

PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

AKLIEF
(trifarotene cream)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

Med D
Ref # 3363-A

FDA-APPROVED INDICATIONS

Aklief Cream is a retinoid indicated for the topical treatment of acne vulgaris in patients 9 years of age and older.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for acne vulgaris in a patient 9 years of age or older

RATIONALE

These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Aklief Cream is a retinoid indicated for the topical treatment of acne vulgaris in patients 9 years of age and older.

REFERENCES

1. Aklief cream [package insert]. Fort Worth, TX: Galderma Laboratories, LP; October 2019.
2. Lexicomp Online, Lexi-Drugs Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed October 2019.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed October 2019.

Written by: UM Development (RP)
Date Written: 10/2019
Revised:
Reviewed: Medical Affairs (AN) 10/2019
External Review: 12/2019

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for acne vulgaris in a patient 9 years of age or older?	Yes	No
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Guidelines for Approval	
Duration of Approval 12 Months	
Set 1	
Yes to question(s)	No to question(s)
1	None

Mapping Instructions		
	Yes	No
1.	Approve, 12 months	Deny

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS ATYPICAL ANTIPSYCHOTICS

BRAND NAME
(generic)

SECUADO
(asenapine transdermal)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

Med D
Ref # 3488-A

FDA-APPROVED INDICATIONS

Secuado is indicated for the treatment of adults with schizophrenia.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the treatment of an adult with schizophrenia

AND

- The patient experienced an inadequate treatment response, intolerance, or contraindication to one of the following: A) aripiprazole, B) lurasidone, C) olanzapine, D) paliperidone, E) quetiapine, F) risperidone, G) ziprasidone

RATIONALE

These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Secuado is indicated for the treatment of adults with schizophrenia.

The American Psychiatric Association (APA) considers certain atypical (second-generation) antipsychotic agents (e.g., aripiprazole, olanzapine, quetiapine, risperidone, ziprasidone) first-line drugs for the management of the acute phase of schizophrenia (including first psychotic episodes), principally because of the decreased risk of adverse extrapyramidal effects and tardive dyskinesia, with the understanding that the relative advantages, disadvantages, and cost-effectiveness of conventional and atypical antipsychotic agents remain controversial. The APA states, with the possible exception of clozapine for the management of treatment-resistant symptoms, there currently is no definitive evidence that one atypical antipsychotic agent will have superior efficacy compared with another agent in the class, although meaningful differences in response may be observed in individual patients. Patient response and tolerance to antipsychotic agents are variable, and patients who do not respond to or tolerate one drug may be successfully treated with an agent from a different class or with a different adverse effect profile.⁴

Therefore, if the patient had an inadequate treatment response, intolerance, or a contraindication to one of the following: aripiprazole, lurasidone (Latuda), olanzapine, paliperidone, quetiapine, risperidone, or ziprasidone, the requested drug should be approved.

REFERENCES

1. Secuado [package insert]. Miami, Florida: Noven Therapeutics, LLC,; October 2019
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed January 2020.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed January 2020.
4. American Psychiatric Association. Practice guideline for the treatment of patients with schizophrenia. *Am J Psychiatry*. 2004; 161: (Suppl) 1-56. Available at: https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/schizophrenia.pdf. Accessed January 2020.

Written by: UM Development (ME)

Date Written: 01/2020

Revised:

Reviewed: Medical Affairs (MMF) 01/2020

External Review: 01/2020

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for the treatment of an adult with schizophrenia?	Yes	No
2	Has the patient experienced an inadequate treatment response, intolerance, or contraindication to one of the following: A) aripiprazole, B) lurasidone, C) olanzapine, D) paliperidone, E) quetiapine, F) risperidone, G) ziprasidone?	Yes	No

Guidelines for Approval

Duration of Approval 12 Months

Set 1

Yes to question(s)

No to question(s)

1 None

2

Mapping Instructions

	Yes	No
1.	Go to 2	Deny
2.	Approve, 12 months	Deny

PRIOR AUTHORIZATION CRITERIA

**BRAND NAME
(generic)**

**SYMLIN
(pramlintide acetate)**

**SYMLINPEN
(pramlintide acetate)**

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

Med D
Ref # 1461-A

FDA-APPROVED INDICATIONS

Symlin/SymlinPen are indicated as an adjunctive treatment in patients with type 1 or type 2 diabetes who use mealtime insulin therapy and who have failed to achieve desired glucose control despite optimal insulin therapy.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has a diagnosis of diabetes mellitus

AND

- The patient has failed to achieve desired glucose control despite receiving optimal insulin therapy, including mealtime insulin

RATIONALE

These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Symlin/SymlinPen are indicated as an adjunctive treatment in patients with type 1 or type 2 diabetes who use mealtime insulin therapy and who have failed to achieve desired glucose control despite optimal insulin therapy.¹

REFERENCES

1. Symlin/SymlinPen [package insert]. San Diego, CA: Amylin Pharmaceuticals, Inc.; April 2016.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed July 2018.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed July 2018.
4. Standards of Medical Care in Diabetes-2018: American Diabetes Association (ADA). *Diabetes Care* January 2018;41(Supplement1).
5. Garber AJ, et al. AACE/ACE Comprehensive Diabetes Management Algorithm 2018, *Endocr Pract.* 2018; 24 (No 1).
6. Handelsman Y, Bloomgarden ZT, Grunberger G, et al. American Association of Clinical Endocrinologists and American College of Endocrinology – Clinical Practice Guidelines for developing a diabetes mellitus comprehensive care plan. *Endocr Pract.* 2015;21(Suppl 1):1-87.

Written by: UM Development (JG)
Date Written: 07/2005
Revised: (MG) 08/2006; (NB) 08/2007; (MS) 07/2008; (NB) 08/2009; (SE) 08/2010, 08/2011; (CY) 08/2012; (PL) 10/2012 (created MDC-2 due to extended commercial duration); (MS) 07/2013, 07/2014, (SE) 04/2015 (CMS Mandated Change), (LN) 05/2015 (added denial reasons); (MS) 07/2015, 10/2015 (changes from external review), (SE) 06/2016 (created separate Med D), 06/2016 (editorial changes for readability); (KM) 07/2016 (no clinical changes); (SF) 02/2017; (DS) 07/2017; (RP) 07/2018 (no clinical changes)
Reviewed: Medical Affairs 07/2005, 08/2006, 08/2007; (WF) 07/2008, 08/2009; (KP) 08/2010, 08/2011; (LB) 08/2012; (DC) 07/2013, (SS) 07/2014, (DHR) 04/2015; (KU) 07/2015; (AD) 10/2015; (MC) 03/2017; (ME) 07/2017
External Review: 12/2006, 02/2008, 12/2008, 12/2009, 12/2010, 12/2011, 10/2012, 10/2013, 10/2014, 10/2015, 10/2016, 04/2017, 10/2017, 10/2018

CRITERIA FOR APPROVAL

1	Does the patient have a diagnosis of diabetes mellitus?	Yes	No
2	Has the patient failed to achieve desired glucose control despite receiving optimal insulin therapy, including mealtime insulin?	Yes	No

Guidelines for Approval	
Duration of Approval	12 Months
Set 1	
Yes to question(s)	No to question(s)
1	None
2	

Mapping Instructions	
	Yes
1.	Go to 2
2.	Approve, 12 months
	Deny
	Deny

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS **GLP-1 AGONIST**

BRAND NAME
(generic)

VICTOZA
(liraglutide)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

Med D
Ref # 1476-A

FDA-APPROVED INDICATIONS

Victoza is indicated:

- as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
- to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease.

Important Limitations of Use

- Victoza is not a substitute for insulin. Victoza should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis, as it would not be effective in these settings.
- The concurrent use of Victoza and prandial insulin has not been studied.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has been receiving GLP-1 (glucagon-like peptide 1) Agonist therapy for at least 3 months
AND
- The patient has any of the following: A) demonstrated a reduction in A1c (hemoglobin A1c) since starting GLP-1 (glucagon-like peptide 1) Agonist therapy, B) established cardiovascular disease
OR
- The patient has a diagnosis of type 2 diabetes mellitus
AND
 - The patient established cardiovascular disease
OR
 - The patient has experienced an inadequate treatment response, intolerance or contraindication to metformin
OR
 - The patient requires combination therapy AND has an A1c (hemoglobin A1c) of 7 percent or greater

RATIONALE

These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Victoza is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Victoza is also indicated to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease. Victoza can be administered once daily at any time

of day, independently of meals, and can be injected subcutaneously in the abdomen, thigh or upper arm. The injection site and timing can be changed without dose adjustment.¹⁻³

Clinical guidelines for the management of hyperglycemia in type 2 diabetes indicate that most patients should begin with life-style changes (lifestyle counseling, weight-loss education, exercise, etc.). Clinical guidelines for the management of hyperglycemia in type 2 diabetes indicate that metformin monotherapy should be started at diagnosis of type 2 diabetes unless there are contraindications. Metformin is effective and safe, is inexpensive, and may reduce risk of cardiovascular events and death. Compared with sulfonylureas, metformin as first-line therapy has beneficial effects on A1c (hemoglobin A1c), weight and cardiovascular mortality. If the A1c target is not achieved after approximately 3 months and patient does not have atherosclerotic cardiovascular disease (ASCVD), consider a combination of metformin and one of the preferred six treatment options: sulfonylurea, thiazolidinedione, DPP-4 inhibitors, SGLT2 inhibitors, GLP-1 (glucagon-like peptide 1) receptor agonists, or basal insulin; the choice of which agent to add is based on drug-specific effects and patient factors. For patients with ASCVD, add a second agent with evidence of cardiovascular risk reduction (currently empagliflozin and liraglutide) after consideration of drug-specific and patient factors. If A1c target is still not achieved after approximately 3 months of dual therapy proceed to a three-drug combination. If not already included in the treatment regimen, addition of an agent with evidence of cardiovascular risk reduction should be considered in patients with ASCVD beyond dual therapy, with continuous reevaluation of patient factors to guide treatment.^{4,5}

In patients with an initial A1c of 7.5% or greater, or in patients who are unable to achieve their glycemic goals with monotherapy, combination therapy is recommended.⁶ The guidelines set goals for therapeutic effectiveness which must be evaluated frequently (e.g., every 3 months) until stable, then at least twice a year, using multiple criteria, including A1c. If A1c targets are not achieved, treatment intensification is based on the addition of another agent with a complementary mechanism of action from a different class.⁴⁻⁶

Based upon guidelines, Victoza (liraglutide) will be approved for patients who have had an inadequate treatment response, intolerance or contraindication to metformin or who require combination therapy and have an A1c greater than 7.5%

The American Diabetes Association reports that because A1c is thought to reflect average glycemia over several months, and has strong predictive value for diabetes complications, A1c testing should be performed routinely in all patients with diabetes, at initial assessment and as part of continuing care. Measurement approximately every 3 months determines whether the patient's glycemic targets have been reached and maintained.⁴ Therefore, continuation of therapy will also be approved for patients that have demonstrated a reduction in A1c since starting GLP-1 Agonist therapy for at least three months.

The LEADER trial was a multi-national, multi-center, placebo-controlled, double-blind trial. Patients with inadequately controlled type 2 diabetes and atherosclerotic cardiovascular disease were randomized to Victoza 1.8 mg or placebo. During the trial, investigators could modify anti-diabetic and cardiovascular medications to achieve local standard of care treatment targets with respect to blood glucose, lipid, and blood pressure.¹ Treatment with subcutaneous liraglutide daily in addition to standard care significantly reduced the rate of composite cardiovascular events (cardiovascular death, nonfatal stroke, and nonfatal myocardial infarction) compared with placebo.¹ Therefore, Victoza (liraglutide) will be approved for initial therapy and continuation of therapy for patients have established cardiovascular disease.

REFERENCES

1. Victoza [package insert]. Princeton, NJ: Novo Nordisk; January 2018.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed July 2018.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed July 2018.
4. American Diabetes Association (ADA) Standards of Medical Care in Diabetes-2018—*Diabetes Care*. 2018; 41(Supplement 1).
5. Garber AJ, et al. AACE/ACE Comprehensive Diabetes Management Algorithm 2018, *Endocr Pract*. 2018; 24 (No 1).
6. Handelsman Y, Bloomgarden ZT, Grunberger G, et al. American Association of Clinical Endocrinologists and American College of Endocrinology – Clinical Practice Guidelines for developing a diabetes mellitus comprehensive care plan. *Endocr Pract*. 2015; 21(Suppl 1):1-87.

Written by: UM Development (NB)
Date Written: 02/2010
Revised: (SE) 08/2010, 04/2011 (revised renewal question) 08/2010 (2)), (SE/SB) 08/2011, 08/2012, (PL) 10/2012 (extended duration), (SE) 11/2012, (SE) 07/2013 (created MDC-2 version/DOA 12 months/removed quantity limits); (PL) 07/2013, (PL) 12/2013 (clarified Q#2), (PL) 07/2014, (SE) 04/2015 (Removed examples of GLP-1 agonists within criteria question), 04/2015 (CMS Mandated Change); (CF) 07/2015, (SE) 06/2016 (created separate Med D), 06/2016 (editorial changes for readability), (SF) 07/2016, 09/2016 (CMS requested changes), 07/2017, 08/2017 (added CV indication), 07/2018 (updated renewal question)
Reviewed: Medical Affairs (WF, MD) 02/2010, (KP) 08/2010, 04/2011, 08/2011, (DHR) 08/2012, 10/2012, (KP) 11/2012; (DNC) 07/2013, 07/2014; (DHR) 04/2015; (DNC) 07/2015; (MES) 07/2016, 07/2017, (MC) 09/2017, (ME) 07/2018
External Review: 03/2010, 12/2010, 12/2011, 10/2012, 10/2013, 10/2014, 10/2015, 10/2016, 10/2017, 10/2018

CRITERIA FOR APPROVAL

- | | | | |
|---|---|-----|----|
| 1 | Has the patient been receiving GLP-1 (glucagon-like peptide 1) Agonist therapy for at least 3 months?
[If no, then skip to question 3.] | Yes | No |
| 2 | Does the patient have any of the following: A) demonstrated a reduction in A1c (hemoglobin A1c) since starting GLP-1 (glucagon-like peptide 1) Agonist therapy, B) established cardiovascular disease?
[No further questions.] | Yes | No |
| 3 | Does the patient have a diagnosis of type 2 diabetes mellitus? | Yes | No |
| 4 | Does the patient have established cardiovascular disease?
[If yes, then no further questions.] | Yes | No |
| 5 | Has the patient experienced an inadequate treatment response, intolerance, or contraindication to metformin?
[If yes, then no further questions.] | Yes | No |
| 6 | Does the patient require combination therapy AND have an A1c (hemoglobin A1c) of 7 percent or greater? | Yes | No |

Guidelines for Approval

Duration of Approval				12 Months			
Set 1		Set 2		Set 3		Set 4	
Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)
1	None	3	1	3	1	3	1
2		4		5	4	6	4
							5

Mapping Instructions

	Yes	No
1.	Go to 2	Go to 3
2.	Approve, 12 months	Deny
3.	Go to 4	Deny
4.	Approve, 12 months	Go to 5

5.	Approve, 12 months	Go to 6
6.	Approve, 12 months	Deny

SPECIALTY GUIDELINE MANAGEMENT

Abraxane (paclitaxel, albumin-bound)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. **Metastatic Breast Cancer**
Abraxane is indicated for the treatment of breast cancer after failure of combination chemotherapy for metastatic disease or relapse within 6 months of adjuvant chemotherapy. Prior therapy should have included an anthracycline unless clinically contraindicated.
2. **Non-Small Cell Lung Cancer**
Abraxane is indicated for the first-line treatment of locally advanced or metastatic non-small cell lung cancer, in combination with carboplatin, in patients who are not candidates for curative surgery or radiation therapy.
3. **Adenocarcinoma of the Pancreas**
Abraxane is indicated for the first-line treatment of patients with metastatic adenocarcinoma of the pancreas, in combination with gemcitabine.

B. Compendial Uses

1. Breast cancer
2. Non-small cell lung cancer
3. Pancreatic adenocarcinoma
4. Cutaneous melanoma
5. Epithelial ovarian cancer/fallopian tube cancer/primary peritoneal cancer
6. Bladder cancer, primary carcinoma of the urethra, upper genitourinary (GU) tract tumors, and urothelial carcinoma of the prostate
7. Acquired immune deficiency syndrome (AIDS)-related Kaposi sarcoma
8. Endometrial carcinoma
9. Hepatobiliary cancer: intrahepatic and extrahepatic cholangiocarcinoma
10. Uveal melanoma
11. Cervical cancer
12. Small bowel adenocarcinoma

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Pancreatic adenocarcinoma**

Authorization of 6 months may be granted for treatment of pancreatic adenocarcinoma.

B. Breast cancer

Authorization of 6 months may be granted for treatment of recurrent or metastatic breast cancer.

C. Non-small cell lung cancer (NSCLC)

Authorization of 6 months may be granted for treatment of recurrent, locally advanced, advanced or metastatic NSCLC.

D. Cutaneous melanoma

Authorization of 6 months may be granted for treatment of metastatic or unresectable cutaneous melanoma, as a single-agent second-line or subsequent therapy.

E. Epithelial ovarian cancer/fallopian tube cancer/primary peritoneal cancer

Authorization of 6 months may be granted for treatment of persistent or recurrent epithelial ovarian cancer, fallopian tube cancer, and primary peritoneal cancer.

F. Bladder cancer, Primary Carcinoma of the Urethra, Upper Genitourinary Tract Tumors, and Urothelial Carcinoma of the Prostate

1. Bladder cancer

Authorization of 6 months may be granted for treatment of bladder cancer, as a single-agent subsequent therapy.

2. Upper genitourinary tract tumors and urothelial carcinoma of the prostate

Authorization of 6 months may be granted for treatment of metastatic upper genitourinary tract tumors or metastatic urothelial carcinoma of the prostate, as a single-agent subsequent therapy.

3. Primary carcinoma of the urethra

Authorization of 6 months may be granted for treatment of recurrent or metastatic primary carcinoma of the urethra, as a single-agent subsequent therapy.

G. AIDS-related Kaposi sarcoma

Authorization of 6 months may be granted for treatment of AIDS-related Kaposi sarcoma.

H. Endometrial carcinoma

Authorization of 6 months may be granted for treatment of endometrial carcinoma.

I. Hepatobiliary cancer

Authorization of 6 months may be granted for treatment of unresectable or metastatic hepatobiliary cancer (including intrahepatic and extrahepatic cholangiocarcinoma) as primary treatment in combination with gemcitabine.

J. Uveal melanoma

Authorization of 6 months may be granted for treatment of uveal melanoma, as a single-agent therapy for distant metastatic disease.

K. Cervical cancer

Authorization of 6 months may be granted for treatment of recurrent or metastatic cervical cancer, as a single-agent second-line therapy.

L. Small Bowel Adenocarcinoma

Reference number(s)
1669-A

Authorization of 6 months may be granted for treatment of advanced or metastatic small bowel adenocarcinoma, as a single agent or in combination with gemcitabine.

III. CONTINUATION OF THERAPY

Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who are experiencing clinical benefit from therapy or who have not experienced an unacceptable toxicity.

IV. REFERENCES

1. Abraxane [package insert]. Summit, NJ: Celgene Corporation; August 2018.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. Available at: <https://www.nccn.org>. Accessed September 10, 2019.
3. The NCCN Clinical Practice Guidelines in Oncology® Breast Cancer (Version 3.2019). © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed September 10, 2019.
4. The NCCN Clinical Practice Guidelines in Oncology® Non-Small Cell Lung Cancer (Version 7.2019). © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed September 10, 2019.
5. The NCCN Clinical Practice Guidelines in Oncology® Pancreatic Adenocarcinoma (Version 3.2019). © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed September 10, 2019.
6. The NCCN Clinical Practice Guidelines in Oncology® Cutaneous Melanoma (Version 2.2019). © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed September 10, 2019.
7. The NCCN Clinical Practice Guidelines in Oncology® Ovarian Cancer (Version 1.2019). © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed September 10, 2019.
8. The NCCN Clinical Practice Guidelines in Oncology® Bladder Cancer (Version 4.2019). © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed September 10, 2019.
9. The NCCN Clinical Practice Guidelines in Oncology® AIDS-Related Kaposi Sarcoma (Version 2.2019). © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed September 10, 2019.
10. The NCCN Clinical Practice Guidelines in Oncology® Uterine Neoplasms (Version 3.2019). © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed September 11, 2019.
11. The NCCN Clinical Practice Guidelines in Oncology® Hepatobiliary Cancers (Version 3.2019). © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed September 11, 2019.
12. The NCCN Clinical Practice Guidelines in Oncology® Uveal Melanoma (Version 1.2019). © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed September 11, 2019.
13. The NCCN Clinical Practice Guidelines in Oncology® Cervical Cancer (Version 5.2019). © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed September 16, 2019.
14. The NCCN Clinical Practice Guidelines in Oncology® Small Bowel Adenocarcinoma (Version 1.2020). © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed September 16, 2019.

STEP THERAPY CRITERIA

DRUG CLASS*	ACNE PRODUCTS TOPICAL (BRAND ONLY)
BRAND NAME (generic)	
	ACZONE (dapsonsone)
	ACANYA (clindamycin phosphate-benzoyl peroxide)
	AMZEEQ (minocycline)
	BENZAACLIN (clindamycin phosphate-benzoyl peroxide)
	CLEOCIN-T (clindamycin phosphate)
	CLINDACIN ETZ (clindamycin phosphate)
	CLINDACIN PAC (clindamycin phosphate)
	CLINDACIN-P (clindamycin phosphate)
	CLINDAGEL (clindamycin phosphate)
	DUAC (clindamycin phosphate-benzoyl peroxide)
	EVOCLIN (clindamycin phosphate)
	KLARON (sulfacetamide sodium)
	NEUAC (clindamycin phosphate-benzoyl peroxide)

Status: CVS Caremark Criteria

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS**Aczone**

Aczone is indicated for the topical treatment of acne vulgaris.

Acanya

Acanya is indicated for the topical treatment of acne vulgaris in patients 12 years or older.

Amzeeq

Amzeeq is indicated for the topical treatment of inflammatory lesions of non-nodular moderate to severe acne vulgaris in adults and pediatric patients 9 years of age and older

Limitations of Use

This formulation of minocycline has not been evaluated in the treatment of infections. To reduce the development of drug-resistant bacteria as well as to maintain the effectiveness of other antibacterial drugs, Amzeeq should be used only as indicated

BenzaClin

BenzaClin is indicated for the topical treatment of acne vulgaris.

Clindamycin Phosphate

Clindamycin phosphate products are indicated in the treatment of acne vulgaris. In view of the potential for diarrhea, bloody diarrhea and pseudomembranous colitis, the physician should consider whether other agents are more appropriate.

Duac

Duac (clindamycin phosphate and benzoyl peroxide) is indicated for the topical treatment of inflammatory acne vulgaris in patients 12 years and older.

Limitations of Use

Duac has not been demonstrated to have any additional benefit when compared with benzoyl peroxide alone in the same vehicle when used for the treatment of non-inflammatory acne.

Klaron

Klaron is indicated in the topical treatment of acne vulgaris.

Neuac

Neuac (clindamycin phosphate and benzoyl peroxide) is indicated for the topical treatment of inflammatory acne vulgaris.

Limitations of Use

Neuac has not been demonstrated to have any additional benefit when compared with benzoyl peroxide alone in the same vehicle when used for the treatment of non-inflammatory acne.

INITIAL STEP THERAPY

If the patient has filled a prescription for at least a 30 day supply of a generic acne product (benzoyl peroxide, clindamycin topical, clindamycin/benzoyl peroxide, erythromycin topical, erythromycin/benzoyl peroxide, sodium sulfacetamide, or sodium sulfacetamide/sulfur) within the past 180 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit. If the patient does not meet the initial step therapy criteria, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for acne vulgaris.

AND

- The patient has demonstrated an inadequate treatment response or intolerance to a generic acne product.

RATIONALE

If the patient has filled a prescription for at least a 30 day supply of a generic acne product (benzoyl peroxide, clindamycin topical, clindamycin/benzoyl peroxide, erythromycin topical, erythromycin/benzoyl peroxide, sodium sulfacetamide, or sodium sulfacetamide/sulfur) within the past 180 days under a prescription benefit administered by CVS Caremark, then the requested branded drug will be paid under that prescription benefit.

If the patient does not meet the initial step therapy criteria, then prior authorization is required.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Aczone, Acanya, BenzaClin, Clindamycin Phosphate, Duac, Klaron, and Neuac are indicated for the topical treatment of acne vulgaris. Acanya and Duac are only indicated in patients 12 years and older. Duac and Neuac are indicated specifically for inflammatory acne vulgaris. Amzeeq is indicated for the topical treatment of inflammatory lesions of non-nodular moderate to severe acne vulgaris in adults and pediatric patients 9 years of age and older

If the patient has demonstrated an inadequate treatment response or intolerance to a topical generic acne product and the requested drug is being prescribed for acne vulgaris, then the requested brand drug will be approved.

REFERENCES

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10. Klaron [package insert]. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; June 2017.
11. Neuac [package insert]. Fairfield, NJ: Medimetrix Pharmaceuticals, Inc.; November 2015.
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13. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed June 2019.
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Written by: UM Development (CF)

Date Written: 06/2016

Revised: (SF) 06/2017 (no clinical changes), 06/2018 (no clinical changes), (ME) 06/2019 (removed Clindamax), (SF) 11/2019 (added Amzeeq)

Reviewed: Medical Affairs: (GAD) 06/2016, (CHART) 12/5/2019

External Review: 10/2016, 10/2017, 10/2018, 10/2019, 01/2020

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for acne vulgaris?	Yes	No
2	Has the patient experienced an inadequate treatment response or intolerance to a topical generic acne product?	Yes	No

Mapping Instructions			
	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have acne vulgaris. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
2.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have tried a topical generic acne product and it did not work for you. Your request has been denied based on the information we have. [Short description: No inadequate treatment response or intolerance to topical generic acne products]

SPECIALTY GUIDELINE MANAGEMENT

ACTEMRA (tocilizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more disease-modifying antirheumatic drugs (DMARDs).
2. Patients 2 years of age and older with active polyarticular juvenile idiopathic arthritis.
3. Patients 2 years of age and older with active systemic juvenile idiopathic arthritis.
4. Adult patients with giant cell arteritis.
5. Adults and pediatric patients 2 years of age and older with chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome.

B. Compendial Uses

1. Unicentric Castleman's disease
2. Multicentric Castleman's disease
3. Oligoarticular juvenile idiopathic arthritis
4. Refractory/severe immunotherapy-related inflammatory arthritis not responding to corticosteroids and anti-inflammatory agents

All other indications are considered experimental/investigational and are not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Moderately to severely active rheumatoid arthritis (RA)**

1. Authorization of 12 months may be granted for members who have previously received a biologic or targeted synthetic DMARD (e.g., Rinvoq, Xeljanz) indicated for moderately to severely active rheumatoid arthritis.
2. Authorization of 12 months may be granted for treatment of moderately to severely active RA when any of the following criteria is met:
 - a. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to 20 mg/week).
 - b. Member has an intolerance or contraindication to methotrexate (see Appendix A).

B. **Active articular juvenile idiopathic arthritis**

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for active articular juvenile idiopathic arthritis.
2. Authorization of 12 months may be granted for the treatment of active articular juvenile idiopathic arthritis when any of the following criteria are met:

- a. The member had an inadequate response to methotrexate or another non-biologic DMARD administered at an adequate dose and duration.
- b. The member has risk factors (See Appendix B) and the member also meets one of the following:
 - i. High-risk joints are involved (e.g., cervical spine, wrist, or hip).
 - ii. High disease activity.
 - iii. Are judged to be at high risk for disabling joint disease.

C. Active Systemic Juvenile Idiopathic Arthritis (sJIA)

Authorization of 12 months may be granted for members who have previously received a biologic indicated for active systemic juvenile idiopathic arthritis.

Authorization of 12 months may be granted for the treatment of active sJIA when any of the following criteria is met:

1. Member has an inadequate response to at least a 1-month trial of NSAIDs.
2. Member has an inadequate response to at least a 2-week trial of corticosteroids.
3. Member has an inadequate response to at least a 3-month trial of methotrexate or leflunomide.

D. Giant Cell Arteritis

Authorization of 12 months may be granted for the treatment of giant cell arteritis when the patient's diagnosis was confirmed by the following:

1. Temporal artery biopsy or cross-sectional imaging; or
2. Acute-phase reactant elevation (i.e., high erythrocyte sedimentation rate [ESR] and/or high serum C-reactive protein [CRP])

E. Chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome

Authorization of 1 month may be granted for the treatment of chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome.

F. Unicentric Castleman's Disease

Authorization of 12 months may be granted for treatment of unicentric Castleman's disease when all of the following are met:

1. The member is HIV-negative.
2. The member is human herpesvirus-8-negative.
3. The requested drug will be used as monotherapy.
4. The requested drug is being used as second-line therapy for relapsed/refractory disease.

G. Multicentric Castleman's Disease

Authorization of 12 months may be granted for treatment of multicentric Castleman's disease when both of the following are met:

1. The requested drug will be used as monotherapy.
2. The requested drug is being used as second-line therapy for relapsed/refractory or progressive disease.

H. Immunotherapy-related Inflammatory Arthritis

Authorization of 12 months may be granted for treatment of severe/refractory immunotherapy-related inflammatory arthritis that is not responding to corticosteroids and anti-inflammatory agents.

III. CONTINUATION OF THERAPY

Chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome and immunotherapy-related inflammatory arthritis

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

All other diagnoses

Authorization of 12 months may be granted for all members (including new members) who are using Actemra for an indication outlined in section II and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

For all indications: Member has had a documented negative TB test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic DMARDs or targeted synthetic DMARDs (e.g., Rinvoq, Xeljanz), and repeated yearly for members with risk factors** for TB that are continuing therapy with biologics.

* If the screening testing for TB is positive, there must be documentation of further testing to confirm there is no active disease. Do not administer tocilizumab to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of tocilizumab.

** Risk factors for TB include: Persons with close contact to people with infectious TB disease; persons who have recently immigrated from areas of the world with high rates of TB (e.g., Africa, Asia, Eastern Europe, Latin America, Russia); children less than 5 years of age who have a positive TB test; groups with high rates of TB transmission (e.g., homeless persons, injection drug users, persons with HIV infection); persons who work or reside with people who are at an increased risk for active TB (e.g., hospitals, long-term care facilities, correctional facilities, homeless shelters).

For all indications: Member cannot use Actemra concomitantly with any other biologic DMARD or targeted synthetic DMARD.

V. APPENDIX A: Examples of contraindications to methotrexate

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
4. Elevated liver transaminases
5. History of intolerance or adverse event
6. Hypersensitivity
7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
8. Myelodysplasia
9. Pregnancy or planning pregnancy
10. Renal impairment
11. Significant drug interaction

APPENDIX B: Risk factors for articular juvenile idiopathic arthritis

1. Positive rheumatoid factor
2. Positive anti-cyclic citrullinated peptide antibodies
3. Pre-existing joint damage

Reference number
1959-A

VI. REFERENCES

1. Actemra [package insert]. South San Francisco, CA: Genentech, Inc.; June 2019.
2. National Comprehensive Cancer Network. The NCCN Drugs & Biologics Compendium. <https://www.nccn.org>. Accessed June 14, 2019.
3. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. *Arthritis Rheumatol*. 2016;68(1):1-26.
4. Smolen JS, Landewé R, Billsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. *Ann Rheum Dis*. 2017;0:1-18.
5. Beukelman T, Patkar NM, Saag KG, et al. 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: initiation and safety monitoring of therapeutic agents for the treatment of arthritis and systemic features. *Arthritis Care Res*. 2011;63(4):465-482.
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7. Ringold S, Angeles-Han S, Beukelman T, et al. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Treatment of Juvenile Idiopathic Arthritis: Therapeutic Approaches for Non-Systemic Polyarthritis, Sacroiliitis, and Enthesitis. *American College of Rheumatology*. 2019;1-18.
8. Stone, J. H., Tuckwell, K., Dimonaco, S., et al. Efficacy and safety of tocilizumab in patients with giant cell arteritis: Primary and secondary outcomes from a phase 3, randomized, double-blind, placebo-controlled trial. 2016 ACR/ARHP Annual meeting. Abstract number 911.
9. Tuberculosis (TB). TB risk factors. Centers for Disease Control and Prevention. Retrieved on 21 June 2019 from: <https://www.cdc.gov/tb/topic/basics/risk.htm>.

INDICATION-SPECIFIC SPECIALTY GUIDELINE MANAGEMENT

ACTHAR GEL (repository corticotropin injection)

POLICY

I. INDICATIONS

The indication-specific Specialty Guideline Management (SGM) program provides coverage for specific, but not all FDA labeled or compendial supported drug use based on plan design and the scope of the pharmacy benefit. This program provides coverage for Acthar Gel for the treatment of infantile spasms and exacerbations of multiple sclerosis if all of the approval criteria are met.

- A. **Infantile spasms:** as monotherapy for the treatment of infantile spasms in infants and children under 2 years of age
- B. **Multiple Sclerosis:** treatment of acute exacerbations of multiple sclerosis in adults

The use of Acthar for the treatment of all other indications listed in the FDA product labeling has not been proven to be superior to conventional therapies (e.g., corticosteroids, immunosuppressive agents) and has a significantly higher cost than the standard of care agents. Use of Acthar for these conditions is considered not medically necessary and is not a covered benefit.

- A. **Rheumatic Disorders:** as adjunctive therapy for short-term administration (to tide the patient over an acute episode or exacerbation) in: psoriatic arthritis; rheumatoid arthritis, including juvenile rheumatoid arthritis, ankylosing spondylitis¹
- B. **Collagen Diseases:** during an exacerbation or as maintenance therapy in selected cases of: systemic lupus erythematosus, systemic dermatomyositis (polymyositis)¹
- C. **Dermatologic Diseases:** severe erythema multiforme, Stevens-Johnson syndrome¹
- D. **Allergic States:** serum sickness¹
- E. **Ophthalmic Diseases:** severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa such as: keratitis, iritis, iridocyclitis, diffuse posterior uveitis and choroiditis, optic neuritis, chorioretinitis, anterior segment inflammation¹
- F. **Respiratory Diseases:** symptomatic sarcoidosis¹
- G. **Edematous State:** to induce a diuresis or a remission of proteinuria in the nephrotic syndrome without uremia of the idiopathic type or that due to lupus erythematosus¹

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review for requests for treatment of multiple sclerosis exacerbations: chart notes detailing the outcomes of the most recent trial with IV methylprednisolone, including dosage and duration of treatment.

III. CRITERIA FOR INITIAL APPROVAL

A. Infantile Spasms

Authorization of 4 weeks may be granted for treatment of infantile spasms in members who are less than 2 years of age.

Reference number(s)
1848-A

B. Multiple Sclerosis

Authorization of 3 weeks may be granted for treatment of acute exacerbations of multiple sclerosis when the member has had an inadequate response to a trial of IV methylprednisolone (for the current exacerbation).

IV. CONTINUATION OF THERAPY

A. Infantile Spasms

Authorization of 4 weeks may be granted to members requesting Acthar Gel for continuation of therapy when the member has shown substantial clinical benefit from therapy.

B. Multiple sclerosis

Authorization of 3 weeks may be granted for members requesting re-authorization for Acthar therapy when all initial authorization criteria are met.

V. REFERENCES

1. Acthar Gel [package insert]. Hazelwood, MO: Mallinckrodt Pharmaceuticals, Inc.; July 2019.
2. Pellock JM, Hrachovy R, Shinnar S, et al. Infantile spasms: A U.S. consensus report. *Epilepsia*. 2010;51:2175-2189.
3. Go CY, Mackay MT, Weiss SK, et al. Evidence-based guideline update: Medical treatment of infantile spasms: Report of the Guideline Development Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. *Neurology*. 2012;78:1974-1980.
4. Hancock EC, Osborne JP, Edwards SW. Treatment of infantile spasms. *Cochrane Database Syst Rev*. 2013;6:CD001770.
5. Riikonen R. Recent advances in pharmacotherapy of infantile spasms. *CNS Drugs* 2014; 28:279-290.
6. Pavone P, et al. Infantile spasms syndrome, West Syndrome and related phenotypes: what we know in 2013. *Brain & Development* 2014; 739-751.
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8. Thompson AJ, Kennard C, Swash M, et al. Relative efficacy of intravenous methylprednisolone and ACTH in the treatment of acute relapse in MS. *Neurology* 1989; 39:969-971.
9. Berkovich R, Agius MA. Mechanisms of action of ACTH in the management of relapsing forms of multiple sclerosis. *Ther Adv Neurol Disord* 2014; 7(2):83-96.
10. Frohman EM, Shah A, Eggenberger E, et al. Corticosteroids for multiple sclerosis: I. Application for treatment exacerbations. *Neurotherapeutics* 2007; 4(4): 618-626.
11. Sellebjerg F, Barnes D, Filippini G, et al. EFNS guidelines on treatment of multiple sclerosis relapses: report of an EFNS task force on treatment of multiple sclerosis. *European Journal of Neurology* 2005; 12:939-946.

SPECIALTY GUIDELINE MANAGEMENT

ACTIMMUNE (interferon gamma-1b)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Actimmune is indicated for reducing the frequency and severity of serious infections associated with chronic granulomatous disease (CGD).
2. Actimmune is indicated for delaying time to disease progression in patients with severe, malignant osteopetrosis (SMO).

B. Compendial Uses

1. Mycosis fungoides/Sezary syndrome
2. Atopic dermatitis

All other indications are considered experimental/investigational and are not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Chronic Granulomatous Disease**

Authorization of 12 months may be granted for the treatment of chronic granulomatous disease.

B. **Severe, Malignant Osteopetrosis**

Authorization of 12 months may be granted for treatment of severe, malignant osteopetrosis.

C. **Mycosis Fungoides/Sezary Syndrome**

Authorization of 12 months may be granted for the treatment of mycosis fungoides or Sezary syndrome.

D. **Atopic Dermatitis**

Authorization of 12 months may be granted for the treatment of atopic dermatitis.

III. CONTINUATION OF THERAPY

Authorization of 12 months will be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

IV. REFERENCES

1. Actimmune [package insert]. Lake Forest, IL: Horizon Pharma USA, Inc.; May 2017.
2. The NCCN Drugs & Biologics Compendium 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed May 30, 2019.
3. The NCCN Clinical Practice Guidelines in Oncology Primary Cutaneous Lymphomas (Version 2.2019) 2019 National Comprehensive Cancer Network, Inc. Available at: <https://www.nccn.org>. Accessed May 30, 2019.
4. IBM Micromedex DRUGDEX (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: <https://www.micromedexsolutions.com>. (cited: 05/30/2019).

PRIOR AUTHORIZATION CRITERIA

BRAND NAME* (generic)

CARAC
(fluorouracil)

FLUOROPLEX
(fluorouracil)

PICATO
(ingenol mebutate)

TOLAK
(fluorouracil)

ZYCLARA
(imiquimod)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

Ref # 1378-A

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Carac

Carac is indicated for the topical treatment of multiple actinic or solar keratoses of the face and anterior scalp.

Fluoroplex

Fluoroplex cream is indicated for the topical treatment of multiple actinic (solar) keratoses.

Picato

Picato gel is indicated for the topical treatment of actinic keratosis.

Tolak

Tolak cream is indicated for the topical treatment of actinic keratosis lesions of the face, ears and/or scalp.

Zyclara

Actinic Keratosis

Zyclara Cream, 2.5% and 3.75% are indicated for the topical treatment of clinically typical visible or palpable, actinic keratoses (AK), of the full face or balding scalp in immunocompetent adults.

External Genital Warts

Zyclara Cream, 3.75% is indicated for the treatment of external genital and perianal warts (EGW)/condyloma acuminata in patients 12 years or older.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has the diagnosis of actinic keratosis or external genital warts

RATIONALE

These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Carac is indicated for the topical treatment of multiple actinic or solar keratoses of the face and anterior scalp. Fluoroplex cream is indicated for is indicated for the topical treatment of multiple actinic (solar) keratoses. Tolak cream is indicated for the topical treatment of actinic keratosis lesions of the face, ears and/or scalp. Picato gel is indicated for the topical treatment of actinic keratosis. Zyclara cream is indicated for actinic keratosis and external genital warts.

REFERENCES

1. Carac [package insert]. Bridgewater, NJ: Valeant Pharmaceuticals North America; May 2017.
2. Fluoroplex [package insert]. West Chester, PA: Aqua Pharmaceuticals; July 2016.
3. Picato [package insert]. Parsippany, NJ: LEO Pharma; June 2017.
4. Tolak [package insert]. Sanford, FL: Hill Dermaceuticals; Inc. March 2017.
5. Zyclara [package insert]. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; June 2017.
6. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed June 2019.
7. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed June 2019.

Date Written: 06/2016
Revised: (SF) 08/2016 (added target drugs); 06/2017 (no clinical changes), (ME) 06/2018 (no clinical changes), 06/2019 (Removed MDC from Title)
Reviewed: Medical Affairs (MM) 06/2016
External Review: 08/2016, 10/2017, 10/2018, 08/2019

CRITERIA FOR APPROVAL

1	Does the patient have the diagnosis of actinic keratosis or external genital warts?	Yes	No
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Guidelines for Approval	
Duration of Approval	12 Months
Set 1	
Yes to question(s)	No to question(s)
1	None

Mapping Instructions			
	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have actinic keratosis or external genital warts. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]

SPECIALTY GUIDELINE MANAGEMENT

ADAGEN (pegademase bovine) injection

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Adagen is indicated for enzyme replacement therapy for adenosine deaminase (ADA) deficiency in patients with severe combined immunodeficiency disease (SCID) who are not suitable candidates for—or who have failed—bone marrow transplantation. Adagen is recommended for use in infants from birth or in children of any age at the time of diagnosis.

All other indications are considered experimental/investigational and are not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: enzyme assay or genetic testing results supporting diagnosis of ADA deficiency.

III. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of severe combined immunodeficiency disease (SCID) associated with adenosine deaminase (ADA) deficiency when the condition has failed to respond to a bone marrow transplant (BMT) or the member is not currently a suitable candidate for BMT.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for SCID associated with ADA deficiency who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

V. REFERENCE

1. Adagen [package insert]. Gaithersburg, MD: Leadiant Biosciences, Inc.; November 2017.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME (generic)	ADAKVEO (crizanlizumab-tmca)
Status: CVS Caremark Criteria Type: Initial Prior Authorization	MDC Ref # 3415-A

FDA-APPROVED INDICATIONS

Adakveo is indicated to reduce the frequency of vasoocclusive crises (VOCs) in adults and pediatric patients aged 16 years and older with sickle cell disease.¹

B vs D CRITERIA FOR DETERMINATION

1	Is the requested drug being supplied from the physician and/or office stock supply and billed as part of a physician service (i.e., the drug is being furnished "incident to a physician's service")? [If yes, no further questions.]	Yes	No
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CRITERIA FOR APPROVAL

2	Does the patient have a diagnosis of sickle cell disease? [If no, no further questions.]	Yes	No
3	Will the requested drug be used to reduce the frequency of vasoocclusive crises (VOCs)? [If no, no further questions.]	Yes	No
4	Is the patient 16 years of age or older?	Yes	No

Continue to Clinical Questions if:

Guidelines for Determination	
Process through Medicare Part D	
Set 1	
Yes to question(s)	No to question(s)
None	1

For any other scenarios other than the Set above, close PA, drug is not covered as Part D

Approve if:

Guidelines for Approval	
Duration of Approval	12 Months
Set 1: SCD	
Yes to question(s)	No to question(s)
2	None
3	
4	

Mapping Instructions		
	Yes	No
1.	Close PA, drug is not covered as Part D	Go to 2
2.	Go to 3	Deny
3.	Go to 4	Deny
4.	Approve, 12 months	Deny

RATIONALE

These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to:

1. Determine if the medication should be processed through Medicare Part D.
2. Ensure that patients follow selection elements noted in labeling and/or practice guidelines in order to decrease the potential for inappropriate utilization.

REFERENCES

1. Adakveo [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; November 2019.
2. Medicare Part B versus Part D Coverage Issues. July 2005. <https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovContra/downloads/BvsDCoverageIssues.pdf> Accessed June 2019.
3. Medicare Prescription Drug Benefit Manual. Chapter 6- Part D Drugs and Formulary Requirements. (Rev. 18, 01-15-16). <https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovContra/Downloads/Part-D-Benefits-Manual-Chapter-6.pdf> Accessed June 2019.

DOCUMENT HISTORY

Created: Specialty Clinical Development (IP) 11/2019
Revised:
Reviewed: CDPR / MMF 11/2019
External Review: 12/2019

SPECIALTY GUIDELINE MANAGEMENT

ADCETRIS (brentuximab vedotin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Classical Hodgkin Lymphoma (CHL)
 - i. Treatment of CHL after failure of autologous hematopoietic stem cell transplantation (auto-HSCT) or after failure of at least two prior multi-agent chemotherapy regimens in patients who are not auto-HSCT candidates
 - ii. Treatment of CHL at high risk of relapse or progression as post-auto-HSCT consolidation
 - iii. Previously untreated Stage III or IV classical Hodgkin lymphoma (CHL), in combination with doxorubicin, vinblastine, and dacarbazine
2. Systemic anaplastic large cell lymphoma (sALCL)
 - a. Treatment of systemic anaplastic large cell lymphoma (sALCL) after failure of at least one prior multi-agent chemotherapy regimen
 - b. Previously untreated systemic anaplastic large cell lymphoma (sALCL) or other CD30-expressing peripheral T-cell lymphomas (PTCL), including angioimmunoblastic T-cell lymphoma and PTCL not otherwise specified, in combination with cyclophosphamide, doxorubicin, and prednisone
3. Treatment of primary cutaneous anaplastic large cell lymphoma (pcALCL) or CD30-expressing mycosis fungoides (MF) in patients who have received prior systemic therapy

B. Compendial Uses

- Non-Hodgkin's Lymphoma (NHL)
1. CD30+ adult T-cell leukemia/lymphoma
 2. Breast implant-associated anaplastic large cell lymphoma (ALCL)
 3. Mycosis Fungoides (MF)/Sezary Syndrome (SS)
 4. Lymphomatoid papulosis (LyP)
 5. CD30+ peripheral T-cell lymphoma (PTCL)
 6. CD30+ angioimmunoblastic T-cell lymphoma
 7. Diffuse large B-cell lymphoma
 8. Extranodal NK/T-cell Lymphoma (nasal type)
 9. Hepatosplenic gamma-delta T-cell lymphoma
 10. Histologic transformation of follicular lymphoma to diffuse large B-cell lymphoma
 11. Histologic transformation of marginal zone lymphoma to diffuse large B-Cell lymphoma
 12. High-grade B-Cell lymphomas
 13. AIDS-related B-Cell lymphomas
 14. Post-transplant lymphoproliferative disorders

All other indications are considered experimental/investigational and are not medically necessary.

II. DOCUMENTATION

Testing or analysis confirming CD30 expression on the surface of the cell (initial requests).

III. CRITERIA FOR INITIAL APPROVAL

A. Classical Hodgkin lymphoma (CHL)

Authorization of 12 months may be granted for treatment of CHL when any of the following are met:

- a. Adcetris will be used as a single agent, or
- b. Adcetris will be used in combination with doxorubicin, vinblastine, and dacarbazine, or
- c. Adcetris will be used in combination with bendamustine, or
- d. Adcetris will be used in combination with dacarbazine.

B. Non-Hodgkin's lymphoma (NHL)

Authorization of 12 months may be granted for treatment of NHL with any of the following subtypes:

1. CD30+ adult T-cell leukemia/lymphoma when either of the following are met:
 - a. Adcetris will be used a single agent, or
 - b. Adcetris will be used in combination with cyclophosphamide, doxorubicin, and prednisone.
2. Systemic anaplastic large cell lymphoma when either of the following are met:
 - a. Adcetris will be used as a single agent, or
 - b. Adcetris will be used in combination the cyclophosphamide, doxorubicin, and prednisone (CHP).
3. Cutaneous anaplastic large cell lymphoma when either of the following are met:
 - a. Adcetris will be used as a single agent, or
 - b. Adcetris will be used in combination with cyclophosphamide, doxorubicin, and prednisone (CHP).
4. Breast implant associated anaplastic large cell lymphoma (ALCL) when either of the following are met:
 - a. Adcetris will be used a single agent, or
 - b. Adcetris will be used in combination with cyclophosphamide, doxorubicin, and prednisone.
5. Mycosis fungoides (MF)/Sezary syndrome (SS)
6. Lymphomatoid papulosis (LyP) when both of the following are met:
 - a. Adcetris will be used a single agent, and
 - b. The disease is relapsed or refractory.
7. CD30+ peripheral T-cell lymphoma (PTCL) when either of the following are met:
 - a. Adcetris will be used a single agent, or
 - b. Adcetris will be used in combination with cyclophosphamide, doxorubicin, and prednisone.
8. CD30+ angioimmunoblastic T-cell lymphoma when both of the following are met:
 - a. Adcetris will be used a single agent, or
 - b. Adcetris will be used in combination with cyclophosphamide, doxorubicin, and prednisone.
9. Diffuse large B-cell lymphoma when both of the following are met:
 - a. Adcetris will be used as second-line or subsequent therapy, and
 - b. The patient is not a candidate for transplant.
10. Extranodal NK/T-cell lymphoma (nasal type) when all of the following are met:
 - a. Adcetris will be used a single agent, and
 - b. Patient has relapsed or refractory disease, and
 - c. Patient has had an inadequate response or contraindication to asparaginase-based therapy (e.g., pegaspargase).
11. Hepatosplenic gamma-delta T-cell lymphoma when either of the following are met:
 - a. Adcetris will be used a single agent after two or more previous lines of chemotherapy, or
 - b. Adcetris will be used in combination with cyclophosphamide, doxorubicin, and prednisone.
12. Histologic transformation of marginal zone lymphoma to diffuse large B-cell lymphoma when the patient has received at least two chemoimmunotherapy regimens.
13. High-grade B-cell lymphomas when both of the following are met:
 - a. Adcetris will be used for second-line or subsequent therapy, and

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- b. The patient is not a candidate for transplant.
- 14. AIDS-Related B-cell lymphomas when both of the following are met:
 - a. Adcetris will be used for second-line or subsequent therapy, and
 - b. The patient is not a candidate for transplant.
- 15. Post-transplant lymphoproliferative disorders when used for second-line or subsequent therapy.
- 16. Histologic transformation of follicular lymphoma to diffuse large B-cell lymphoma when the patient has received at least two chemoimmunotherapy regimens.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES

1. Adcetris [package insert]. Bothell, WA: Seattle Genetics, Inc; November 2017.
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SPECIALTY GUIDELINE MANAGEMENT

Adempas (riociguat)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

A. Pulmonary Arterial Hypertension (PAH)

Adempas is indicated for the treatment of adults with pulmonary arterial hypertension (PAH), (World Health Organization [WHO] Group 1), to improve exercise capacity, WHO functional class and to delay clinical worsening.

B. Chronic Thromboembolic Pulmonary Hypertension (CTEPH)

Adempas is indicated for the treatment of adults with persistent/recurrent chronic thromboembolic pulmonary hypertension (CTEPH), (WHO Group 4) after surgical treatment, or inoperable CTEPH, to improve exercise capacity and WHO functional class.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Pulmonary Arterial Hypertension (PAH)

Authorization of 12 months may be granted for treatment of PAH when ALL of the following criteria are met:

1. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (Refer to Appendix)
2. PAH was confirmed by right heart catheterization with all of the following pretreatment results:
 - i. mPAP \geq 25 mmHg
 - ii. PCWP \leq 15 mmHg
 - iii. PVR $>$ 3 Wood units

B. Chronic Thromboembolic Pulmonary Hypertension (CTEPH)

Authorization of 12 months may be granted for treatment of CTEPH when ALL of the following criteria are met:

1. Member has CTEPH defined as WHO Group 4 class of pulmonary hypertension (Refer to Appendix)
2. Member meets either criterion (i) or criterion (ii) below:
 - i. Recurrent or persistent CTEPH after pulmonary endarterectomy (PEA)
 - ii. Inoperable CTEPH with diagnosis confirmed by BOTH of the following (a. and b.):
 - a. Computed tomography (CT)/magnetic resonance imaging (MRI) angiography or pulmonary angiography
 - b. Pretreatment right heart catheterization with all of the following results:
 - mPAP \geq 25 mmHg
 - PCWP \leq 15 mmHg
 - PVR $>$ 3 Wood units

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with an indication listed in Section II who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

IV. APPENDIX

WHO Classification of Pulmonary Hypertension

1 PAH

- 1.1 Idiopathic (PAH)
- 1.2 Heritable PAH
- 1.3 Drug- and toxin-induced PAH
- 1.4. PAH associated with:
 - 1.4.1 Connective tissue diseases
 - 1.4.2 HIV infection
 - 1.4.3 Portal hypertension
 - 1.4.4 Congenital heart diseases
 - 1.4.5 Schistosomiasis
- 1.5 PAH long-term responders to calcium channel blockers
- 1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement
- 1.7 Persistent PH of the newborn syndrome

2 PH due to left heart disease

- 2.1 PH due to heart failure with preserved LVEF
- 2.2 PH due to heart failure with reduced LVEF
- 2.3 Valvular heart disease
- 2.4 Congenital/acquired cardiovascular conditions leading to post-capillary PH

3 PH due to lung diseases and/or hypoxia

- 3.1 Obstructive lung disease
- 3.2 Restrictive lung disease
- 3.3 Other lung disease with mixed restrictive/obstructive pattern
- 3.4 Hypoxia without lung disease
- 3.5 Developmental lung disorders

4 PH due to pulmonary artery obstruction

- 4.1 Chronic thromboembolic PH
- 4.2 Other pulmonary artery obstructions
 - 4.2.1 Sarcoma (high or intermediate grade) or angiosarcoma
 - 4.2.2 Other malignant tumors
 - Renal carcinoma
 - Uterine carcinoma
 - Germ cell tumours of the testis
 - Other tumours
 - 4.2.3 Non-malignant tumours
 - Uterine leiomyoma
 - 4.2.4 Arteritis without connective tissue disease
 - 4.2.5 Congenital pulmonary artery stenosis
 - 4.2.6 Parasites
 - Hydatidosis

5 PH with unclear and/or multifactorial mechanisms

- 5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders
- 5.2 Systemic and metabolic disorders: Pulmonary Langerhans cell histiocytosis, Gaucher disease, glycogen storage disease, neurofibromatosis, sarcoidosis
- 5.3 Others: chronic renal failure with or without hemodialysis, fibrosing mediastinitis
- 5.4 Complex congenital heart disease

V. REFERENCES

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2. Chin KM, Rubin LJ. Pulmonary arterial hypertension. *J Am Coll Cardiol*. 2008;51(16):1527-1538.
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PRIOR AUTHORIZATION CRITERIA

DRUG CLASS **GLUCAGON-LIKE PEPTIDE 1 (GLP-1) RECEPTOR AGONIST**

BRAND NAME*
(generic)

ADLYXIN
(lixisenatide)

Status: CVS Caremark Criteria

Type: Initial Prior Authorization with Quantity Limit

Ref #1511-C

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Adlyxin is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use

- Adlyxin has not been studied in patients with chronic pancreatitis or a history of unexplained pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.
- Adlyxin is not a substitute for insulin. Adlyxin is not indicated for use in patients with type 1 diabetes mellitus or for treatment of diabetic ketoacidosis
- The concurrent use of Adlyxin with short acting insulin has not been studied and is not recommended
- Adlyxin has not been studied in patients with gastroparesis and is not recommended in patients with gastroparesis.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has been receiving GLP-1 Agonist therapy for at least 3 months and has demonstrated a reduction in A1c (hemoglobin A1c) since starting GLP-1 Agonist therapy
[Note: Examples of GLP-1 Agonists are Adlyxin, Bydureon, Byetta, Ozempic, Tanzeum, Trulicity, Victoza]
OR
- The patient has a diagnosis of type 2 diabetes mellitus
AND
 - The patient has experienced an inadequate treatment response, intolerance, or contraindication to metformin
OR
 - The patient requires combination therapy **AND** has an A1c (hemoglobin A1c) of 7.5 percent or greater

Quantity Limits apply.

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Adlyxin is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Adlyxin should be initiated at 10 mcg administered subcutaneously once daily within one hour before the first meal of the day for 14 days. On Day 15, increase dosage to 20 mcg once daily. ¹⁻³

Clinical guidelines from the American Diabetes Association and the American Association of Clinical Endocrinologists and American College of Endocrinology for the management of hyperglycemia in type 2 diabetes indicate that metformin monotherapy should be started at diagnosis of type 2 diabetes unless there are contraindications. Metformin is effective

and safe, is inexpensive, and may reduce risk of cardiovascular events and death. In patients with contraindications or intolerance of metformin, initial therapy should be based on patient factors; consider a drug from another class.^{4,5}

The clinical guidelines also state that the A1c test is the major tool for assessing glycemic control and has strong predictive value for diabetes complications. Thus, A1c testing should be performed routinely in all patients with diabetes at initial assessment and as part of continuing care. The guidelines set goals for therapeutic effectiveness which must be evaluated frequently (e.g., every 3 months) until stable, using multiple criteria, including A1c. Less frequent monitoring is acceptable once targets are achieved.⁴⁻⁵ Therefore; continued use of any GLP-1 Agonist (e.g., Adlyxin, Byetta, Bydureon, Ozempic, Tanzeum, Trulicity, and Victoza) will be approved for patients who have demonstrated a reduction in A1c since starting GLP-1 Agonist therapy for at least three months.

If the A1c target is not achieved after approximately 3 months and patient does not have atherosclerotic cardiovascular disease (ASCVD) or chronic kidney disease (CKD), consider a combination of metformin and one of the preferred six treatment options: sulfonylurea, thiazolidinedione, dipeptidyl peptidase 4 (DPP-4) inhibitors, sodium-glucose cotransporter 2 (SGLT2) inhibitors, glucagon-like peptide 1 (GLP-1) receptor agonists, or basal insulin; the choice of which agent to add is based on drug-specific effects and patient factors. For patients in whom ASCVD, Heart Failure, or CKD predominates, the best choice for a second agent is a GLP-1 receptor agonist or SGLT2 inhibitor with demonstrated cardiovascular risk reduction, after consideration of drug-specific and patient factors.

In patients with an initial A1c of 7.5% or greater, or in patients who are unable to achieve their glycemic goals with monotherapy, combination therapy is recommended.⁵

Lixisenatide slows gastric emptying, which reduces the rate at which meal-derived glucose appears in the circulation, reduces food intake, and is associated with weight loss.¹⁻³ A quantity limit is in place to aid proper utilization of Adlyxin. At maximum approved dosing for Adlyxin, two (2) pens will be allowed for a 28 day supply (6 pens per 84 day supply).

REFERENCES

1. Adlyxin [package insert]. Bridgewater, NJ: Sanofi-Aventis U.S. LLC; January 2019.
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3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed July 2019.
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Written by: UM Development (SF)
Date Written: 07/2016
Revised: 07/2017, 07/2018 (no clinical changes), 07/2019 (no clinical changes)
Reviewed: Medical Affairs (MES) 07/2016, 07/2017, (CHART) 08/01/2019
External Review: 08/2016, 10/2017, 10/2018, 10/2019

CRITERIA FOR APPROVAL

- | | | | |
|---|--|-----|----|
| 1 | Has the patient been receiving GLP-1 Agonist therapy for at least 3 months?
[Note: Examples of GLP-1 Agonists are Adlyxin, Bydureon, Byetta, Ozempic, Tanzeum, Trulicity, Victoza]
[If no, then skip to question 3.] | Yes | No |
| 2 | Has the patient demonstrated a reduction in A1c (hemoglobin A1c) since starting GLP-1 | Yes | No |

Agonist therapy?
[If yes, then skip to question 6.]

- | | | | |
|---|---|-----|----|
| 3 | Does the patient have a diagnosis of type 2 diabetes mellitus? | Yes | No |
| 4 | Has the patient experienced an inadequate treatment response, intolerance, or contraindication to metformin?
[If yes, then skip to question 6.] | Yes | No |
| 5 | Does the patient require combination therapy AND have an A1c (hemoglobin A1c) of 7.5 percent or greater? | Yes | No |
| 6 | Does the patient require more than 2 prefilled pens per month (or 6 prefilled pens per 3 months)?
[RPh Note: If yes, then deny and enter a partial approval for 2 pens (6 ml) per 21 days (or 6 pens (18 ml) per 63 days)] | Yes | No |

Mapping Instructions

DENIAL REASONS – DO NOT USE FOR MEDICARE PART D

	Yes	No	
1.	Go to 2	Go to 3	
2.	Go to 6	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions:</p> <ul style="list-style-type: none"> - You have been receiving this drug or another drug in the same class for at least 3 months - You had a reduction in A1c (hemoglobin A1c) since starting therapy <p>Your request has been denied based on the information we have.</p> <p>[Short Description: Continuation of therapy, no response to treatment]</p>
3.	Go to 4	Deny	<p>You do not meet the requirements of your plan.</p> <p>Your plan covers this drug when you have type 2 diabetes mellitus. Your request has been denied based on the information we have.</p> <p>[Short Description: No approvable diagnosis]</p>
4.	Go to 6	Go to 5	
5.	Go to 6	Deny	<p>You do not meet the requirements of your plan.</p> <p>Your plan covers this drug when you meet one of these conditions:</p> <ul style="list-style-type: none"> - You have tried metformin it did not work for you or you cannot use it - You require combination therapy and you have an A1c (hemoglobin A1c) of 7.5 percent or greater <p>Your request has been denied based on the information we have.</p> <p>[Short description: No inadequate treatment response, intolerance or contraindication to metformin, no requirement for combination therapy]</p>
6.	Deny	Approve, 36 Months, 2 pens (6 ml) /21 days* (6 pens (18 ml)/63 days*)	<p>You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 2 prefilled pens per month (or 6 prefilled pens per 3 months). You have been approved for the maximum quantity that your plan covers for a duration of 36 months. Your request for additional quantities of the requested drug and strength has been denied.</p> <p>[Short description: Over max quantity]</p>

**The duration of 21 days is used for a 28-day fill period and 63 days is used for an 84-day fill period to allow time for refill processing.*

SPECIALTY GUIDELINE MANAGEMENT

AFINITOR (everolimus)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. **Hormone Receptor-Positive, HER2-Negative Breast Cancer**
Afinitor is indicated for the treatment of postmenopausal women with advanced hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer in combination with exemestane, after failure of treatment with letrozole or anastrozole.
2. **Neuroendocrine Tumors (NET)**
 - a. Afinitor is indicated for the treatment of adult patients with progressive neuroendocrine tumors of pancreatic origin (PNET) with unresectable, locally advanced or metastatic disease.
 - b. Afinitor is indicated for the treatment of adult patients with progressive, well-differentiated, non-functional neuroendocrine tumors (NET) of gastrointestinal (GI) or lung origin with unresectable, locally advanced or metastatic disease.
3. **Renal Cell Carcinoma (RCC)**
Afinitor is indicated for the treatment of adult patients with advanced renal cell carcinoma (RCC) after failure of treatment with sunitinib or sorafenib.
4. **Tuberous Sclerosis Complex (TSC)-Associated Renal Angiomyolipoma**
Afinitor is indicated for the treatment of adult patients with renal angiomyolipoma and tuberous sclerosis complex (TSC), not requiring immediate surgery.
5. **Tuberous Sclerosis Complex (TSC)-Associated Subependymal Giant Cell Astrocytoma (SEGA)**
Afinitor and Afinitor Disperz are indicated in adult and pediatric patients aged 1 year and older with tuberous sclerosis complex (TSC) for the treatment of subependymal giant cell astrocytoma (SEGA) that requires therapeutic intervention but cannot be curatively resected.
6. **Tuberous Sclerosis Complex (TSC)-Associated Partial-Onset Seizures**
Afinitor Disperz is indicated for the adjunctive treatment of adult and pediatric patients aged 2 years and older with TSC-associated partial-onset seizures.

B. Compendial Uses

1. Relapsed or stage IV renal cell carcinoma:
 - a. Single agent or in combination with lenvatinib as subsequent therapy for clear cell histology
 - b. Single-agent systemic therapy for non-clear histology
 - c. In combination with lenvatinib as systemic therapy for non-clear cell histology
 - d. In combination with bevacizumab as systemic therapy for non-clear cell histology
2. Soft tissue sarcoma subtypes:
 - a. Perivascular epithelioid cell tumors (PEComa), single-agent therapy
 - b. Recurrent angiomyolipoma, single-agent therapy
 - c. Lymphangioleiomyomatosis, single-agent therapy
3. Gastrointestinal stromal tumors (GIST), in combination with either imatinib, sunitinib, or regorafenib for disease progression after single-agent therapy with imatinib, sunitinib, and regorafenib
4. Neuroendocrine tumors of the gastrointestinal tract, lung and thymus (carcinoid tumors)
5. Neuroendocrine tumors of the pancreas, single-agent therapy

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6. Thymomas and thymic carcinomas, second-line therapy as a single agent
7. Classic Hodgkin lymphoma, third-line or subsequent systemic therapy as a single agent for relapsed or refractory disease
8. Central nervous system cancers:
 - a. Meningiomas
 - b. Glioma
 - c. Subependymal giant cell astrocytoma (SEGA); adjuvant treatment as a single agent
9. Thyroid carcinoma (papillary carcinoma, Hürthle cell carcinoma, and follicular carcinoma), if clinical trials or other systemic therapies are not available or appropriate for treatment of progressive and/or symptomatic iodine-refractory
10. Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma, single-agent therapy for previously treated disease that does not respond to primary therapy or for progressive or relapsed disease
11. Endometrial carcinoma, in combination with letrozole or as adjuvant treatment for surgically staged patients in combination with letrozole
12. Invasive breast cancer
Recurrent or stage IV (M1) hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer with no visceral crisis in postmenopausal women treated with prior endocrine therapy within 1 year or in premenopausal women treated with ovarian ablation/suppression treated with prior endocrine therapy within 1 year in combination with exemestane, fulvestrant, or tamoxifen.
13. Tuberous sclerosis complex

All other indications are considered experimental/investigational and are not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Breast Cancer

Authorization of 12 months may be granted for treatment of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative recurrent or metastatic breast cancer when prescribed in combination with exemestane, fulvestrant, or tamoxifen and the member has received endocrine therapy within 1 year.

B. Renal Cell Carcinoma

Authorization of 12 months may be granted for treatment of relapsed or metastatic RCC when any of the following criteria are met:

1. Afinitor is given as a single agent or in combination with lenvatinib as subsequent therapy for clear cell histology; OR
2. Afinitor is given as single-agent systemic therapy for non-clear cell histology; OR
3. Afinitor is given in combination with lenvatinib as systemic therapy for non-clear cell histology; OR
4. Afinitor is given in combination with bevacizumab as systemic therapy for non-clear cell histology.

C. Neuroendocrine Tumors

1. Authorization of 12 months may be granted for treatment of progressive neuroendocrine tumors (PNET) of pancreatic origin in members with unresectable, locally advanced, or metastatic disease.
2. Authorization of 12 months may be granted for treatment of progressive, well-differentiated, non-functional neuroendocrine tumors (NET) of gastrointestinal, lung, or thymic origin with unresectable, locally advanced or metastatic disease.

D. Tuberous Sclerosis Complex (TSC)

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Authorization of 12 months may be granted for treatment of TSC.

E. Soft Tissue Sarcoma

Authorization of 12 months may be granted for treatment of any of the following subtypes of soft tissue sarcoma as single agent therapy: perivascular epithelioid cell (PEComa), recurrent angiomyolipoma, or lymphangioliomyomatosis.

F. Gastrointestinal Stromal Tumor (GIST)

Authorization of 12 months may be granted for treatment of gastrointestinal stromal tumors in combination with either imatinib, sunitinib, or regorafenib for disease progression after single-agent therapy with imatinib, sunitinib, and regorafenib.

G. Thymoma and Thymic Carcinoma

Authorization of 12 months may be granted for treatment of thymoma or thymic carcinoma for second-line therapy as a single agent.

H. Classic Hodgkin Lymphoma

Authorization of 12 months may be granted for treatment of relapsed or refractory classic Hodgkin lymphoma for third-line or subsequent systemic therapy as a single agent.

I. Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma

Authorization of 12 months may be granted for treatment of Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma as a single-agent therapy for previously treated disease that does not respond to primary therapy or for progressive relapsed disease.

J. Thyroid Carcinoma

Authorization of 12 months may be granted for treatment of progressive and/or symptomatic iodine-refractory thyroid carcinoma with any of the following histologies: papillary, Hurthle cell, or follicular.

K. Endometrial Carcinoma

Authorization of 12 months may be granted for treatment of endometrial carcinoma when either of the following criteria are met:

1. Afinitor is given in combination with letrozole; OR
2. Afinitor is given in combination with letrozole as adjuvant treatment for surgically staged members.

L. Central Nervous System Cancers

1. Authorization of 12 months may be granted for the treatment of glioma (including glioblastoma) or meningioma.
2. Authorization of 12 months may be granted for the adjuvant treatment of subependymal giant cell astrocytoma (SEGA) as a single agent.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication in Section II who have not experienced disease progression or an unacceptable toxicity.

IV. REFERENCES

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PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

AFREZZA
(insulin human inhalation powder)

Status: CVS Caremark Criteria

Type: Initial Prior Authorization

Ref # 1238-A

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Afrezza is a rapid acting inhaled insulin indicated to improve glycemic control in adult patients with diabetes mellitus.

Limitations of Use:

- Afrezza is not a substitute for long-acting insulin. Afrezza must be used in combination with long-acting insulin in patients with type 1 diabetes mellitus.
- Afrezza is not recommended for the treatment of diabetic ketoacidosis.
- The safety and efficacy of Afrezza in patients who smoke have not been established. The use of Afrezza is not recommended in patients who smoke or who have recently stopped smoking.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has been evaluated with spirometry (FEV₁) to rule out any potential lung disease
[Note: Afrezza is contraindicated in patients with chronic lung disease and not recommended in patients who smoke or who have recently stopped smoking.]

AND

- The patient has been receiving the requested drug for at least 3 months AND the patient has demonstrated a reduction in A1c (hemoglobin A1c) since starting this therapy

OR

- The requested drug is being prescribed for an adult with type 1 diabetes mellitus AND
 - The patient has experienced a contraindication or intolerance to an injectable rapid-acting insulin
- The requested drug will be used in combination with long-acting insulin

OR

- The requested drug is being prescribed for an adult with type 2 diabetes mellitus AND
 - The patient has experienced a contraindication or intolerance to an injectable rapid-acting insulin OR is unable to administer injectable insulin
- The patient has experienced an inadequate treatment response, contraindication, or intolerance to metformin

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Afrezza (insulin human inhalation powder) is a rapid acting inhaled insulin indicated to improve glycemic control in adult patients with diabetes mellitus.

Afrezza is not a substitute for long-acting insulin. Afrezza must be used in combination with long-acting insulin in patients with type 1 diabetes mellitus.¹ Most people with type 1 diabetes should be treated with multiple daily injections of prandial and basal insulin, or continuous subcutaneous insulin infusion.⁴

Afrezza is contraindicated in patients with chronic lung disease such as asthma or chronic obstructive pulmonary disease (COPD), because of the risk of acute bronchospasm. Afrezza causes a decline in lung function over time as measured by spirometry (FEV₁). In patients who have a decline of $\geq 20\%$ in FEV₁ from baseline, consider discontinuing Afrezza. Consider more frequent monitoring of pulmonary function in patients with pulmonary symptoms such as wheezing, bronchospasm, breathing difficulties, or persistent or recurring cough. If symptoms persist, discontinue Afrezza. The safety and efficacy of Afrezza in patients who smoke has not been established. The use of Afrezza is not recommended in patients who smoke or who have recently stopped smoking. Before initiating Afrezza, a medical history, physical examination and spirometry (FEV₁) should be performed to identify potential lung disease in all patients. Assess pulmonary function at baseline, after the first 6 months of therapy, and annually thereafter, even in the absence of pulmonary symptoms.¹

Clinical guidelines from the American Diabetes Association and the American Association of Clinical Endocrinologists and American College of Endocrinology for the management of hyperglycemia in type 2 diabetes indicate that metformin monotherapy should be started at diagnosis of type 2 diabetes unless there are contraindications. Metformin is effective and safe, is inexpensive, and may reduce risk of cardiovascular events and death. In patients with contraindications or intolerance of metformin, initial therapy should be based on patient factors; consider a drug from another class.^{4,5}

If the A1c target is not achieved after approximately 3 months and patient does not have atherosclerotic cardiovascular disease (ASCVD) or chronic kidney disease (CKD), consider a combination of metformin and one of the preferred six treatment options: sulfonylurea, thiazolidinedione, dipeptidyl peptidase 4 (DPP-4) inhibitors, sodium-glucose cotransporter 2 (SGLT2) inhibitors, glucagon-like peptide 1 (GLP-1) receptor agonists, or basal insulin; the choice of which agent to add is based on drug-specific effects and patient factors. For patients in whom ASCVD, Heart Failure, or CKD predominates, the best choice for a second agent is a GLP-1 receptor agonist or SGLT2 inhibitor with demonstrated cardiovascular risk reduction, after consideration of drug-specific and patient factors. Many patients with type 2 diabetes eventually require and benefit from insulin therapy. Insulin has the advantage of being effective where other agents are not and should be considered as part of any combination regimen when hyperglycemia is severe.^{4,5}

Patients with inadequately controlled type 1 diabetes participated in a 24-week, open-label, active-controlled study to evaluate the glucose lowering effect of mealtime Afrezza used in combination with a basal insulin. Following a 4-week basal insulin optimization period, 344 patients were randomized to Afrezza (n=174) or insulin aspart (n=170) administered at each meal of the day. Afrezza provided less A1c reduction than insulin aspart, and the difference was statistically significant. More subjects in the insulin aspart group achieved the A1c target of $\leq 7\%$.¹ Considering the results of this study, Afrezza will be approved if the patient experienced a contraindication or intolerance to an injectable rapid-acting insulin. Study data comparing Afrezza to a rapid-acting insulin in patients with type 2 diabetes is not available¹; therefore, Afrezza will also be approved if a patient with type 2 diabetes is unable to administer injectable insulin.

The clinical guidelines also state that the A1c test is the major tool for assessing glycemic control and has strong predictive value for diabetes complications. Thus, A1c testing should be performed routinely in all patients with diabetes at initial assessment and as part of continuing care. The guidelines set goals for therapeutic effectiveness which must be evaluated frequently (e.g., every 3 months) until stable, using multiple criteria, including A1c. Less frequent monitoring is acceptable once targets are achieved.⁴⁻⁵ Therefore, continued use of Afrezza (insulin human inhalation powder) will be approved for patients who have demonstrated a reduction in A1c (hemoglobin A1c) since starting Afrezza therapy for at least three months.

REFERENCES

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Written by: UM Development (CF)
 Date Written: 02/2015
 Revised: 04/2015 (updated injectable insulin question); 08/2015 (reordered questions); (KM) 07/2016 (no clinical changes); (RP) 07/2017, 07/2018 (no clinical changes); (DFW) 07/2019 (no clinical changes/removed MDC designation from title/document)
 Reviewed: Medical Affairs (KRU) 02/2015, 03/2015, 04/2015; (LCB) 08/2015; (ME) 07/2017, (CHART) 8/1/2019
 External Review: 04/2015, 10/2015, 10/2016, 10/2017, 10/2018, 10/2019

CRITERIA FOR APPROVAL

1	Has the patient been evaluated with spirometry (FEV1) to rule out any potential lung disease? [Note: Afrezza is contraindicated in patients with chronic lung disease and not recommended in patients who smoke or who have recently stopped smoking.]	Yes	No
2	Has the patient been receiving the requested drug for at least 3 months? [If no, then skip to question 4.]	Yes	No
3	Has the patient demonstrated a reduction in A1c (hemoglobin A1c) since starting this therapy? [No further questions.]	Yes	No
4	Is the requested drug being prescribed for an adult with type 1 diabetes mellitus? [If no, then skip to question 7.]	Yes	No
5	Has the patient experienced a contraindication or intolerance to an injectable rapid-acting insulin?	Yes	No
6	Will the requested drug be used in combination with long-acting insulin? [No further questions.]	Yes	No
7	Is the requested drug being prescribed for an adult with type 2 diabetes mellitus?	Yes	No
8	Has the patient experienced a contraindication or intolerance to an injectable rapid-acting insulin OR is unable to administer injectable insulin?	Yes	No
9	Has the patient experienced an inadequate treatment response, contraindication, or intolerance to metformin?	Yes	No

Guidelines for Approval

Duration of Approval 36 Months

Set 1		Set 2		Set 3	
Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)
1	None	1	2	1	2
2		4		7	4
3		5		8	
		6		9	

Mapping Instructions

	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Deny	You do not meet the requirements of your plan.

			<p>Your plan covers this drug when you have been tested with spirometry (FEV₁) to make sure you do not have a lung disease.</p> <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No confirmation of spirometry]</p>
2.	Go to 3	Go to 4	
3.	Approve, 36 months	Deny	<p>You do not meet the requirements of your plan.</p> <p>Your plan covers this drug when you meet these conditions:</p> <ul style="list-style-type: none"> - You have been receiving the requested drug for at least 3 months - You have had a reduction in A1c (hemoglobin A1c) since starting this therapy <p>Your request has been denied based on the information we have.</p> <p>[Short Description: Continuation of therapy, No response to treatment]</p>
4.	Go to 5	Go to 7	
5.	Go to 6	Deny	<p>You do not meet the requirements of your plan.</p> <p>Your plan covers this drug when you tried an injectable rapid-acting insulin first and it did not work for you or you cannot use it</p> <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No intolerance or contraindication to injectable rapid-acting insulin]</p>
6.	Approve, 36 months	Deny	<p>You do not meet the requirements of your plan.</p> <p>Your plan covers this drug when you will use a long-acting insulin with the requested drug.</p> <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No use of long-acting insulin]</p>
7.	Go to 8	Deny	<p>You do not meet the requirements of your plan.</p> <p>Your plan covers this drug when you are an adult with type 1 or type 2 diabetes.</p> <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No approvable diagnosis]</p>
8.	Go to 9	Deny	<p>You do not meet the requirements of your plan.</p> <p>Your plan covers this drug when you meet any of these conditions:</p> <ul style="list-style-type: none"> - You are unable to inject yourself with insulin - You tried an injectable rapid-acting insulin first and it did not work for you or you cannot use it <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No intolerance or contraindication to injectable rapid-acting insulin or able to use injectable insulin]</p>
9.	Approve, 36 months	Deny	<p>You do not meet the requirements of your plan.</p> <p>Your plan covers this drug when you have tried metformin and it either did not work for you or you cannot use it.</p> <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No inadequate response, intolerance or contraindication to metformin]</p>

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

AKLIEF
(trifarotene)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

Ref # 3362-A

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Aklief Cream is a retinoid indicated for the topical treatment of acne vulgaris in patients 9 years of age and older.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for acne vulgaris in a patient 9 years of age or older

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Aklief Cream is a retinoid indicated for the topical treatment of acne vulgaris in patients 9 years of age and older.

REFERENCES

1. Aklief cream [package insert]. Fort Worth, TX: Galderma Laboratories, LP; October 2019.
2. Lexicomp Online, Lexi-Drugs Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed October 2019.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed October 2019.

Written by: UM Development (RP)
Date Written: 10/2019
Revised:
Reviewed: Medical Affairs (CHART) 10/17/2019
External Review: 12/2019

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for acne vulgaris in a patient 9 years of age or older?	Yes	No
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Mapping Instructions

		Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Approve, 12 Months		Deny	You do not meet the requirements of your plan. Your plan covers this drug when you are 9 years of age or older and are using it for acne vulgaris. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis.]

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

AKYNZEO CAPSULES
(netupitant/palonosetron)

AKYNZEO INJECTION
(fosnetupitant/palonosetron)

Status: CVS Caremark Criteria

Type: Post Limit Prior Authorization

Ref # 1212-J

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated*

FDA-APPROVED INDICATIONS

Akynzeo capsules is indicated in combination with dexamethasone in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of cancer chemotherapy, including, but not limited to, highly emetogenic chemotherapy. Akynzeo capsules is a combination of palonosetron and netupitant: palonosetron prevents nausea and vomiting during the acute phase and netupitant prevents nausea and vomiting during both the acute and delayed phase after cancer chemotherapy.

Akynzeo for injection is indicated in combination with dexamethasone in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy. Akynzeo for injection is a combination of palonosetron and fosnetupitant, a prodrug of netupitant: palonosetron prevents nausea and vomiting during the acute phase and fosnetupitant prevents nausea and vomiting during both the acute and delayed phase after cancer chemotherapy.

Limitations of Use

Akynzeo for injection has not been studied for the prevention of nausea and vomiting associated with anthracycline plus cyclophosphamide chemotherapy.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of cancer chemotherapy

Quantity Limits apply.

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Akynzeo capsules is indicated in combination with dexamethasone in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of cancer chemotherapy, including, but not limited to, highly emetogenic chemotherapy. Akynzeo for injection is indicated in combination with dexamethasone in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy.

The recommended oral dosage in adults for highly emetogenic chemotherapy, including cisplatin based chemotherapy, is one capsule of Akynzeo administered approximately 1 hour prior to the start of chemotherapy with dexamethasone 12 mg administered orally 30 minutes prior to chemotherapy on day 1; followed by dexamethasone 8 mg orally once daily on days 2 to 4. The recommended dosage in adults for anthracyclines and cyclophosphamide based chemotherapy and chemotherapy not considered highly emetogenic is one capsule of Akynzeo approximately 1 hour prior to the start of

chemotherapy with dexamethasone 12 mg administered orally 30 minutes prior to chemotherapy on day 1. Administration of dexamethasone on days 2 to 4 is not necessary.

The recommended injection dosage in adults for highly emetogenic chemotherapy, including cisplatin based chemotherapy, is one vial of Akynzeo administered approximately 30 minutes prior to the start of chemotherapy with dexamethasone 12 mg administered orally 30 minutes prior to chemotherapy on day 1; followed by dexamethasone 8 mg orally once daily on days 2 to 4. Akynzeo for injection has not been studied for the prevention of nausea and vomiting associated with anthracycline plus cyclophosphamide chemotherapy.

Akynzeo has been studied in patients who completed cycle 1 and continued treatment in a multiple-cycle extension, up to a maximum of 8 treatment cycles; the majority of patients completed at least 4 cycles but only a limited number of patients received treatment beyond cycle 6. Antiemetic activity of Akynzeo was maintained throughout repeat cycles for those patients continuing in each of the multiple cycles.¹ In a separate study, patients undergoing initial and repeat cycles of chemotherapy (including carboplatin, cisplatin, oxaliplatin, and doxorubicin regimens) received Akynzeo; efficacy was maintained throughout all cycles during the acute, delayed, and overall (0-120 hr) phase after the start of chemotherapy.¹

The risk of nausea/vomiting for patients receiving highly and moderately emetogenic chemotherapy lasts for at least 3 days for high and 2 days for moderate after the last dose of chemotherapy. The period of risk for delayed emesis after chemotherapy administration depends on the specific regimen and the emetogenic potential of the last chemotherapy agent administered in the regimen. Patients need to be protected throughout the full period of risk. For multi-drug regimens, antiemetic therapy is based on the drug with the highest emetic risk.⁴ Therefore, the Akynzeo post limit quantity has been determined based on the drug regimen with the highest emetic risk.

The limit is designed to allow for the prevention of acute or delayed onset nausea and vomiting associated with chemotherapy at the recommended dose of Akynzeo. The limit allows a quantity sufficient for four chemotherapy cycles per month (i.e., one chemotherapy cycle every week).

REFERENCES

1. Akynzeo [package insert]. Iselin, NJ: Helsinn Therapeutics.; April 2018.
2. AHFS DI (Adult and Pediatric) [database online]. Hudson, OH: Lexi-Comp, Inc.; http://online.lexi.com/lco/action/index/dataset/complete_ashp [available with subscription]. Accessed January 2018.
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4. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Antiemesis. V.2.2016. Available at: www.nccn.org. Accessed May 2018.

Written by: UM Development (RP)
Date Written: 10/2014
Revised: 01/2015, 05/2015 (added denial reasons); (MS) 01/2016 (no clinical changes), 01/2017, (ME) 01/2018 (no clinical changes) (ME) 05/2018 (added injection)
Reviewed: Medical Affairs (SES) 10/2014, 01/2015; (JG) 01/2017, (ME) 05/2018
External Review: 11/2014, 04/2015, 04/2016, 04/2017, 04/2018, 06/2018

CRITERIA FOR APPROVAL

- | | | | |
|---|---|-----|----|
| 1 | Is the requested drug being prescribed for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of cancer chemotherapy? | Yes | No |
| 2 | Does the patient require use of MORE than 4 capsules or vials per 28 days of Akynzeo? | Yes | No |

[RPh Note: If yes, then deny and enter a partial approval for 4 capsules or vials per 21 days of Akynzeo.]

Mapping Instructions			
	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Deny	Your plan covers this drug when it is being used to prevent nausea or vomiting from chemotherapy. Your use of this drug does not meet the requirement. This is based on the information we have. [Short Description: No approvable diagnosis]
2.	Deny	Approve, 6 months, 4 capsules or vials / 21 days*	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 4 capsules or vials per 28 days of Akynzeo. You have been approved for the maximum quantity that your plan covers for a duration of 6 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity]

* The duration of 21 days is used for a 28-day fill period.

* This drug is indicated for short-term acute use; therefore, the mail limit will be the same as the retail limit.

STEP THERAPY CRITERIA

BRAND NAME*
(generic)

ALDARA (BRAND ONLY)
(imiquimod)

ZYCLARA (BRAND ONLY)
(imiquimod)

Status: CVS Caremark Criteria

Type: Initial Step Therapy with Quantity Limit;

Post Step Therapy Prior Authorization with Quantity Limit

Ref # 1377-E

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Aldara

Actinic Keratosis

Aldara Cream is indicated for the topical treatment of clinically typical, nonhyperkeratotic, nonhypertrophic actinic keratoses on the face or scalp in immunocompetent adults.

Superficial Basal Cell Carcinoma

Aldara Cream is indicated for the topical treatment of biopsy-confirmed, primary superficial basal cell carcinoma (sBCC) in immunocompetent adults, with a maximum tumor diameter of 2.0 cm, located on the trunk (excluding anogenital skin), neck, or extremities (excluding hands and feet), only when surgical methods are medically less appropriate and patient follow-up can be reasonably assured. The histological diagnosis of superficial basal cell carcinoma should be established prior to treatment, since safety and efficacy of Aldara Cream have not been established for other types of basal cell carcinomas, including nodular and morpheaform (fibrosing or sclerosing) types.

External Genital Warts

Aldara Cream is indicated for the treatment of external genital and perianal warts/condyloma acuminata in patients 12 years or older.

Limitations of Use

Aldara Cream has been evaluated in children ages 2 to 12 years with molluscum contagiosum and these studies failed to demonstrate efficacy.

Unevaluated Populations

The safety and efficacy of Aldara Cream in immunosuppressed patients have not been established. Aldara Cream should be used with caution in patients with pre-existing autoimmune conditions. The efficacy and safety of Aldara Cream have not been established for patients with Basal Cell Nevus Syndrome or Xeroderma Pigmentosum.

Zyclara

Actinic Keratosis

Zyclara Cream, 2.5% and 3.75% are indicated for the topical treatment of clinically typical, visible or palpable actinic keratoses (AK) of the full face or balding scalp in immunocompetent adults.

External Genital Warts

Zyclara Cream, 3.75% is also indicated for the treatment of external genital (EGW) and perianal warts/condyloma acuminata in patients 12 years or older.

INITIAL STEP THERAPY with QUANTITY LIMIT*

If the patient has filled a prescription for at least a 30 day supply of generic imiquimod 5% cream within the past 120 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.* If the patient does not meet the initial step therapy criteria, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

*If the patient meets the initial step therapy criteria, then the initial limit criteria will apply. If the patient is requesting more than the initial quantity limit the claim will reject with a message indicating that a PA is required.

***INITIAL QUANTITY LIMIT**

Drug	4 Week Limit*	12 Week Limit*
Aldara packets	2 boxes (24 packets) / 21 days	6 boxes (72 packets) / 63 days
Zyclara packets	1 box (28 packets) / 21 days	3 boxes (84 packets) / 63 days
Zyclara pump	1 pump (7.5gm) / 21 days	3 pumps (7.5gms each) / 63 days

**The duration of 21 days is used for a 28-day fill period and 63 days is used for an 84-day fill period to allow time for refill processing.*

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has experienced an inadequate treatment response, intolerance, or contraindication to generic imiquimod 5 percent cream

AND

- The request is for the treatment of superficial basal cell carcinoma with Aldara
- OR**
- The request is for the treatment of actinic keratosis or external genital warts

Quantity Limit applies.

RATIONALE

If the patient has filled a prescription for at least a 30 day supply of generic imiquimod 5% cream within the past 120 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit. The quantity limit is set at 2 boxes of Aldara or 1 box of Zyclara or 1 pump of Zyclara per month.

If the patient does not meet the initial step therapy criteria, then prior authorization (PA) is required. If the patient is requesting more than the initial quantity limit the claim will reject with a message indicating that a PA is required.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Aldara cream is indicated for actinic keratosis, superficial basal cell carcinoma, and external genital warts. Zyclara cream is indicated for actinic keratosis and external genital and perianal warts in patients 12 years or older.

Imiquimod 5% cream is indicated for the topical treatment of clinically typical, nonhyperkeratotic, nonhypertrophic actinic keratoses on the face or scalp in immunocompetent adults. According to the American Academy of Dermatology, no one treatment works on all actinic keratosis⁵. Clearance rates are dependent on patient adherence and there is limited evidence regarding comparative efficacy of topical medications⁶. Therefore, the patient must have experienced an inadequate treatment response or intolerance to generic imiquimod 5% cream.

For actinic keratosis, Aldara Cream should be applied 2 times per week for a full 16 weeks to a defined treatment area on the face or scalp (but not both concurrently). The treatment area is defined as one contiguous area of approximately 25 cm² (e.g., 5 cm x 5 cm) on the face (e.g., forehead or one cheek) or on the scalp. For superficial basal cell carcinoma, Aldara Cream should be applied 5 times per week for a full 6 weeks to a biopsy-confirmed superficial basal cell carcinoma. For external genital/perianal warts, Aldara Cream should be applied 3 times per week. Aldara Cream treatment should continue until there is total clearance of the genital/perianal warts or for a maximum of 16 weeks. New warts may develop during therapy, as Aldara Cream is not a cure.

Aldara Cream is packaged in single-use packets each of which contains 250 mg of the cream, equivalent to 12.5 mg of imiquimod, with 12 packets supplied per box. Therefore, the quantity limit is set to 2 boxes (24 packets) per 4 weeks which allows a quantity sufficient for all Food and Drug Administration (FDA) approved indications.

For actinic keratosis, Zyclara Cream should be applied once per day before bedtime to the affected treatment area on the face or scalp for two 2-week treatment cycles divided by a 2-week no-treatment period. The treatment area is defined as one contiguous area of approximately 25 cm² (e.g., 5 cm x 5 cm²) on the face (e.g., forehead or one cheek) or on the scalp. Patients may apply up to 0.5 grams or 2 packets or 2 full actuations of the pump to each treatment area and left on the skin for approximately 8 hours. For external genital and perianal warts, Zyclara Cream should be applied once per day until total clearance or for up to 8 weeks. Patients may apply up to 0.25 grams or one packet or one full actuation of the pump to each treatment area and left on the skin for approximately 8 hours. No more than 2 boxes (56 packets) or two 7.5 gram pumps should be prescribed per two 2-week treatment cycles and treatment cycles should not be extended due to missed doses.

Zyclara 3.75% Cream is packaged in single-use packets, with 28 packets supplied per box and a 7.5 gram pump. Each pump, when actuated after priming delivers 0.235 grams of cream. Each 3.75% Cream packet delivers 0.25 grams of cream. Therefore, the quantity limit is set to 1 box (28 packets) and 1 pump (7.5gm) per 4 weeks which allows a quantity sufficient for all Food and Drug Administration (FDA) approved indications.

Recommended Dosing Chart ¹⁻²					
Brand Name	Diagnosis	Dosage	Treatment Course Duration	Quantity per 4 weeks	Quantity per treatment course
Aldara 12 packets per box	Superficial basal cell carcinoma	1 packet 5 times per week	6 weeks	20 packets up to 2 boxes	30 packets up to 3 boxes
Aldara 12 packets per box	Actinic Keratosis	1 packet 2 times per week	16 weeks	8 packets up to 1 box	32 packets up to 3 boxes
Aldara 12 packets per box	External genital warts	1 packet 3 times per week	16 weeks	12 packets 1 box	48 packets 4 boxes
Zyclara 3.75% 28 packets per box	Actinic Keratosis	2 packets per day	two 2-weeks divided by 2-weeks off	28 packets 1 box	56 packets 2 boxes
Zyclara 3.75% 28 packets per box	External genital warts	1 packet per day	8 weeks	28 packets 1 box	56 packets 2 boxes
Zyclara 28 actuations per 7.5 gram pump	Actinic Keratosis	2 actuations per day	two 2-weeks divided by 2-weeks off	28 actuations one 7.5gm pump	56 actuations two 7.5gm pumps
Zyclara 28 actuations per 7.5 gram pump	External genital warts	1 actuation per day	8 weeks	28 actuations one 7.5gm pump	56 actuations two 7.5gm pumps

REFERENCES

1. Aldara [package insert]. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; April 2018.
2. Zyclara [package insert]. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; June 2017.
3. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed June 2019.
4. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed June 2019.
5. Bhatia ND. Medical Management of Actinic Keratoses. Focus session presented at the 2011 American Academy of Dermatology Summer Academy Meeting: New York City. Aug 2011.
6. Shoimer I, Rosen N, Muhn C. Current management of actinic keratoses. Skin Therapy Lett. 2010 May;15(5):5-7

Written by: UM Development (MS)
 Date Written: 06/2016
 Revised: (CF) 06/2017 (no clinical changes), (JK/AJ) 03/2018 (addition of Zyclara, revise Aldara Qty), (ME) 06/2019 (no clinical changes)
 Reviewed: Medical Affairs (MM) 06/2016, (AN) 07/2018
 External Review: 10/2016, 10/2017, 10/2018, 08/2019

CRITERIA FOR APPROVAL

- | | | | |
|---|--|-----|----|
| 1 | Is this request for the treatment of any of the following: A) actinic keratosis, B) external genital warts, C) superficial basal cell carcinoma with Aldara? | Yes | No |
| 2 | Has the patient experienced an inadequate treatment response, intolerance, or contraindication to generic imiquimod 5 percent cream? | Yes | No |
| 3 | Does the patient require MORE than any of the following per month: A) 2 boxes (24 packets) of Aldara, B) 1 box (28 packets) of Zyclara, C) one 7.5 gram pump of Zyclara? | Yes | No |

[RPh Note: If yes, then deny and enter a partial approval for 2 boxes (24 packets) per 21 days of brand Aldara, or 1 box (28 packets) or one 7.5 gram pump per 21 days of brand Zyclara.]

Mapping Instructions			
	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have any of the following: - actinic keratosis - external genital warts - superficial basal cell carcinoma (Aldara only). Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
2.	Go to 3	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have tried generic imiquimod 5 percent cream and it either did not work for you or you cannot use it. Your request has been denied based on the information we have. [Short Description: No inadequate response, intolerance or contraindication to generic imiquimod 5 percent cream]
3.	Deny	Approve, 12 months, See Quantity Limits Chart*	You do not meet the requirements of your plan. You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to one of the following per month: - 2 boxes (24 packets) of brand Aldara - 1 box (28 packets) of brand Zyclara - one 7.5 gram pump of brand Zyclara. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. Your request has been denied based on the information we have. [Short Description: Over max quantity]

*** QUANTITY LIMITS CHART**

Drug	4 Week Limit*	12 Week Limit*
Aldara packets	2 boxes (24 packets) / 21 days	6 boxes (72 packets) / 63 days
Zyclara packets	1 box (28 packets) / 21 days	3 boxes (84 packets) / 63 days
Zyclara pump	1 pump (7.5gm) / 21 days	3 pumps (7.5gms each) / 63 days

*The duration of 21 days is used for a 28-day fill period and 63 days is used for an 84-day fill period to allow time for refill processing.

SPECIALTY GUIDELINE MANAGEMENT

ALDURAZYME (laronidase)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Aldurazyme is indicated for patients with Hurler and Hurler-Scheie forms of Mucopolysaccharidosis I (MPS I) and for patients with the Scheie form who have moderate to severe symptoms. The risks and benefits of treating mildly affected patients with the Scheie form have not been established.

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: alpha-L-iduronidase enzyme assay or genetic testing results supporting diagnosis.

III. CRITERIA FOR INITIAL APPROVAL

Mucopolysaccharidosis I (MPS I)

Authorization of 12 months may be granted for treatment of MPS I when both of the following criteria are met:

- A. Diagnosis of MPS I was confirmed by enzyme assay demonstrating a deficiency of alpha-L-iduronidase enzyme activity or by genetic testing.
- B. Member has the Hurler or Hurler-Scheie form of MPS I OR the member has the Scheie form (Scheie syndrome) with moderate to severe symptoms (e.g., normal intelligence, less progressive physical problems, corneal clouding, joint stiffness, valvular heart disease, death in later decades).

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for Mucopolysaccharidosis I (MPS I) who are responding to therapy (e.g., improvement, stabilization, or slowing of disease progression for pulmonary function or walking capacity).

V. REFERENCES

1. Aldurazyme [package insert]. Cambridge, MA: Genzyme Corporation; April 2013.
2. Wraith JE, Clarke LA, Beck M, et al. Enzyme replacement therapy for mucopolysaccharidosis I: a randomized, double-blinded, placebo-controlled, multinational study of recombinant human alpha-L-iduronidase (laronidase). *J Pediatr*. 2004;144:581-588.

Reference number(s)
2049-A

SPECIALTY GUIDELINE MANAGEMENT

ALECENSA (alectinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Alecensa is indicated for the treatment of patients with anaplastic lymphoma kinase (ALK)-positive, metastatic non-small cell lung cancer (NSCLC) as detected by an FDA-approved test.

B. Compendial Uses

1. Recurrent or advanced NSCLC, ALK rearrangement-positive
2. Brain metastases from ALK rearrangement-positive NSCLC

All other indications are considered experimental/investigational and are not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: ALK mutation status

III. CRITERIA FOR INITIAL APPROVAL

Non-Small Cell Lung Cancer (NSCLC)

Authorization of 12 months may be granted for treatment of recurrent, advanced or metastatic ALK-positive NSCLC (including brain metastases from NSCLC).

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced an unacceptable toxicity.

V. REFERENCES

1. Alecensa [package insert]. South San Francisco, CA: Genentech USA, Inc.; June 2018.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed February 27, 2019.
3. The NCCN Clinical Practice Guidelines in Oncology® Non-Small Cell Lung Cancer Version 3.2019. National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed February 27, 2019.

Reference number(s)
2150-A

4. The NCCN Clinical Practice Guidelines in Oncology® Central Nervous System Cancers Version 1.2019. ©2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 7, 2019.

SPECIALTY GUIDELINE MANAGEMENT

ALIMTA (pemetrexed)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Non-squamous non-small cell lung cancer (NSCLC)
 - a. Alimta is indicated in combination with pembrolizumab and platinum chemotherapy, for the initial treatment of patients with metastatic non-squamous NSCLC, with no EGFR or ALK genomic tumor aberrations.
 - b. Alimta is indicated in combination with cisplatin for the initial treatment of patients with locally advanced or metastatic, non-squamous, non-small cell lung cancer (NSCLC).
 - c. Alimta is indicated as a single agent for the maintenance treatment of patients with locally advanced or metastatic, non-squamous NSCLC whose disease has not progressed after four cycles of platinum-based first-line chemotherapy.
 - d. Alimta is indicated as a single agent for the treatment of patients with recurrent, metastatic non-squamous, NSCLC after prior chemotherapy.

Limitations of use: Alimta is not indicated for the treatment of patients with squamous cell, non-small cell lung cancer (NSCLC).

2. Mesothelioma
Alimta is indicated, in combination with cisplatin, for the treatment of patients with malignant pleural mesothelioma whose disease is unresectable or who are otherwise not candidates for curative surgery.

B. Compendial Uses

1. Bladder cancer, primary carcinoma of the urethra, upper genitourinary (GU) tract tumors, and urothelial carcinoma of the prostate
2. Malignant pleural mesothelioma
3. Nonsquamous non-small cell lung cancer (NSCLC)
4. Ovarian cancer, fallopian tube cancer, and primary peritoneal cancer: epithelial ovarian cancer, fallopian tube cancer, and primary peritoneal cancer
5. Primary central nervous system (CNS) lymphoma
6. Thymomas and thymic carcinomas
7. Malignant peritoneal mesothelioma
8. Cervical cancer

All other indications are considered experimental/investigational and are not medically necessary.

II. EXCLUSIONS

Reference number(s)
1900-A

Coverage will not be provided for members with any of the following exclusions: Squamous cell NSCLC

III. CRITERIA FOR INITIAL APPROVAL

A. Bladder Cancer, Primary Carcinoma of the Urethra, Upper Genitourinary Tract Tumors, and Urothelial Carcinoma of the Prostate

1. Bladder Cancer

Authorization of 6 months may be granted for treatment of bladder cancer, as a single agent as subsequent therapy.

2. Upper Genitourinary Tract Tumors and Urothelial Carcinoma of the Prostate

Authorization of 6 months may be granted for treatment of metastatic upper genitourinary tract tumors or urothelial carcinoma of the prostate, as a single agent as subsequent therapy.

3. Primary Carcinoma of the Urethra

Authorization of 6 months may be granted for treatment of recurrent or metastatic primary carcinoma of the urethra, as a single agent as subsequent therapy.

B. Malignant Pleural Mesothelioma (MPM)

Authorization of 6 months may be granted for treatment of MPM in members when any of the following criteria are met:

1. Alimta will be used as a single agent or in combination with cisplatin or carboplatin; or
2. Alimta will be used in combination with bevacizumab and either cisplatin or carboplatin.

C. Non-Small Cell Lung Cancer (Non-Squamous Histology)

Authorization of 6 months may be granted for treatment of non-squamous non-small cell lung cancer in members when Alimta will be used in any of the following regimens:

1. As a single agent; or
2. Alimta in combination with cisplatin or carboplatin; or
3. Alimta in combination with pembrolizumab or bevacizumab; or
4. Alimta in combination with pembrolizumab and either cisplatin or carboplatin; or
5. Alimta in combination with bevacizumab and either cisplatin or carboplatin.

D. Epithelial Ovarian Cancer, Fallopian Tube Cancer, and Primary Peritoneal Cancer

Authorization of 6 months may be granted for treatment of persistent or recurrent epithelial ovarian cancer, fallopian tube cancer, or primary peritoneal cancer, as single agent therapy.

E. Primary Central Nervous System (CNS) Lymphoma

Authorization of 6 months may be granted for treatment of relapsed or refractory primary CNS lymphoma, as a single agent.

F. Thymomas and Thymic Carcinomas

Authorization of 6 months may be granted for treatment of thymoma or thymic carcinoma, as a single agent for second-line therapy.

G. Malignant Peritoneal Mesothelioma (MPeM)

Authorization of 6 months may be granted for treatment of MPeM.

H. Cervical Cancer

Authorization of 6 months may be granted for treatment of persistent or recurrent cervical cancer.

Reference number(s)
1900-A

IV. CONTINUATION OF THERAPY

Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for an indication in Section III who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES

1. Alimta [package insert]. Indianapolis, IN: Eli Lilly and Company USA, LLC; January 2019.
2. The NCCN Drugs & Biologics Compendium 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed July 03, 2019.
3. Lexicomp [database online]. Hudson, OH: Lexi-Comp, Inc.; http://online.lexi.com/lco/action/index/dataset/complete_ashp [available with subscription]. Accessed (July 2019).

SPECIALTY GUIDELINE MANAGEMENT

ALIQOPA (copanlisib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Aliqopa is indicated for the treatment of adult patients with relapsed follicular lymphoma (FL) who have received at least two prior systemic therapies.

Accelerated approval was granted for this indication based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

B. Compendial Uses

1. Follicular lymphoma, second-line or subsequent therapy for relapsed or refractory disease after 2 prior therapies
2. Gastric MALT lymphoma, subsequent therapy for relapsed or refractory disease after 2 prior therapies
3. Non-gastric MALT lymphoma, subsequent therapy for relapsed or refractory disease after 2 prior therapies
4. Nodal marginal zone lymphoma, subsequent therapy for relapsed or refractory disease after 2 prior therapies
5. Splenic marginal zone lymphoma, subsequent therapy for relapsed or refractory disease after 2 prior therapies

All other indications are considered experimental/investigational and are not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Follicular lymphoma (FL)**

Authorization of 12 months may be granted to members with follicular lymphoma (FL) when the requested medication will be used as second-line or subsequent therapy.

B. **Gastric MALT Lymphoma and Non-gastric MALT Lymphoma**

Authorization of 12 months may be granted to members with gastric or non-gastric MALT lymphoma when the requested medication will be used as subsequent therapy after at least two prior therapies.

C. **Nodal Marginal Zone lymphoma**

Authorization of 12 months may be granted to members with nodal marginal zone lymphoma when the requested medication will be used as subsequent therapy after at least two prior therapies.

D. **Splenic Marginal Zone Lymphoma**

Authorization of 12 months may be granted to members with splenic marginal zone lymphoma when the requested medication will be used as subsequent therapy after at least two prior therapies.

Reference number
2329-A

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Aliqopa [package insert]. Whippany, NJ: Bayer HealthCare Pharmaceuticals, Inc.; May 2019.
2. National Comprehensive Cancer Network. The NCCN Drugs & Biologics Compendium. <http://www.nccn.org>. Accessed July 02, 2019.

SPECIALTY GUIDELINE MANAGEMENT

Alpha₁-Proteinase Inhibitors

ARALAST NP (alpha₁-proteinase inhibitor [human])
GLASSIA (alpha₁-proteinase inhibitor [human])
PROLASTIN-C (alpha₁-proteinase inhibitor [human])
ZEMAIRA (alpha₁-proteinase inhibitor [human])

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

1. Aralast NP
Chronic augmentation therapy in adults with clinically evident emphysema due to severe congenital deficiency of alpha₁-proteinase inhibitor (alpha₁-antitrypsin deficiency)
2. Glassia
Chronic augmentation and maintenance therapy in adults with clinically evident emphysema due to severe hereditary deficiency of alpha₁-proteinase inhibitor (alpha₁-antitrypsin deficiency)
3. Prolastin-C
Chronic augmentation and maintenance therapy in adults with clinical evidence of emphysema due to severe hereditary deficiency of alpha₁-proteinase inhibitor (alpha₁-antitrypsin deficiency)
4. Zemaira
Chronic augmentation and maintenance therapy in adults with alpha₁-proteinase inhibitor deficiency and clinical evidence of emphysema

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

1. Pretreatment serum alpha₁-antitrypsin (AAT) level
2. Pretreatment post-bronchodilation forced expiratory volume in 1 second (FEV₁)
3. AAT protein phenotype

III. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of emphysema due to alpha₁-antitrypsin (AAT) deficiency when all of the following criteria are met:

1. The member's pretreatment serum AAT level is less than 11 micromol/L (80 mg/dL by radial immunodiffusion or 50 mg/dL by nephelometry).
2. The member's pretreatment post-bronchodilation forced expiratory volume in 1 second (FEV₁) is greater than or equal to 25% and less than or equal to 80% of the predicted value.
3. The member has a documented PiZZ, PiZ (null), or Pi (null, null) phenotype (homozygous) AAT deficiency or other phenotype associated with serum AAT concentrations of less than 11 micromol/L (80 mg/dL by radial immunodiffusion or 50 mg/dL by nephelometry).
4. The member does not have the PiMZ or PiMS phenotype AAT deficiency.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment of emphysema due to alpha₁-antitrypsin (AAT) deficiency when the member is experiencing beneficial clinical response from therapy.

V. OTHER

Note: If the member is a current smoker, they should be counseled on the harmful effects of smoking on pulmonary conditions and available smoking cessation options.

VI. REFERENCES

1. Aralast NP [package insert]. Westlake Village, CA: Baxalta US Inc.; September 2015.
2. Glassia [package insert]. Westlake Village, CA: Baxalta US Inc.; June 2017.
3. Prolastin-C [package insert]. Research Triangle Park, NC: Grifols Therapeutics Inc.; September 2017.
4. Zemaira [package insert]. Kankakee, IL: CSL Behring LLC; September 2015.
5. American Thoracic Society/European Respiratory Society statement: standards for the diagnosis and management of individuals with alpha-1 antitrypsin deficiency. *Am J Respir Crit Care Med*. 2003;168:818-900.
6. Marciniuk DD, Hernandez P, Balter M, et al. Alpha-1 antitrypsin deficiency targeted testing and augmentation therapy: a Canadian Thoracic Society clinical practice guideline. *Can Respir J*. 2012;19:109-116.
7. Sandhaus RA, Turino G, Brantly ML, et al. The diagnosis and management of alpha-1 antitrypsin deficiency in the adult. *Chronic Obstr Pulm Dis*. 2016;3(3):668-82.

SPECIALTY GUIDELINE MANAGEMENT

ALUNBRIG (brigatinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Alunbrig is indicated for the treatment of patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC) who have progressed on or are intolerant to crizotinib.

This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

B. Compendial Uses

1. Recurrent, advanced or metastatic ALK rearrangement-positive NSCLC: as first line therapy, after progression on or intolerance to crizotinib, or as continuation of therapy if used first line
2. Brain metastases from ALK rearrangement-positive NSCLC

All other indications are considered experimental/investigational and are not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: ALK mutation status

III. CRITERIA FOR INITIAL APPROVAL

Non-Small Cell Lung Cancer (NSCLC)

Authorization of 12 months may be granted for treatment of recurrent, advanced or metastatic ALK-positive NSCLC (including brain metastases from NSCLC).

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced an unacceptable toxicity.

V. REFERENCES

1. Alunbrig [package insert]. Cambridge, MA: ARIAD Pharmaceuticals, Inc.; December 2018.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed February 27, 2019.

Reference number(s)
1815-A

3. The NCCN Clinical Practice Guidelines in Oncology® Non-Small Cell Lung Cancer Version 3.2019. National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed February 27, 2019.
4. The NCCN Clinical Practice Guidelines in Oncology® Central Nervous System Cancers Version 1.2019. ©2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 7, 2019.

Reference number(s)
1836-A

SPECIALTY GUIDELINE MANAGEMENT

AMPYRA (dalfampridine)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication: Ampyra is indicated as a treatment to improve walking in adult patients with multiple sclerosis. This was demonstrated by an increase in walking speed.

All other indications are considered experimental/investigational and are not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 30 days may be granted to members with a diagnosis of multiple sclerosis if the member has sustained walking impairment (prior to initiating therapy with Ampyra).

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted to members with multiple sclerosis if the member has experienced an improvement in walking speed or other objective measure of walking ability since starting Ampyra.

IV. REFERENCES

1. Ampyra [package insert]. Ardsley, NY: Acorda Therapeutics, Inc.; September 2017.

STEP THERAPY CRITERIA

CATEGORY	ANTIDIABETIC AGENTS
DRUG CLASS	
BRAND NAME* (generic)	<p>AMYLIN ANALOG: SYMLINPEN (pramlintide acetate)</p> <p>GLUCAGON-LIKE PEPTIDE-1 (GLP-1) RECEPTOR AGONIST: ADLYXIN (lixisenatide)</p> <p>BYDUREON (exenatide extended-release)</p> <p>BYDUREON BCISE (exenatide extended-release)</p> <p>BYETTA (exenatide)</p> <p>OZEMPIC (semaglutide)</p> <p>RYBELSUS (semaglutide)</p> <p>TANZEUM (albiglutide)</p> <p>TRULICITY (dulaglutide)</p> <p>VICTOZA (liraglutide)</p> <p>SODIUM-GLUCOSE COTRANSPORTER 2 (SGLT2) INHIBITOR: FARXIGA (dapagliflozin)</p> <p>INVOKANA (canagliflozin)</p>

JARDIANCE
(empagliflozin)

STEGLATRO
(ertugliflozin)

SGLT2 INHIBITOR / METFORMIN:

INVOKAMET
(canagliflozin / metformin HCl)

INVOKAMET XR
(canagliflozin / metformin HCl extended-release)

SEGLUROMET
(ertugliflozin / metformin HCl)

SYNJARDY
(empagliflozin / metformin HCl)

SYNJARDY XR
(empagliflozin / metformin HCl extended-release)

XIGDUO XR
(dapagliflozin / metformin HCl)

SGLT2 INHIBITOR / DIPEPTIDYL PEPTIDASE-4 (DPP-4) INHIBITOR:

GLYXAMBI
(empagliflozin / linagliptin)

QTERN
(dapagliflozin / saxagliptin)

STEGLUJAN
(ertugliflozin / sitagliptin)

SGLT2 INHIBITOR / DPP4 INHIBITOR / METFORMIN:

QTERNMET XR
(dapagliflozin / saxagliptin / metformin HCl extended-release)

TRIJARDY XR
(empagliflozin / linagliptin / metformin HCl extended-release)

LONG ACTING INSULIN/GLP-1 RECEPTOR AGONIST:

SOLIQUA

(insulin glargine / lixisenatide injection)

XULTOPHY

(insulin degludec / liraglutide injection)

Status: CVS Caremark Criteria

Type: Initial Step Therapy; Post Step Therapy Prior Authorization

Ref # 676-D

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA APPROVED INDICATIONS

AMYLIN ANALOG:

SymlinPen

SymlinPen is indicated as an adjunctive treatment in patients with type 1 or type 2 diabetes who use mealtime insulin therapy and who have failed to achieve desired glucose control despite optimal insulin therapy.

GLP-1 RECEPTOR AGONIST:

Adlyxin

Adlyxin is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use

- Adlyxin has not been studied in patients with chronic pancreatitis or a history of unexplained pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.
- Adlyxin is not a substitute for insulin. Adlyxin is not indicated for use in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis.
- The concurrent use of Adlyxin with short acting insulin has not been studied and is not recommended.
- Adlyxin has not been studied in patients with gastroparesis and is not recommended in patients with gastroparesis.

Bydureon/Bydureon BCise

Bydureon and Bydureon BCise are indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use

- Bydureon/Bydureon BCise are not recommended as first-line therapy for patients who have inadequate glycemic control on diet and exercise because of the uncertain relevance of the rat thyroid C-cell tumor findings to humans.
- Bydureon/Bydureon BCise are not a substitute for insulin. Bydureon/Bydureon BCise should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis, as it would not be effective in these settings.
- The concurrent use of Bydureon/Bydureon BCise with insulin has not been studied.
- Bydureon/Bydureon BCise are extended-release formulations of exenatide. Bydureon/Bydureon BCise should not be used with other products containing the active ingredient exenatide.
- Bydureon/Bydureon BCise have not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.

Byetta

Byetta (exenatide) is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use

- Byetta is not a substitute for insulin. Byetta should not be used for the treatment of type 1 diabetes or diabetic ketoacidosis, as it would not be effective in these settings.
- The concurrent use of Byetta with prandial insulin has not been studied and cannot be recommended.
- Based on postmarketing data Byetta has been associated with acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis. Byetta has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at increased risk for pancreatitis while using Byetta. Other antidiabetic therapies should be considered in patients with a history of pancreatitis.

Ozempic

Ozempic is indicated:

- as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus
- to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction or non-fatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease

Limitations of Use

- Ozempic has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.
- Ozempic is not a substitute for insulin. Ozempic is not indicated for use in patients with type 1 diabetes mellitus or for the treatment of patients with diabetic ketoacidosis, as it would not be effective in these settings.

Rybelsus

Rybelsus is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use

- Rybelsus is not recommended as a first-line therapy for patients who have inadequate glycemic control on diet and exercise because of the uncertain relevance of rodent C-cell tumor findings to humans
- Rybelsus has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis
- Rybelsus is not indicated for use in patients with type 1 diabetes mellitus or for the treatment of patients with diabetic ketoacidosis, as it would not be effective in these settings.

Tanzeum

Tanzeum is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use

- Tanzeum is not recommended as first-line therapy for patients inadequately controlled on diet and exercise because of the uncertain relevance of the rodent C-cell tumor findings to humans. Prescribe Tanzeum only to patients for whom the potential benefits are considered to outweigh the potential risk.
- Tanzeum has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.
- Tanzeum is not indicated in the treatment of patients with type 1 diabetes mellitus or for the treatment of patients with diabetic ketoacidosis. Tanzeum is not a substitute for insulin in these patients.
- Tanzeum has not been studied in patients with severe gastrointestinal disease, including severe gastroparesis. The use of Tanzeum is not recommended in patients with pre-existing severe gastrointestinal disease.
- Tanzeum has not been studied in combination with prandial insulin.

Trulicity

Trulicity is indicated:

- as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
- to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus who have established cardiovascular disease or multiple cardiovascular risk factors.

Limitations of Use

- Trulicity has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.
- Trulicity should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis. Trulicity is not a substitute for insulin.
- Trulicity has not been studied in patients with severe gastrointestinal disease, including severe gastroparesis. The use of Trulicity is not recommended in patients with pre-existing severe gastrointestinal disease.

Victoza

Victoza is indicated:

- as an adjunct to diet and exercise to improve glycemic control in patients 10 years and older with type 2 diabetes mellitus
- to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease

Limitations of Use

- Victoza should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis, as it would not be effective in these settings.

- The concurrent use of Victoza and prandial insulin has not been studied.

SGLT2 INHIBITOR:

Farxiga

Farxiga (dapagliflozin) is indicated:

- as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus
- to reduce the risk of hospitalization for heart failure in adults with type 2 diabetes mellitus and established cardiovascular disease (CVD) or multiple cardiovascular (CV) risk factors

Limitation of Use

Farxiga is not recommended for patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis.

Invokana

Invokana (canagliflozin) is indicated:

- as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
- to reduce the risk of major adverse cardiovascular events (cardiovascular death, nonfatal myocardial infarction and nonfatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease (CVD).
- to reduce the risk of end-stage kidney disease (ESKD), doubling of serum creatinine, cardiovascular (CV) death, and hospitalization for heart failure in adults with type 2 diabetes mellitus and diabetic nephropathy with albuminuria > 300 mg/day.

Limitations of Use

Invokana is not recommended in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis.

Jardiance

Jardiance is indicated:

- as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus,
- to reduce the risk of cardiovascular death in adult patients with type 2 diabetes mellitus and established cardiovascular disease

Limitation of Use

Jardiance is not recommended for patients with type 1 diabetes or for the treatment of diabetic ketoacidosis.

Steglatro

Steglatro is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use

Steglatro is not recommended in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis.

SGLT2 INHIBITOR / METFORMIN:

Invokamet, Invokamet XR

Invokamet and Invokamet XR are a combination of canagliflozin and metformin hydrochloride (HCl) indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both canagliflozin and metformin HCl is appropriate.

Canagliflozin is indicated to reduce the risk of major adverse cardiovascular events (cardiovascular death, nonfatal myocardial infarction and nonfatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease (CVD). However, the effectiveness of Invokamet/Invokamet XR on reducing major cardiovascular events in adults with type 2 diabetes and cardiovascular disease has not been established.

Limitations of Use

Not recommended in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis.

Segluromet

Segluromet is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus who are not adequately controlled on a regimen containing ertugliflozin or metformin, or in patients who are already treated with both ertugliflozin and metformin.

Limitations of Use

Segluromet is not recommended in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis.

Synjardy, Synjardy XR

Synjardy and Synjardy XR are a combination of empagliflozin and metformin hydrochloride indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both empagliflozin and metformin is appropriate. Empagliflozin is indicated to reduce the risk of cardiovascular death in adults with type 2 diabetes mellitus and established cardiovascular disease. However, the effectiveness of Synjardy/Synjardy XR on

reducing the risk of cardiovascular death in adults with type 2 diabetes mellitus and cardiovascular disease has not been established.

Limitation of Use

Synjardy/Synjardy XR is not recommended for patients with type 1 diabetes or for the treatment of diabetic ketoacidosis.

Xigduo XR

Xigduo XR (dapagliflozin and metformin HCl extended-release) is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both dapagliflozin and metformin is appropriate.

Limitation of Use

Xigduo XR is not recommended for patients with type 1 diabetes mellitus or diabetic ketoacidosis.

SGLT2 INHIBITOR / DPP-4 INHIBITOR:

Glyxambi

Glyxambi is a combination of empagliflozin and linagliptin indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both empagliflozin and linagliptin is appropriate.

Empagliflozin is indicated to reduce the risk of cardiovascular death in adults with type 2 diabetes mellitus and established cardiovascular disease. However, the effectiveness of Glyxambi on reducing the risk of cardiovascular death in adults with type 2 diabetes mellitus and cardiovascular disease has not been established.

Limitations of Use

- Glyxambi is not recommended for patients with type 1 diabetes or for the treatment of diabetic ketoacidosis.
- Glyxambi has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at an increased risk for the development of pancreatitis while using Glyxambi.

Qtern

Qtern (dapagliflozin and saxagliptin) is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use

Qtern is not indicated for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis.

Steglujan

Steglujan is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both ertugliflozin and sitagliptin is appropriate.

Limitations of Use

Steglujan is not recommended in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis. Steglujan has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at increased risk for the development of pancreatitis while using Steglujan.

SGLT2 INHIBITOR / DPP-4 INHIBITOR / METFORMIN:

Qternmet XR

Qternmet XR (dapagliflozin, saxagliptin, and metformin hydrochloride) extended-release tablets is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use

Qternmet XR is not indicated for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis.

Qternmet XR initiation is intended only for patients currently taking metformin.

Trijardy XR

Trijardy XR is a combination of empagliflozin, linagliptin, and metformin hydrochloride (HCl) indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use

Trijardy XR is not recommended for patients with type 1 diabetes or for the treatment of diabetic ketoacidosis.

Trijardy XR has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at an increased risk for the development of pancreatitis while using Trijardy XR.

LONG ACTING INSULIN / GLP-1 RECEPTOR AGONIST:

Soliqua

Soliqua 100/33 is a combination of insulin glargine and lixisenatide and is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use:

- Soliqua 100/33 has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis
- Soliqua 100/33 is not recommended for use in combination with any other product containing a
- GLP-1 receptor agonist
- Soliqua 100/33 is not indicated for use in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis
- Soliqua 100/33 has not been studied in patients with gastroparesis and is not recommended in patients with gastroparesis
- Soliqua 100/33 has not been studied in combination with prandial insulin

Xultophy

Xultophy 100/3.6 is a combination of insulin degludec and liraglutide and is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use:

- Xultophy 100/3.6 is not recommended as first-line therapy for patients who have inadequate glycemic control on diet and exercise because of the uncertain relevance of the rodent C-cell tumor findings to humans
- Xultophy 100/3.6 is not recommended for use in combination with any other product containing liraglutide or another GLP-1 receptor agonist
- Xultophy 100/3.6 is not indicated for use in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis
- Xultophy 100/3.6 has not been studied in combination with prandial insulin

INITIAL STEP THERAPY*

**Include Rx and OTC products unless otherwise stated.*

INITIAL STEP THERAPY For AMYLIN ANALOGS (SymlinPen):

If the patient has filled a prescription for at least a 30 day supply of a rapid-acting insulin or short-acting insulin or pre-mixed insulin [e.g., insulin aspart (Novolog), insulin glulisine (Apidra), insulin lispro (Humalog), insulin regular R (Afrezza, Humulin R, Novolin R)] within the past 120 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit. If the patient does not meet the initial step therapy criteria, then the system will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

INITIAL STEP THERAPY For GLP-1 RECEPTOR AGONISTS, SGLT2 INHIBITORS, COMBINATIONS:

If the patient has filled a prescription for at least a 30 day supply of metformin within the past 180 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit. If the patient does not meet the initial step therapy criteria, then the system will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has been receiving the requested drug for at least 3 months **AND**
 - The patient has demonstrated a reduction in A1c (hemoglobin A1c) since starting this therapy
OR
 - The request is for Farxiga (dapagliflozin), Invokana (canagliflozin), Jardiance (empagliflozin), Ozempic (semaglutide), Trulicity (dulaglutide), or Victoza (liraglutide) **AND** the patient has established cardiovascular disease
OR
 - The request is for Invokana (canagliflozin) **AND** the patient has diabetic nephropathy with albuminuria greater than 300 mg per day
OR

- The request is for Farxiga (dapagliflozin) or Trulicity (dulaglutide) AND the patient has multiple cardiovascular risk factors

OR

- The request is for SymlinPen (pramlintide acetate) **AND**
 - The patient has a diagnosis of diabetes mellitus AND has failed to achieve desired glucose control despite receiving optimal insulin therapy, including mealtime insulin

OR

- The patient has a diagnosis of type 2 diabetes mellitus **AND**
 - The patient experienced an inadequate treatment response, intolerance, or contraindication to metformin

OR

- The patient requires combination therapy AND has an A1c (hemoglobin A1c) of 7.5 percent or greater

OR

- The request is for Farxiga (dapagliflozin), Invokana (canagliflozin), Jardiance (empagliflozin), Ozempic (semaglutide), Trulicity (dulaglutide), or Victoza (liraglutide) AND the patient has established cardiovascular disease

OR

- The request is for Invokana (canagliflozin) AND the patient has diabetic nephropathy with albuminuria greater than 300 mg per day

OR

- The request is for Farxiga (dapagliflozin) or Trulicity (dulaglutide) AND the patient has multiple cardiovascular risk factors

RATIONALE

For Amylin Analogs (SymlinPen), if the patient has filled a prescription for at least a 30 day supply of a rapid-acting insulin or short-acting insulin or premixed insulin [e.g., insulin aspart (Novolog), insulin glulisine (Apidra), insulin lispro (Humalog), insulin regular R (Afrezza, Humulin R, Novolin R)] within the past 120 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.

For GLP-1 (glucagon-like peptide-1) receptor agonists, SGLT2 (sodium-glucose cotransporter 2) Inhibitors, and Combinations, if the patient has filled a prescription for at least a 30 day supply of metformin within the past 180 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.

If the patient does not meet the initial step therapy criteria, then prior authorization is required.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Adlyxin (lixisenatide), Bydureon/Bydureon BCise (exenatide extended-release), Byetta (exenatide), Farxiga (dapagliflozin), Glyxambi (empagliflozin/linagliptin), Invokana (canagliflozin), Invokamet (canagliflozin/metformin), Invokamet XR (canagliflozin/metformin extended-release), Jardiance (empagliflozin), Ozempic (semaglutide), Qtern (dapagliflozin/saxagliptin), Qternmet XR (dapagliflozin/saxagliptin/metformin extended-release), Rybelsus (semaglutide), Segluromet (ertugliflozin /metformin), Steglatro (ertugliflozin), Steglujan (ertugliflozin/ sitagliptin), Synjardy (empagliflozin/metformin), Synjardy XR (empagliflozin/metformin extended-release), Tanzeum (albiglutide), Trijardy XR (empagliflozin/linagliptin/metformin extended-release) Trulicity (dulaglutide), Victoza (liraglutide), and Xigduo XR (dapagliflozin and metformin extended-release) are indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes.

Farxiga (dapagliflozin) is also indicated to reduce the risk of hospitalization for heart failure in adults with type 2 diabetes mellitus and established cardiovascular disease or multiple cardiovascular risk factors.

Invokana (canagliflozin) is also indicated to reduce the risk of major adverse cardiovascular events (cardiovascular death, nonfatal myocardial infarction and nonfatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease (CVD); and to reduce the risk of end-stage kidney disease (ESKD), doubling of serum creatinine, cardiovascular (CV) death, and hospitalization for heart failure in adults with type 2 diabetes mellitus and diabetic nephropathy with

albuminuria > 300 mg/day. However, the effectiveness of canagliflozin combination products such as Invokamet and Invokamet XR for these indications has not been established.

Jardiance (empagliflozin) is also indicated to reduce the risk of cardiovascular death in adults with type 2 diabetes mellitus and established cardiovascular disease. However, the effectiveness of empagliflozin combination products such as Glyxambi, Synjardy, and Synjardy XR on reducing the risk of cardiovascular death in adults with type 2 diabetes mellitus and cardiovascular disease has not been established.

Ozempic (semaglutide) is also indicated to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction or non-fatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease.

Trulicity (dulaglutide) is also indicated to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus who have established cardiovascular disease or multiple cardiovascular risk factors.

Victoza (liraglutide) is also indicated to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease.

SymlinPen (pramlintide acetate) is indicated as an adjunctive treatment in patients with type 1 or type 2 diabetes who use mealtime insulin therapy and who have failed to achieve desired glucose control despite optimal insulin therapy.

Soliqua (insulin glargine and lixisenatide) is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. The recommended starting doses are determined based on the following: patients naïve to basal insulin or GLP-1 receptor agonist; patients currently on a GLP-1 receptor agonist; patients currently on less than 30 units of basal insulin daily; patients currently on 30-60 units of basal insulin, with or without a GLP-1 receptor agonist.

Xultophy (insulin degludec and liraglutide) is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. The recommended starting doses are determined based on the following: patients naïve to basal insulin or GLP-1 receptor agonist; patients currently on basal insulin or a GLP-1 receptor agonist.

Clinical guidelines from the American Diabetes Association and the American Association of Clinical Endocrinologists and American College of Endocrinology for the management of hyperglycemia in type 2 diabetes indicate that metformin monotherapy should be started at diagnosis of type 2 diabetes unless there are contraindications. Metformin is effective and safe, is inexpensive, and may reduce risk of cardiovascular events and death. In patients with contraindications or intolerance of metformin, initial therapy should be based on patient factors; consider a drug from another class.^{27, 28}

The clinical guidelines also state that the A1c test is the major tool for assessing glycemic control and has strong predictive value for diabetes complications. Thus, A1c testing should be performed routinely in all patients with diabetes at initial assessment and as part of continuing care.²⁷ The guidelines set goals for therapeutic effectiveness which must be evaluated frequently (e.g., every 3 months) until stable, using multiple criteria, including A1c. Less frequent monitoring is acceptable once targets are achieved.^{27, 28}

If the A1c target is not achieved after approximately 3 months and patient does not have atherosclerotic cardiovascular disease (ASCVD) or chronic kidney disease (CKD), consider a combination of metformin and one of the preferred six treatment options: sulfonylurea, thiazolidinedione, dipeptidyl peptidase 4 (DPP-4) inhibitors, SGLT2 inhibitors, GLP-1 receptor agonists, or basal insulin; the choice of which agent to add is based on drug-specific effects and patient factors. For patients in whom ASCVD, Heart Failure, or CKD predominates, the best choice for a second agent is a GLP-1 receptor agonist or SGLT2 inhibitor with demonstrated cardiovascular risk reduction, after consideration of drug-specific and patient factors.^{27, 28}

In patients with an initial A1c of 7.5% or greater, or in patients who are unable to achieve their glycemic goals with monotherapy, combination therapy is recommended.²⁸ Add-on therapy clinical studies with dapagliflozin plus saxagliptin in

patients on metformin (i.e., Qternmet XR) were conducted – in one study (24-week randomized, double-blind, active-controlled, parallel group study in patients with an HbA1c $\geq 7.5\%$ and $\leq 10.0\%$) patients were on a stable dose of metformin HCl (≥ 1500 mg per day) for at least 8 weeks prior to being randomized to one of three double-blind treatment groups to receive 5 mg dapagliflozin and 5 mg saxagliptin added to metformin, 5 mg saxagliptin and placebo added to metformin, or 5 mg dapagliflozin and placebo added to metformin. At Week 24, concomitant addition of 5 mg dapagliflozin and 5 mg saxagliptin plus metformin resulted in statistically significant decreases in HbA1c, and a larger proportion of patients achieving the therapeutic glycemic goal of HbA1c $< 7\%$, compared to dapagliflozin plus metformin or saxagliptin plus metformin.¹² An add-on therapy clinical study with empagliflozin and linagliptin in patients on metformin (i.e., Trijardy XR) was conducted - the double-blind, active-controlled study evaluated the efficacy and safety of empagliflozin 10 mg or 25 mg in combination with linagliptin 5 mg, compared to the individual components. Patients with type 2 diabetes inadequately controlled on at least 1500 mg of metformin per day entered a single-blind placebo run-in period for 2 weeks. At the end of the run-in period, patients who remained inadequately controlled and had an HbA1c between 7 and 10.5% were randomized to one of 5 active-treatment arms of empagliflozin 10 mg or 25 mg, linagliptin 5 mg, or linagliptin 5 mg in combination with 10 mg or 25 mg empagliflozin as a fixed dose combination tablet. At Week 24, empagliflozin 10 mg or 25 mg used in combination with linagliptin 5 mg provided statistically significant improvement in HbA1c (p-value < 0.0001) and FPG (p-value < 0.001) compared to the individual components in patients who had been inadequately controlled on metformin.³¹ Additionally, the combination of basal insulin with a GLP1 receptor agonist (i.e., Soliqua, Xultophy) may offer greater efficacy than the oral agents.²⁸ This combination also has potent glucose lowering actions and less weight gain and hypoglycemia compared with intensified insulin regimens.²⁷

Invokana (canagliflozin), Jardiance (empagliflozin), Ozempic (semaglutide), and Victoza (liraglutide) will be approved for initial therapy and continuation of therapy for type 2 diabetes mellitus patients who have established cardiovascular disease per the following: The CANVAS and CANVAS-R trials compared the risk of Major Adverse Cardiovascular Event (MACE) between canagliflozin and placebo when these were added to and used concomitantly with standard of care treatments for diabetes and atherosclerotic cardiovascular disease. Concomitant antidiabetic and atherosclerotic therapies could be adjusted, at the discretion of investigators, to ensure participants were treated according to standard of care for these diseases.⁷ The EMPA-REG OUTCOME study compared the risk of experiencing a MACE between empagliflozin and placebo. Coadministered antidiabetic medications were to be kept stable for the first 12 weeks of the trial. Thereafter, antidiabetic and atherosclerotic therapies could be adjusted, at the discretion of investigators, to ensure participants were treated according to the standard of care for these diseases.⁹ The SUSTAIN 6 trial compared the risk of Major Adverse Cardiovascular Event (MACE) between semaglutide and placebo when these were added to and used concomitantly with standard of care treatments for diabetes and cardiovascular disease.¹⁰ In the LEADER trial, patients with inadequately controlled type 2 diabetes and atherosclerotic cardiovascular disease were randomized to liraglutide 1.8 mg or placebo. During the trial, investigators could modify anti-diabetic and cardiovascular medications to achieve local standard of care treatment targets with respect to blood glucose, lipid, and blood pressure.²²

Farxiga (dapagliflozin) and Trulicity (dulaglutide) will be approved for initial therapy and continuation of therapy for type 2 diabetes mellitus patients who have established cardiovascular disease or multiple cardiovascular risk factors per the following: The DECLARE trial compared the effect of dapagliflozin 10mg relative to placebo on cardiovascular outcomes when added to current background therapy. Concomitant antidiabetic and atherosclerotic therapies could be adjusted, at the discretion of the investigators, to ensure participants were treated according to the standard of care for these diseases.⁵ The REWIND trial compared the risk of Major Adverse Cardiovascular Events (MACE) outcome (which included CV death, non-fatal myocardial infarction (MI), and non-fatal stroke) between Trulicity 1.5 mg and placebo, both added to standard of care. During the trial, investigators were to modify antidiabetic and cardiovascular medications to achieve local standard of care treatment targets with respect to blood glucose, lipids, and blood pressure, and manage patients recovering from an acute coronary syndrome or stroke event per local treatment guidelines.²¹

Invokana (canagliflozin) will also be approved for initial therapy and continuation of therapy for type 2 diabetes mellitus patients who have diabetes with established nephropathy per the following: The CREDENCE trial compared canagliflozin with placebo in patients with type 2 diabetes mellitus, an estimated glomerular filtration rate ≥ 30 to < 90 mL/min/1.73 m² and albuminuria (urine albumin/creatinine > 300 to ≤ 5000 mg/g) who were receiving standard of care including a maximum-tolerated, labeled daily dose of an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker. Patients were randomized to receive canagliflozin 100 mg or placebo and treatment was continued until the initiation of dialysis or renal transplantation.⁸ The use of other background therapy for glycemic management and control of cardiovascular risk factors was recommended in accordance with local guidelines.³⁰

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Reviewed: Medical Affairs: (KP) 06/2011, 02/2012, 08/2012; (LS) 05/2013; (LCB) 12/2013, (LMS) 07/2014, (DR) 08/2014, (MM) 08/2014, (SES) 09/2014; (AD) 03/2015, (DC) 07/2015, (ADA) 08/2015, (AD) 10/2015; (ME) 07/2016, 12/2016, 01/2017, (DNC) 03/2017; (SD) 07/2017; (MC) 09/2017; (AN) 12/2017; (GAD) 12/2017; (EPA) 01/2018; (ME) 07/2018, 11/2018; (MCM) 05/2019; (CHART) 08/01/2019, (CHART) 09/26/2019, (CHART) 10/03/2019, (CHART) 11/21/2019, 02/06/2020, 03/12/2020

External Review: 08/2011, 04/2012, 10/2012, 08/2013, 02/2014, 08/2014, 10/2014, 10/2015, 08/2016, 02/2017, 10/2017, 02/2018, 10/2018, 12/2018, 06/2019, 10/2019, 12/2019 (FYI), 02/2020 (FYI), 04/2020 (FYI)

CRITERIA FOR APPROVAL

1	Has the patient been receiving the requested drug for at least 3 months? [If no, then skip to question 4.]	Yes	No
2	Has the patient demonstrated a reduction in A1c (hemoglobin A1c) since starting this therapy? [If yes, then no further questions.]	Yes	No
3	Is this request for Farxiga (dapagliflozin), Invokana (canagliflozin), Jardiance (empagliflozin), Ozempic (semaglutide), Trulicity (dulaglutide), or Victoza (liraglutide)? [If yes, then skip to question 9.] [If no, then no further questions.]	Yes	No
4	Is this request for SymlinPen (pramlintide acetate)? [If yes, then skip to question 14.]	Yes	No
5	Does the patient have a diagnosis of type 2 diabetes mellitus?	Yes	No
6	Has the patient experienced an inadequate treatment response, intolerance, or contraindication to metformin? [If yes, then no further questions.]	Yes	No
7	Does the patient require combination therapy AND have an A1c (hemoglobin A1c) of 7.5 percent or greater? [If yes, then no further questions.]	Yes	No
8	Is this request for Farxiga (dapagliflozin), Invokana (canagliflozin), Jardiance (empagliflozin), Ozempic (semaglutide), Trulicity (dulaglutide), or Victoza (liraglutide)?	Yes	No
9	Does the patient have established cardiovascular disease? [If yes, then no further questions.]	Yes	No
10	Is this request for Invokana (canagliflozin)? [If no, then skip to question 12.]	Yes	No
11	Does the patient have diabetic nephropathy with albuminuria greater than 300 mg per day? [No further questions.]	Yes	No
12	Is this request for Farxiga (dapagliflozin) or Trulicity (dulaglutide)?	Yes	No
13	Does the patient have multiple cardiovascular risk factors? [No further questions.]	Yes	No
14	Does the patient have a diagnosis of diabetes mellitus?	Yes	No
15	Has the patient failed to achieve desired glucose control despite receiving optimal insulin therapy, including mealtime insulin?	Yes	No

Mapping Instructions

	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Go to 4	
2.	Approve, 36 months	Go to 3	
3.	Go to 9	Deny	<p>You do not meet the requirements of your plan.</p> <p>Your plan covers this drug when you meet these conditions:</p> <ul style="list-style-type: none"> - You have been taking the requested drug for at least 3 months - You had a reduction in A1c (hemoglobin A1c) since starting this therapy <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No response to treatment]</p>
4.	Go to 14	Go to 5	
5.	Go to 6	Deny	<p>You do not meet the requirements of your plan.</p> <p>Your plan covers this drug when you have type 2 diabetes mellitus.</p> <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No approvable diagnosis]</p>
6.	Approve, 36 months	Go to 7	
7.	Approve, 36 months	Go to 8	
8.	Go to 9	Deny	<p>You do not meet the requirements of your plan.</p> <p>Your plan covers this drug when you meet any of these conditions:</p> <ul style="list-style-type: none"> - You have tried metformin and it did not work for you, or you cannot use it - You require combination therapy and you have an A1c (hemoglobin A1c) of 7.5 percent or greater <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No inadequate response, intolerance or contraindication to metformin, No combination therapy requirement]</p>
9.	Approve, 36 months	Go to 10	
10.	Go to 11	Go to 12	
11.	Approve, 36 months	Deny	<p>You do not meet the requirements of your plan.</p> <p>Your plan covers this drug when you meet any of these conditions:</p> <ul style="list-style-type: none"> - You have been taking the requested drug for at least 3 months and you had a reduction in A1c (hemoglobin A1c) since starting this therapy - You have tried metformin and it did not work for you, or you cannot use it - You require combination therapy and you have an A1c (hemoglobin A1c) of 7.5 percent or greater - You have cardiovascular (heart) disease - You have diabetic nephropathy (kidney disease) with albuminuria greater than 300 mg per day <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No response to treatment, No inadequate response, intolerance or contraindication to metformin, No combination therapy requirement, No established CV disease or diabetic nephropathy with albuminuria greater than 300 mg/day for Invokana]</p>
12.	Go to 13	Deny	<p>You do not meet the requirements of your plan.</p> <p>Your plan covers this drug when you meet any of these conditions:</p> <ul style="list-style-type: none"> - You have been taking the requested drug for at least 3 months and you had a reduction in A1c (hemoglobin A1c) since

			<p>starting this therapy</p> <ul style="list-style-type: none"> - You have tried metformin and it did not work for you, or you cannot use it - You require combination therapy and you have an A1c (hemoglobin A1c) of 7.5 percent or greater - You have cardiovascular (heart) disease <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No response to treatment, No inadequate response, intolerance or contraindication to metformin, No combination therapy requirement, No CV disease for Jardiance, Ozempic, Victoza]</p>
13.	Approve, 36 months	Deny	<p>You do not meet the requirements of your plan.</p> <p>Your plan covers this drug when you meet any of these conditions:</p> <ul style="list-style-type: none"> - You have been taking the requested drug for at least 3 months and you had a reduction in A1c (hemoglobin A1c) since starting this therapy - You have tried metformin and it did not work for you, or you cannot use it - You require combination therapy and you have an A1c (hemoglobin A1c) of 7.5 percent or greater - You have cardiovascular (heart) disease - You have multiple cardiovascular risk factors <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No response to treatment, No inadequate response, intolerance or contraindication to metformin, No combination therapy requirement, No CV disease or multiple CV risk factors for Farxiga, Trulicity]</p>
14.	Go to 15	Deny	<p>You do not meet the requirements of your plan.</p> <p>Your plan covers this drug when you have diabetes mellitus.</p> <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No approvable diagnosis]</p>
15.	Approve, 36 months	Deny	<p>You do not meet the requirements of your plan.</p> <p>Your plan covers this drug when you meet these conditions:</p> <ul style="list-style-type: none"> - You receive optimal insulin treatment - Your treatment includes mealtime insulin - You have not achieved desired glucose control <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No approvable diagnosis]</p>

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	ANTIEMETIC AGENTS – 5HT3 ANTAGONISTS
BRAND NAME* (generic)	ALOXI INJECTION (palonosetron hydrochloride) ANZEMET (dolasetron mesylate) (granisetron hydrochloride) (ALL PRODUCTS) (palonosetron hydrochloride injection) SANCUSO (granisetron transdermal system) SUSTOL (granisetron extended-release injection) ZOFRAN (ALL DOSAGE FORMS) (ondansetron, ondansetron hydrochloride) ZUPLENZ (ondansetron oral soluble film)
Status: CVS Caremark Criteria Type: Post Limit Prior Authorization	
Ref # 16-J	

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Aloxi Injection

Chemotherapy-Induced Nausea and Vomiting in Adults

Aloxi is indicated for:

- Moderately emetogenic cancer chemotherapy - prevention of acute and delayed nausea and vomiting associated with initial and repeat courses
- Highly emetogenic cancer chemotherapy - prevention of acute nausea and vomiting associated with initial and repeat courses

Chemotherapy-Induced Nausea and Vomiting in Pediatric Patients Aged 1 Month to Less than 17 Years

Aloxi is indicated for prevention of acute nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy, including highly emetogenic cancer chemotherapy.

Postoperative Nausea and Vomiting in Adults

Aloxi is indicated for prevention of postoperative nausea and vomiting (PONV) for up to 24 hours following surgery.

Efficacy beyond 24 hours has not been demonstrated.

As with other antiemetics, routine prophylaxis is not recommended in patients in whom there is little expectation that nausea and/or vomiting will occur postoperatively. In patients where nausea and vomiting must be avoided during the postoperative period, Aloxi is recommended even where the incidence of postoperative nausea and/or vomiting is low.

Anzemet Tablets

Anzemet tablets are indicated for the prevention of nausea and vomiting associated with moderately emetogenic cancer chemotherapy, including initial and repeat courses in adults and children 2 years and older.

Granisetron

Granisetron Tablets

Granisetron Hydrochloride Tablets are indicated for the prevention of:

- Nausea and vomiting associated with initial and repeat courses of emetogenic cancer therapy, including high-dose cisplatin.
- Nausea and vomiting associated with radiation, including total body irradiation and fractionated abdominal radiation.

Granisetron Injection:

Granisetron Hydrochloride Injection is a serotonin-3 (5-HT₃) receptor antagonist indicated for:

- The prevention of nausea and/or vomiting associated with initial and repeat courses of emetogenic cancer therapy, including high-dose cisplatin.

Ondansetron Injection

Prevention of Nausea and Vomiting Associated with Initial and Repeat Courses of Emetogenic Cancer Chemotherapy

Ondansetron Injection is indicated for the prevention of nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy, including high-dose cisplatin. Ondansetron is approved for patients aged 6 months and older.

Prevention of Postoperative Nausea and/or Vomiting

Ondansetron Injection is indicated for the prevention of postoperative nausea and/or vomiting. As with other antiemetics, routine prophylaxis is not recommended for patients in whom there is little expectation that nausea and/or vomiting will occur postoperatively. In patients in whom nausea and/or vomiting must be avoided postoperatively, ondansetron injection is recommended even when the incidence of postoperative nausea and/or vomiting is low. For patients who do not receive prophylactic ondansetron injection and experience nausea and/or vomiting postoperatively, ondansetron injection may be given to prevent further episodes. Ondansetron is approved for patients aged 1 month and older.

Palonosetron Hydrochloride Injection

Chemotherapy-Induced Nausea and Vomiting in Adults

Palonosetron Hydrochloride (HCl) Injection is indicated for:

- Moderately emetogenic cancer chemotherapy - prevention of acute and delayed nausea and vomiting associated with initial and repeat courses
- Highly emetogenic cancer chemotherapy - prevention of acute nausea and vomiting associated with initial and repeat courses

Sancuso Transdermal System

Sancuso (granisetron transdermal system) is indicated for the prevention of nausea and vomiting in patients receiving moderately and/or highly emetogenic chemotherapy regimens of up to 5 consecutive days duration.

Sustol Extended-Release Injection

Sustol is indicated in combination with other antiemetics in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic chemotherapy (MEC) or anthracycline and cyclophosphamide (AC) combination chemotherapy regimens.

Zofran Tablets, Zofran ODT, and Zofran Oral Solution

Zofran is indicated for the prevention of nausea and vomiting associated with:

- highly emetogenic cancer chemotherapy, including cisplatin greater than or equal to 50 mg/m².
- initial and repeat courses of moderately emetogenic cancer chemotherapy.
- radiotherapy in patients receiving either total body irradiation, single high-dose fraction to the abdomen, or daily fractions to the abdomen.

Zofran is also indicated for the prevention of postoperative nausea and/or vomiting.

Zuplenz

Prevention of Nausea and Vomiting Associated with Highly Emetogenic Cancer Chemotherapy

Zuplenz (ondansetron) oral soluble film is indicated for the prevention of nausea and vomiting associated with highly emetogenic cancer chemotherapy, including cisplatin ≥ 50 mg/m²

Prevention of Nausea and Vomiting Associated with Moderately Emetogenic Cancer Chemotherapy

Zuplenz is indicated for the prevention of nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy

Prevention of Nausea and Vomiting Associated with Radiotherapy

Zuplenz is indicated for the prevention of nausea and vomiting associated with radiotherapy in patients receiving either total body irradiation, single high-dose fraction to the abdomen, or daily fractions to the abdomen

Prevention of Postoperative Nausea and/or Vomiting

Zuplenz is indicated for the prevention of postoperative nausea and/or vomiting. As with other antiemetics, routine prophylaxis is not recommended for patients in whom there is little expectation that nausea and/or vomiting will occur postoperatively. In patients where nausea and/or vomiting must be avoided postoperatively, Zuplenz is recommended even where the incidence of postoperative nausea and/or vomiting is low.

Compendial Uses:

- Treatment and/or prophylaxis of radiation-induced nausea and vomiting.¹²

Compendial Use Ondansetron Only:

- Hyperemesis Gravidarum^{12,13}

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient is receiving radiation therapy or moderate to highly emetogenic chemotherapy.

OR

- The request is for Zofran, Zuplenz or ondansetron **AND**
- The patient is pregnant with the diagnosis of Hyperemesis Gravidarum and a documented risk for hospitalization **AND**
- The patient has experienced an inadequate treatment response, intolerance, or contraindication to two of the following medications: A) vitamin B6, B) vitamin B6 in combination with doxylamine, C) doxylamine/pyridoxine extended-release (Bonjesta), D) doxylamine/pyridoxine delayed-release (Diclegis), E) promethazine (Phenergan), F) trimethobenzamide (Tigan), G) metoclopramide (Reglan), H) diphenhydramine (Benadryl), I) dimenhydrinate (Dramamine)

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. 5HT-3 antiemetics are indicated for chemotherapy induced nausea and vomiting (CINV). Aloxi, Zofran tablets, ondansetron injection and Zuplenz are also indicated for postoperative nausea and vomiting (PONV). Granisetron tablets, Zofran tablets, ondansetron injection and Zuplenz are also indicated for nausea and vomiting associated with radiotherapy. Some 5HT-3 antiemetics also have compendial support for treatment and/or prophylaxis of radiation-induced nausea and vomiting.¹² Zofran, Zuplenz, and ondansetron have compendial support for use in hyperemesis gravidarum.^{12,13}

The National Comprehensive Cancer Network (NCCN) Guidelines state that the risk of nausea and vomiting for persons receiving chemotherapy of high and moderate emetic risk lasts for at least 3 days for high and 2 days for moderate after the last dose of chemotherapy. Patients need to be protected throughout the full period of risk.¹⁴ The recommended dosing parameters for the prevention of postoperative nausea and vomiting fall within the initial limits.

Patients receiving multiday chemotherapy are at risk for both acute and delayed nausea/vomiting based on the emetogenic potential of the individual chemotherapy agents administered on any given day and their sequence. Acute and delayed emesis may overlap after the initial day of chemotherapy until the last day of chemotherapy. The period of risk for delayed emesis after chemotherapy administration has concluded also depends on the specific regimen and the emetogenic potential of the last chemotherapy agent administered in the regimen. Antiemetic regimens should be chosen based on the drug with the highest emetic risk in the chemotherapy regimen, previous experience with antiemetics, and patient-specific risk factors.¹⁴

The NCCN has also made recommendations for use of antiemetics for radiation-induced emesis. Prophylaxis for radiation-induced nausea and/or vomiting is based on the site of radiation and whether the radiation is combined with anticancer therapy.¹⁴ The American Society of Clinical Oncology recommends that all patients should receive a 5-HT3 antagonist (granisetron and ondansetron are preferred) before each fraction of moderately to highly emetogenic radiation therapy.¹⁵

Hyperemesis gravidarum is the most common indication for admission to the hospital during the first part of pregnancy and is second only to preterm labor as the most common reason for hospitalization during pregnancy. For a diagnosis of hyperemesis gravidarum (HG), the intent is to allow a quantity of ondansetron above the current initial limit allowed for patients with a documented risk for hospitalization who have had an inadequate treatment response, intolerance, or contraindication to two of the following medications: vitamin B6, vitamin B6 in combination with doxylamine, doxylamine/pyridoxine extended-release (Bonjesta), doxylamine/pyridoxine delayed-release (Diclegis), promethazine (Phenergan), trimethoprim (Tigan), metoclopramide (Reglan), diphenhydramine (Benadryl), dimenhydrinate (Dramamine). Evidence is limited on the safety or efficacy of ondansetron for nausea and vomiting of pregnancy. However, because of its effectiveness in reducing chemotherapy-induced emesis, its use appears to be increasing.¹³ Limited data have shown that ondansetron is safe and effective in the management of hyperemesis gravidarum.¹² Safety data are insufficient to recommend ondansetron as a first line agent for HG. The use of ondansetron is supported by the American College of Obstetrician and Gynecologists (ACOG) Guidelines after failure of other first line agents.¹³ Ondansetron is classified in pregnancy as 'fetal risk cannot be ruled out'.¹² There are multiple first line agents for the treatment of hyperemesis gravidarum. Therefore, prior to authorization of the requested drug, an inadequate treatment response, intolerance, or contraindication to two first-line agents will be required.

Chemotherapy is often given for a specific time or for as long as it is effective. Most courses of chemotherapy last 3 months or more.¹⁶ The number of cycles given may be decided before treatment starts, based on the type and stage of cancer; in some cases, this number is flexible and will take into account the efficacy of treatment and the patient's overall health.¹⁷ To balance the variability in the length of chemotherapy courses with limiting disruptions in therapy, the duration of approval will be 6 months. Since the period of risk for nausea and vomiting with hyperemesis gravidarum (HG) during the first part of pregnancy is not expected to last for a long period of time, the duration of approval will be 6 months.

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Written by: UM Development (LS)

Date Written: 12/1996

Revised: 12/1998, 11/1999; (JG) 08/2002; (MG) 07/2003, 10/2004, 04/2005; (AK) 07/2006; (CT) 04/2007, 04/2008, 10/2008(2) (Sancuso added); (SE) 03/2009, 01/2010 (removed Aloxi caps 03/2009(2)); (KD) 03/2010, 07/2010 (Zuplenz added); (SE) 01/2011 (FDA Warning/ CI 03-2010 (2)); (CY) 04/2011(updated algorithms), (CY) 02/2012, 05/2012 (Removed Q10 days/weeks per month and included in Q5&6 for CAS Web compatibility), 07/2012 (removed single use ondansetron 32mg); (PL) 01/2013; (MS) 09/2013, (PL) 01/2014; (CF) 01/2015, 03/2015, (LN) 04/2015 (added denial reasons); (CF) 01/2016, 09/2016 (added palonosetron injection), 12/2016 (added Diclegis and Bonjesta to t/f question); (KM) 01/2017 (added Sustol injection), (ME) 01/2018 (no clinical changes), 01/2019, 01/2020 (no clinical changes)

Reviewed: Medical Affairs 08/2002, 08/2003, 10/2004, 04/2005; (MM) 07/2006, (WLF) 04/2007, 04/2008, 10/2008, 03/2009, 03/2010; (KP) 01/2011, 04/2011, 09/2011, 02/2012; (LB) 07/2012; (LMS) 01/2013, (DR) 09/2013, (DNC) 01/2014; (SES) 01/2015; (DHR) 03/2015; (GAD) 01/2016; (LMS) 09/2016, 12/2016; (JG) 02/2017, (CHART) 01/30/20

External Review: 10/2002, 10/2003, 11/2004, 08/2005, 08/2006, 08/2007, 08/2008, 10/2008, 08/2009, 08/2010, 08/2011, 04/2012, 06/2013, 10/2013, 04/2014, 04/2015, 04/2016, 04/2017, 04/2018, 04/2019, 04/2020

CRITERIA FOR APPROVAL

1	Is this request for Zofran, Zuplenz or ondansetron? [If no, then skip to question 4.]	Yes	No
2	Is the patient pregnant with the diagnosis of Hyperemesis Gravidarum and a documented risk for hospitalization? [If no, then skip to question 4.]	Yes	No
3	Has the patient experienced an inadequate treatment response, intolerance, or contraindication to TWO of the following medications: A) vitamin B6, B) vitamin B6 in combination with doxylamine, C) doxylamine/pyridoxine extended-release (Bonjesta), D) doxylamine/pyridoxine delayed-release (Diclegis), E) promethazine (Phenergan), F) trimethoprim-sulfamethoxazole (Tigan), G) metoclopramide (Reglan), H) diphenhydramine (Benadryl), I) dimenhydrinate (Dramamine)? [No further questions.]	Yes	No
4	Is the patient receiving radiation therapy or moderate to highly emetogenic chemotherapy?	Yes	No

Mapping Instructions			
	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Go to 4	
2.	Go to 3	Go to 4	
3.	Approve, 6 months	Deny	<p>You do not meet the requirements of your plan. Your plan covers additional quantities of this drug when you meet all of these conditions:</p> <ul style="list-style-type: none"> - You have hyperemesis gravidarum - You are at risk for a hospital stay - You tried 2 of the following drugs for nausea first and either they didn't work for you or you cannot use them [vitamin B6, vitamin B6 in combination with doxylamine, doxylamine/pyridoxine extended-release (Bonjesta), doxylamine/pyridoxine delayed-release (Diclegis), promethazine (Phenergan), trimethobenzamide (Tigan), or metoclopramide (Reglan), diphenhydramine (Benadryl), dimenhydrinate (Dramamine)] <p>Your request has been denied based on the information we have. [Short Description: No approvable diagnosis with risk of hospital stay, No inadequate response, intolerance or contraindication to two other nausea drugs]</p>
4.	Approve, 6 months	Deny	<p>You do not meet the requirements of your plan. Your plan covers additional quantities of this drug when you meet one of these conditions:</p> <ul style="list-style-type: none"> - You have hyperemesis gravidarum, are at risk for a hospital stay, and your request is for Zofran, Zuplenz or ondansetron - You are undergoing radiation therapy - You are undergoing moderate to highly emetogenic chemotherapy <p>Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]</p>

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	ANTIEMETIC AGENTS – 5HT3 ANTAGONISTS
BRAND NAME* (generic)	ALOXI INJECTION (palonosetron hydrochloride) ANZEMET (dolasetron mesylate) (granisetron hydrochloride) (ALL PRODUCTS) (palonosetron hydrochloride injection) SANCUSO (granisetron transdermal system) SUSTOL (granisetron extended-release injection) ZOFRAN (ALL DOSAGE FORMS) (ondansetron, ondansetron hydrochloride) ZUPLENZ (ondansetron oral soluble film)
Status: CVS Caremark Criteria Type: Post Limit Prior Authorization	REG Ref # 2821-J

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Aloxi Injection

Chemotherapy-Induced Nausea and Vomiting in Adults

Aloxi is indicated for:

- Moderately emetogenic cancer chemotherapy - prevention of acute and delayed nausea and vomiting associated with initial and repeat courses
- Highly emetogenic cancer chemotherapy - prevention of acute nausea and vomiting associated with initial and repeat courses

Chemotherapy-Induced Nausea and Vomiting in Pediatric Patients Aged 1 Month to Less than 17 Years

Aloxi is indicated for prevention of acute nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy, including highly emetogenic cancer chemotherapy.

Postoperative Nausea and Vomiting in Adults

Aloxi is indicated for prevention of postoperative nausea and vomiting (PONV) for up to 24 hours following surgery. Efficacy beyond 24 hours has not been demonstrated.

As with other antiemetics, routine prophylaxis is not recommended in patients in whom there is little expectation that nausea and/or vomiting will occur postoperatively. In patients where nausea and vomiting must be avoided during the postoperative period, Aloxi is recommended even where the incidence of postoperative nausea and/or vomiting is low.

Anzemet Tablets

Anzemet tablets are indicated for the prevention of nausea and vomiting associated with moderately emetogenic cancer chemotherapy, including initial and repeat courses in adults and children 2 years and older.

Granisetron

Granisetron Tablets

Granisetron Hydrochloride Tablets are indicated for the prevention of:

- Nausea and vomiting associated with initial and repeat courses of emetogenic cancer therapy, including high-dose cisplatin.
- Nausea and vomiting associated with radiation, including total body irradiation and fractionated abdominal radiation.

Granisetron Injection:

Granisetron Hydrochloride Injection is a serotonin-3 (5-HT₃) receptor antagonist indicated for:

- The prevention of nausea and/or vomiting associated with initial and repeat courses of emetogenic cancer therapy, including high-dose cisplatin.

Ondansetron Injection

Prevention of Nausea and Vomiting Associated with Initial and Repeat Courses of Emetogenic Cancer Chemotherapy

Ondansetron Injection is indicated for the prevention of nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy, including high-dose cisplatin. Ondansetron is approved for patients aged 6 months and older.

Prevention of Postoperative Nausea and/or Vomiting

Ondansetron Injection is indicated for the prevention of postoperative nausea and/or vomiting. As with other antiemetics, routine prophylaxis is not recommended for patients in whom there is little expectation that nausea and/or vomiting will occur postoperatively. In patients in whom nausea and/or vomiting must be avoided postoperatively, ondansetron injection is recommended even when the incidence of postoperative nausea and/or vomiting is low. For patients who do not receive prophylactic ondansetron injection and experience nausea and/or vomiting postoperatively, ondansetron injection may be given to prevent further episodes. Ondansetron is approved for patients aged 1 month and older.

Palonosetron Hydrochloride Injection

Chemotherapy-Induced Nausea and Vomiting in Adults

Palonosetron Hydrochloride (HCl) Injection is indicated for:

- Moderately emetogenic cancer chemotherapy - prevention of acute and delayed nausea and vomiting associated with initial and repeat courses
- Highly emetogenic cancer chemotherapy - prevention of acute nausea and vomiting associated with initial and repeat courses

Sancuso Transdermal System

- Sancuso (granisetron transdermal system) is indicated for the prevention of nausea and vomiting in patients receiving moderately and/or highly emetogenic chemotherapy regimens of up to 5 consecutive days duration.

Sustol Extended-Release Injection

Sustol is indicated in combination with other antiemetics in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic chemotherapy (MEC) or anthracycline and cyclophosphamide (AC) combination chemotherapy regimens.

Zofran Tablets, Zofran ODT, and Zofran Oral Solution

Zofran is indicated for the prevention of nausea and vomiting associated with:

- highly emetogenic cancer chemotherapy, including cisplatin greater than or equal to 50 mg/m².
- initial and repeat courses of moderately emetogenic cancer chemotherapy.
- radiotherapy in patients receiving either total body irradiation, single high-dose fraction to the abdomen, or daily fractions to the abdomen.

Zofran is also indicated for the prevention of postoperative nausea and/or vomiting.

Zuplenz

Prevention of nausea and vomiting associated with highly emetogenic cancer chemotherapy

Zuplenz (ondansetron) oral soluble film is indicated for the prevention of nausea and vomiting associated with highly emetogenic cancer chemotherapy, including cisplatin ≥ 50 mg/m²

Prevention of nausea and vomiting associated with moderately emetogenic cancer chemotherapy

Zuplenz is indicated for the prevention of nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy

Prevention of nausea and vomiting associated with radiotherapy

Zuplenz is indicated for the prevention of nausea and vomiting associated with radiotherapy in patients receiving either total body irradiation, single high-dose fraction to the abdomen, or daily fractions to the abdomen

Prevention of postoperative nausea and/or vomiting

Zuplenz is indicated for the prevention of postoperative nausea and/or vomiting. As with other antiemetics, routine prophylaxis is not recommended for patients in whom there is little expectation that nausea and/or vomiting will occur postoperatively. In patients where nausea and/or vomiting must be avoided postoperatively, Zuplenz is recommended even where the incidence of postoperative nausea and/or vomiting is low.

Compendial Uses:

- Treatment and/or prophylaxis of radiation-induced nausea and vomiting.¹⁰

Compendial Use Ondansetron Only:

- Hyperemesis Gravidarum^{12,17}

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient is receiving radiation therapy or moderate to highly emetogenic chemotherapy.

OR

- The request is for Zofran, Zuplenz or ondansetron **AND**
- The patient is pregnant with the diagnosis of Hyperemesis Gravidarum and a documented risk for hospitalization

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. 5HT-3 antiemetics are indicated for chemotherapy induced nausea and vomiting (CINV). Aloxi, Zofran tablets, ondansetron injection and Zuplenz are also indicated for postoperative nausea and vomiting (PONV). Granisetron tablets, Zofran tablets, ondansetron injection and Zuplenz are also indicated for nausea and vomiting associated with radiotherapy. 5HT-3 antiemetics also have compendial support for treatment and/or prophylaxis of radiation-induced nausea and vomiting.¹² Zofran, Zuplenz, and ondansetron have compendial support for use in hyperemesis gravidarum.^{12,13}

The National Comprehensive Cancer Network (NCCN) Guidelines state that the risk of nausea and vomiting for persons receiving chemotherapy of high and moderate emetic risk lasts for at least 3 days for high and 2 days for moderate after the last dose of chemotherapy. Patients need to be protected throughout the full period of risk.¹⁴ The recommended dosing parameters for the prevention of postoperative nausea and vomiting fall within the initial limits.

Patients receiving multiday chemotherapy are at risk for both acute and delayed nausea/vomiting based on the emetogenic potential of the individual chemotherapy agents administered on any given day and their sequence. Acute and delayed emesis may overlap after the initial day of chemotherapy until the last day of chemotherapy. The period of risk for delayed emesis after chemotherapy administration has concluded also depends on the specific regimen and the emetogenic potential of the last chemotherapy agent administered in the regimen. Antiemetic regimens should be chosen based on the drug with the highest emetic risk in the chemotherapy regimen, previous experience with antiemetics, and patient-specific risk factors.¹⁴

The NCCN has also made recommendations for use of antiemetics for radiation-induced emesis. Prophylaxis for radiation-induced nausea and/or vomiting is based on the site of radiation and whether the radiation is combined with anticancer therapy.¹⁴ The American Society of Clinical Oncology recommends that all patients should receive a 5-HT3 antagonist (granisetron and ondansetron are preferred) before each fraction of moderately to highly emetogenic radiation therapy.¹⁵

Chemotherapy is often given for a specific time or for as long as it is effective. Most courses of chemotherapy last 3 months or more.¹⁶ The number of cycles given may be decided before treatment starts, based on the type and stage of cancer; in some cases, this number is flexible and will take into account the efficacy of treatment and the patient's overall health.¹⁷ To balance the variability in the length of chemotherapy courses with limiting disruptions in therapy, the duration of approval will be 6 months. Since the period of risk for nausea and vomiting with hyperemesis gravidarum (HG) in pregnancy is not expected to last for a long period of time, the duration of approval will be 6 months.

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Written by: UM Development (ME)
Date Written: 12/2018 (created REG version from ref # 16-J)
Revised: (ME) 01/2019 (no clinical changes)
Reviewed: Medical Affairs: (ME) 12/2018, (CHART) 01/30/20
External Review: 02/2019 (FYI), 04/2019, 04/2020

CRITERIA FOR APPROVAL

- | | | | |
|---|---|-----|----|
| 1 | Is this request for Zofran, Zuplenz or ondansetron?
[If no, then skip to question 3.] | Yes | No |
| 2 | Is the patient pregnant with the diagnosis of Hyperemesis Gravidarum and a documented risk for hospitalization?
[If yes, then no further questions.] | Yes | No |
| 3 | Is the patient receiving radiation therapy or moderate to highly emetogenic chemotherapy? | Yes | No |

Mapping Instructions			
	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Go to 3	
2.	Approve, 6 months	Go to 3	
3.	Approve, 6 months	Deny	You do not meet the requirements of your plan. Your plan covers additional quantities of this drug when you meet one of these conditions: <ul style="list-style-type: none">- You have hyperemesis gravidarum, are at risk for a hospital stay, and your request is for Zofran, Zuplenz or ondansetron- You are undergoing radiation therapy- You are undergoing moderate to highly emetogenic chemotherapy Your request has been denied based on the information we have. [Short Description: No approvable diagnosis.]

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	TOPICAL ANTIFUNGAL AGENTS (BRAND PRODUCTS ONLY)
BRAND NAME* (generic)	<p>ECOZA (econazole)</p> <p>ERTACZO (sertaconazole)</p> <p>EXELDERM (sulconazole nitrate)</p> <p>LOPROX (ciclopirox shampoo)</p> <p>LOTRISONE (clotrimazole/betamethasone)</p> <p>LUZU (luliconazole)</p> <p>MENTAX (butenafine)</p> <p>NAFTIN (naftifine)</p> <p>OXISTAT (oxiconazole)</p> <p>VUSION (miconazole/zinc oxide/white petrolatum)</p> <p>XOLEGEL (ketoconazole)</p>
<p>Status: CVS Caremark Criteria Type: Initial Prior Authorization</p>	
<p>Ref # 1376-A</p>	

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Ecoza

Ecoza topical 1% foam is indicated for the treatment of interdigital tinea pedis caused by *Trichophyton rubrum*, *Trichophyton mentagrophytes*, and *Epidermophyton floccosum* in patients 12 years of age and older.

Ertaczo

Ertaczo 2% cream is indicated for the topical treatment of interdigital tinea pedis in immunocompetent patients 12 years of age and older, caused by: *Trichophyton rubrum*, *Trichophyton mentagrophytes*, and *Epidermophyton floccosum*.

Exelderm

Exelderm 1% cream is indicated for the treatment of tinea pedis (athlete's foot), tinea cruris, and tinea corporis caused by *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Epidermophyton floccosum*, and *Microsporum canis*, and for the treatment of tinea versicolor.

Exelderm 1% solution is indicated for the treatment of tinea cruris and tinea corporis caused by *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Epidermophyton floccosum*, and *Microsporum canis*; and for the treatment of tinea versicolor.

Effectiveness has not been proven in tinea pedis (athlete's foot). Symptomatic relief usually occurs within a few days after starting Exelderm solution and clinical improvement usually occurs within one week.

Loprox

Loprox 1% shampoo is indicated for the topical treatment of seborrheic dermatitis of the scalp in adults.

Lotrisone

Lotrisone cream is a combination of an azole antifungal and corticosteroid and is indicated for the topical treatment of symptomatic inflammatory tinea pedis, tinea cruris, and tinea corporis due to *Epidermophyton Floccosum*, *Trichophyton Mentagrophytes*, and *Trichophyton rubrum* in patients 17 years and older.

Luzu

Luzu cream is indicated for the topical treatment of interdigital tinea pedis, tinea cruris, and tinea corporis caused by the organisms *Trichophyton rubrum* and *Epidermophyton floccosum*.

Mentax

Mentax 1% cream is indicated for the topical treatment of the dermatologic infection, tinea (pityriasis) versicolor due to *M. furfur* (formerly *P. orbiculare*). Butenafine HCl cream was not studied in immunocompromised patients.

Naftin

Naftin 1% gel is indicated for the topical treatment of tinea pedis, tinea cruris, and tinea corporis caused by the organisms *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Trichophyton tonsurans*, *Epidermophyton floccosum*.

Naftin 2% cream is an allylamine antifungal indicated for the treatment of interdigital tinea pedis, tinea cruris, and tinea corporis caused by the organism *Trichophyton rubrum*.

Naftin 2% gel is an allylamine antifungal indicated for the treatment of interdigital tinea pedis caused by the organisms *Trichophyton rubrum*, *Trichophyton mentagrophytes*, and *Epidermophyton floccosum*.

Oxistat

Oxistat 1% lotion is indicated for the topical treatment of the following dermal infections: tinea pedis, tinea cruris, and tinea corporis due to *Trichophyton rubrum*, *Trichophyton mentagrophytes*, or *Epidermophyton floccosum*.

Oxistat 1% cream is indicated for the topical treatment of the following dermal infections: tinea pedis, tinea cruris, and tinea corporis due to *Trichophyton rubrum*, *Trichophyton mentagrophytes*, or *Epidermophyton floccosum*. Oxistat 1% cream is also indicated for the topical treatment of tinea (pityriasis) versicolor due to *Malassezia furfur*.

Vusion

Vusion ointment is indicated for the adjunctive treatment of diaper dermatitis only when complicated by documented candidiasis (microscopic evidence of pseudohyphae and/or budding yeast), in immunocompetent pediatric patients 4 weeks and older. A positive fungal culture for *Candida albicans* is not adequate evidence of candidal infection since colonization with *C. albicans* can result in a positive culture. The presence of candidal infection should be established by microscopic evaluation prior to initiating treatment.

Vusion should be used as part of a treatment regimen that includes measures directed at the underlying diaper dermatitis, including gentle cleansing of the diaper area and frequent diaper changes.

Vusion should not be used as a substitute for frequent diaper changes. Vusion should not be used to prevent the occurrence of diaper dermatitis, since preventative use may result in the development of drug resistance.

Limitations of Use

The safety and efficacy of Vusion have not been demonstrated in immunocompromised patients, or in infants less than 4 weeks of age (premature or term).

The safety and efficacy of Vusion have not been evaluated in incontinent adult patients. Vusion should not be used to prevent the occurrence of diaper dermatitis, such as in an adult institutional setting, since preventative use may result in the development of drug resistance.

Xolegel

Xolegel is indicated for the topical treatment of seborrheic dermatitis in immunocompetent adults and children 12 years of age and older.

Safety and efficacy of Xolegel for treatment of fungal infections have not been established.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being used for an FDA-Approved indication

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Ecoza topical 1% foam is indicated for the treatment of interdigital tinea pedis in patients 12 years of age and older. Ertaczo 2% cream is indicated for the topical treatment of interdigital tinea pedis in immunocompetent patients 12 years of age and older. Exelderm 1% cream is indicated for the treatment of tinea pedis (athlete's foot), tinea cruris, and tinea corporis and for the treatment of tinea versicolor. Exelderm 1% solution is indicated for the treatment of tinea cruris and tinea corporis and for the treatment of tinea versicolor. Loprox 1% shampoo is indicated for the topical treatment of seborrheic dermatitis of the scalp in adults. Lotrisone cream is indicated for the topical treatment of symptomatic inflammatory tinea pedis, tinea cruris, and tinea corporis. Luzu cream is indicated for the topical treatment of interdigital tinea pedis, tinea cruris, and tinea corporis. Mentax 1% cream is indicated for the topical treatment of the dermatologic infection, tinea (pityriasis) versicolor. Butenafine HCl cream was not studied in immunocompromised patients. Naftin 1% gel is indicated for the topical treatment of tinea pedis, tinea cruris, and tinea corporis. Naftin 2% gel is indicated for the treatment of interdigital tinea pedis. Oxistat 1% cream and lotion are indicated for the topical treatment of tinea pedis, tinea cruris, and tinea corporis. Oxistat 1% cream is also indicated for the topical treatment of tinea (pityriasis) versicolor. Vusion ointment is indicated for the adjunctive treatment of diaper dermatitis only when complicated by documented candidiasis (microscopic evidence of pseudohyphae and/or budding yeast), in immunocompetent pediatric patients 4 weeks and older. Xolegel is indicated for the topical treatment of seborrheic dermatitis in immunocompetent adults and children 12 years of age and older.

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Written by: UM Development (MS)
 Date Written: 06/2016
 Revised: (CT) 08/2016 (added target drugs); (SF) 06/2017 (no clinical changes); (DS) 06/2018 (no clinical changes), 06/2019 (no clinical changes)
 Reviewed: Medical Affairs (MM) 06/2016
 External Review: 09/2016, 10/2017, 10/2018, 10/2019

CRITERIA FOR APPROVAL

1	Is the requested drug being used for an FDA-Approved indication?	Yes	No
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Guidelines for Approval

Duration of Approval		3 Months
Set 1		
Yes to question(s)		No to question(s)
1		None

	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Approve, 3 months	Deny	You do not meet the requirements of your plan. Your plan covers the requested drug when it is used for the FDA-approved use. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]

STEP THERAPY CRITERIA

DRUG CLASS	TOPICAL ANTIFUNGAL AGENTS (BRAND PRODUCTS ONLY)
BRAND NAME* (generic)	<p>ECOZA (econazole)</p> <p>ERTACZO (sertaconazole)</p> <p>EXELDERM (sulconazole nitrate)</p> <p>LOPROX (ciclopirox shampoo)</p> <p>LOTRISONE (clotrimazole/betamethasone)</p> <p>LUZU (luliconazole)</p> <p>MENTAX (butenafine)</p> <p>NAFTIN (naftifine)</p> <p>OXISTAT (oxiconazole)</p> <p>VUSION (miconazole/zinc oxide/white petrolatum)</p> <p>XOLEGEL (ketoconazole)</p>
<p>Status: CVS Caremark Criteria</p> <p>Type: Initial Step Therapy; Post Step Therapy Prior Authorization</p> <p>Ref # 1380-D</p>	

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Ecoza

Ecoza topical 1% foam is indicated for the treatment of interdigital tinea pedis caused by *Trichophyton rubrum*, *Trichophyton mentagrophytes*, and *Epidermophyton floccosum* in patients 12 years of age and older.

Ertaczo

Ertaczo 2% cream is indicated for the topical treatment of interdigital tinea pedis in immunocompetent patients 12 years of age and older, caused by: *Trichophyton rubrum*, *Trichophyton mentagrophytes*, and *Epidermophyton floccosum*.

Exelderm

Exelderm 1% cream is indicated for the treatment of tinea pedis (athlete's foot), tinea cruris, and tinea corporis caused by *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Epidermophyton floccosum*, and *Microsporum canis*, and for the treatment of tinea versicolor.

Exelderm 1% solution is indicated for the treatment of tinea cruris and tinea corporis caused by *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Epidermophyton floccosum*, and *Microsporum canis*; and for the treatment of tinea versicolor.

Effectiveness has not been proven in tinea pedis (athlete's foot). Symptomatic relief usually occurs within a few days after starting Exelderm solution and clinical improvement usually occurs within one week.

Loprox

Loprox 1% shampoo is indicated for the topical treatment of seborrheic dermatitis of the scalp in adults.

Lotrisone

Lotrisone cream is a combination of an azole antifungal and corticosteroid and is indicated for the topical treatment of symptomatic inflammatory tinea pedis, tinea cruris, and tinea corporis due to *Epidermophyton Floccosum*, *Trichophyton Mentagrophytes*, and *Trichophyton rubrum* in patients 17 years and older.

Luzu

Luzu cream is indicated for the topical treatment of interdigital tinea pedis, tinea cruris, and tinea corporis caused by the organisms *Trichophyton rubrum* and *Epidermophyton floccosum*.

Mentax

Mentax 1% cream is indicated for the topical treatment of the dermatologic infection, tinea (pityriasis) versicolor due to *M. furfur* (formerly *P. orbiculare*). Butenafine HCl cream was not studied in immunocompromised patients.

Naftin

Naftin 1% gel is indicated for the topical treatment of tinea pedis, tinea cruris, and tinea corporis caused by the organisms *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Trichophyton tonsurans*, *Epidermophyton floccosum*.

Naftin 2% cream is an allylamine antifungal indicated for the treatment of interdigital tinea pedis, tinea cruris, and tinea corporis caused by the organism *Trichophyton rubrum*.

Naftin 2% gel is an allylamine antifungal indicated for the treatment of interdigital tinea pedis caused by the organisms *Trichophyton rubrum*, *Trichophyton mentagrophytes*, and *Epidermophyton floccosum*.

Oxistat

Oxistat 1% lotion is indicated for the topical treatment of the following dermal infections: tinea pedis, tinea cruris, and tinea corporis due to *Trichophyton rubrum*, *Trichophyton mentagrophytes*, or *Epidermophyton floccosum*.

Oxistat 1% cream is indicated for the topical treatment of the following dermal infections: tinea pedis, tinea cruris, and tinea corporis due to *Trichophyton rubrum*, *Trichophyton mentagrophytes*, or *Epidermophyton floccosum*. Oxistat 1% cream is also indicated for the topical treatment of tinea (pityriasis) versicolor due to *Malassezia furfur*.

Vusion

Vusion ointment is indicated for the adjunctive treatment of diaper dermatitis only when complicated by documented candidiasis (microscopic evidence of pseudohyphae and/or budding yeast), in immunocompetent pediatric patients 4 weeks and older. A positive fungal culture for *Candida albicans* is not adequate evidence of candidal infection since colonization with *C. albicans* can result in a positive culture. The presence of candidal infection should be established by microscopic evaluation prior to initiating treatment.

Vusion should be used as part of a treatment regimen that includes measures directed at the underlying diaper dermatitis, including gentle cleansing of the diaper area and frequent diaper changes.

Vusion should not be used as a substitute for frequent diaper changes. Vusion should not be used to prevent the occurrence of diaper dermatitis, since preventative use may result in the development of drug resistance.

Limitations of Use

The safety and efficacy of Vusion have not been demonstrated in immunocompromised patients, or in infants less than 4 weeks of age (premature or term).

The safety and efficacy of Vusion have not been evaluated in incontinent adult patients. Vusion should not be used to prevent the occurrence of diaper dermatitis, such as in an adult institutional setting, since preventative use may result in the development of drug resistance.

Xolegel

Xolegel is indicated for the topical treatment of seborrheic dermatitis in immunocompetent adults and children 12 years of age and older.

Safety and efficacy of Xolegel for treatment of fungal infections have not been established.

INITIAL STEP THERAPY

If the patient has filled a prescription for at least a 7 day supply of a generic topical antifungal agent within the past 120 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit. If the patient does not meet the initial step therapy criteria, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient experienced an inadequate treatment response, intolerance, or contraindication to a generic topical antifungal agent (e.g., ciclopirox, clotrimazole, ketoconazole, naftifine, oxiconazole)

RATIONALE

If the patient has filled a prescription for at least a 7 day supply of a generic topical antifungal agent within the past 120 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.

If the patient does not meet the initial step therapy criteria, then prior authorization is required.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines.

Ecoza topical 1% foam is indicated for the treatment of interdigital tinea pedis in patients 12 years of age and older. Ertaczo 2% cream is indicated for the topical treatment of interdigital tinea pedis in immunocompetent patients 12 years of age and older. Exelderm 1% cream is indicated for the treatment of tinea pedis (athlete's foot), tinea cruris, and tinea corporis and for the treatment of tinea versicolor. Exelderm 1% solution is indicated for the treatment of tinea cruris and

tinea corporis and for the treatment of tinea versicolor. Loprox 1% shampoo is indicated for the topical treatment of seborrheic dermatitis of the scalp in adults. Lotrisone cream is indicated for the topical treatment of symptomatic inflammatory tinea pedis, tinea cruris, and tinea corporis. Luzu cream is indicated for the topical treatment of interdigital tinea pedis, tinea cruris, and tinea corporis. Mentax 1% cream is indicated for the topical treatment of the dermatologic infection, tinea (pityriasis) versicolor. Butenafine HCl cream was not studied in immunocompromised patients. Naftin 1% gel is indicated for the topical treatment of tinea pedis, tinea cruris, and tinea corporis. Naftin 2% cream is indicated for the treatment of interdigital tinea pedis, tinea cruris, and tinea corporis. Naftin 2% gel is indicated for the treatment of interdigital tinea pedis. Oxistat 1% cream and lotion are indicated for the topical treatment of tinea pedis, tinea cruris, and tinea corporis. Oxistat 1% cream is also indicated for the topical treatment of tinea (pityriasis) versicolor. Vusion ointment is indicated for the adjunctive treatment of diaper dermatitis only when complicated by documented candidiasis (microscopic evidence of pseudohyphae and/or budding yeast), in immunocompetent pediatric patients 4 weeks and older. Xolegel is indicated for the topical treatment of seborrheic dermatitis in immunocompetent adults and children 12 years of age and older.

Treatment for seborrheic dermatitis includes over-the-counter shampoos and topical antifungals, calcineurin inhibitors, and corticosteroids. For long-term control, antifungal shampoos containing ketoconazole 2% or ciclopirox 1% (Loprox) can be used daily or at least two or three times per week for several weeks.^{15,18} If a patient with seborrheic dermatitis shows no clinical improvement after 4 weeks of treatment, the diagnosis should be reviewed.¹⁵

Tinea corporis and tinea cruris generally can be effectively treated using a topical antifungal. Many clinicians consider topical imidazole derivative azole antifungals (e.g., clotrimazole, ketoconazole, oxiconazole) or topical allylamine antifungals (e.g., naftifine) the drugs of first choice for the topical treatment of tinea corporis or tinea cruris, although other antifungals agents (e.g., ciclopirox olamine) also can be effective in the treatment of these infections. Uncomplicated interdigital and vesiculobullous forms of tinea pedis generally can be treated effectively using topical therapy with an imidazole derivative azole antifungal (e.g., clotrimazole, ketoconazole, oxiconazole), an allylamine antifungal (e.g., naftifine), or other topical antifungal agents such as ciclopirox olamine. Like other imidazole derivatives (e.g., clotrimazole, ketoconazole) and ciclopirox olamine, oxiconazole has an advantage over some other topical antifungal agents (e.g., nystatin, tolinaftate) in the treatment of mixed infections or for empiric treatment pending identification of the causative organism, since the drug is active against both dermatophytes and *Candida*.^{15,17} If clinical improvement does not occur after 4 weeks of treatment with topical treatment, the diagnosis should be reevaluated.¹⁵

Pityriasis (tinea) versicolor generally can be treated topically with an imidazole derivative azole antifungal (e.g., clotrimazole, ketoconazole, oxiconazole), ciclopirox olamine.¹⁵ Pityriasis (tinea) versicolor should be treated for 2 weeks to reduce the possibility of recurrence. If clinical improvement does not occur after the recommended treatment period, the diagnosis should be reevaluated.¹⁵

The management of diaper dermatitis includes numerous approaches. Eliminating the causes of diaper dermatitis and using barrier creams may be enough to cure mild cases; however, for the best therapeutic approach, fungal and bacterial investigation should be undertaken when suspected. As candidal infection is quite common in more severe cases of diaper dermatitis, antifungal agents such as clotrimazole, ketoconazole, miconazole, econazole, tioconazole, and ciclopirox can be applied to the diaper area with every diaper change. There is a wide variety of disorders to consider in an infant presenting with an inflamed eruption in the diaper area, and it becomes particularly important to consider other diagnoses when diaper dermatitis fails to respond to therapy.^{19,20}

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Written by: UM Development (CT)
 Date Written: 06/2016
 Revised: 08/2016 (added target drugs); (SF) 06/2017 (no clinical changes); (DS) 06/2018 (no clinical changes), 06/2019 (no clinical changes)
 Reviewed: Medical Affairs (GAD) 06/2016
 External Review: 09/2016, 10/2017, 10/2018, 10/2019

CRITERIA FOR APPROVAL

1	Has the patient experienced an inadequate treatment response, intolerance, or contraindication to a generic topical antifungal agent (e.g., ciclopirox, clotrimazole, ketoconazole, naftifine, oxiconazole)?	Yes	No
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Mapping Instructions

	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Approve, 3 months	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you have tried a generic topical antifungal agent (e.g., ciclopirox, clotrimazole, ketoconazole, naftifine, oxiconazole) and it either did not work for you or you cannot use it.</p> <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No inadequate response, intolerance or contraindication to generic topical antifungals]</p>

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS **ANTI OBESITY AGENTS**

BRAND NAME*
(generic)

benzphetamine products

diethylpropion products

phendimetrazine products

phentermine products

Status: CVS Caremark Criteria

Type: Initial Prior Authorization

Ref # 18-A

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Benzphetamine

Benzphetamine is indicated in the management of exogenous obesity as a short term (a few weeks) adjunct in a regimen of weight reduction based on caloric restriction in patients with an initial body mass index (BMI) of 30 kg/m² or higher who have not responded to appropriate weight reducing regimen (diet and/or exercise) alone. The limited usefulness of agents of this class should be weighed against possible risks inherent in their use. Benzphetamine is indicated for use as monotherapy only.

Limitations of Use:

- The effect on cardiovascular morbidity and mortality has not been established.
- The safety and effectiveness of these agents in combination with other products intended for weight loss, including prescription drugs, over-the-counter drugs, and herbal preparations, have not been established.

Diethylpropion

Diethylpropion is indicated in the management of exogenous obesity as a short-term adjunct (a few weeks) in a regimen of weight reduction based on caloric restriction in patients with an initial body mass index of 30 kg/m² or higher and who have not responded to an appropriate weight reducing regimen (diet and/or exercise) alone. The usefulness of agents of this class should be measured against possible risk factors inherent in their use. Diethylpropion is indicated for use as monotherapy only.

Limitations of Use:

- The effect on cardiovascular morbidity and mortality has not been established.
- The safety and effectiveness of these agents in combination with other products intended for weight loss, including prescription drugs, over-the-counter drugs, and herbal preparations, have not been established.

Phendimetrazine

Phendimetrazine tartrate extended-release capsules are indicated in the management of exogenous obesity as a short term adjunct (a few weeks) in a regimen of weight reduction based on caloric restriction in patients with an initial body mass index (BMI) of greater than or equal to 30 kg/m² or greater than or equal to 27 kg/m² in the presence of other risk factors (e.g., controlled hypertension, diabetes, hyperlipidemia) who have not responded to appropriate weight reducing regimen (diet and/or exercise) alone. The limited usefulness of agents of this class should be weighed against possible risks inherent in their use. Phendimetrazine tartrate is indicated for use as monotherapy only.

Phendimetrazine tartrate is indicated in the management of exogenous obesity as a short term adjunct (a few weeks) in a regimen of weight reduction based on caloric restriction in patients with an initial body mass index (BMI) of 30 kg/m² or

higher who have not responded to appropriate weight reducing regimen (diet and/or exercise) alone. The limited usefulness of agents of this class should be weighed against possible risks inherent in their use. Phendimetrazine tartrate is indicated for use as monotherapy only.

Limitations of Use:

- The effect on cardiovascular morbidity and mortality has not been established.
- The safety and effectiveness of these agents in combination with other products intended for weight loss, including prescription drugs, over-the-counter drugs, and herbal preparations, have not been established.

Phentermine

Phentermine is indicated as a short-term (a few weeks) adjunct in a regimen of weight reduction based on exercise, behavioral modification, and caloric restriction, in the management of exogenous obesity for patients with an initial body mass index greater than or equal to 30 kg/m², or greater than or equal to 27 kg/m² in the presence of other risk factors (e.g., controlled hypertension, diabetes, hyperlipidemia). The limited usefulness of agents of this class should be measured against possible risk factors inherent in their use.

Limitations of Use:

- The effect on cardiovascular morbidity and mortality has not been established.
- The safety and effectiveness of these agents in combination with other products intended for weight loss, including prescription drugs, over-the-counter drugs, and herbal preparations, have not been established.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has not received 3 months of therapy with the requested drug within the past 365 days
AND
- The requested drug will be used with a reduced calorie diet and increased physical activity **AND**
 - The patient has a body mass index (BMI) greater than or equal to 30 kg per square meter
OR
 - The patient has a body mass index (BMI) greater than or equal to 27 kg per square meter **AND** has additional risk factors

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Anoretics are indicated as a short-term (a few weeks) adjunct to a reduced-calorie diet and increased physical activity, in the management of exogenous obesity for patients with an initial body mass index greater than or equal to 30 kg/m² or greater than or equal to 27 kg/m² in the presence of other risk factors (e.g., controlled hypertension, diabetes, hyperlipidemia).¹⁻⁷ The limited usefulness of agents of this class should be measured against possible risk factors inherent in their use.

The guidelines state that the purpose of weight loss and weight maintenance is to reduce health risk.^{8,9} Weight loss programs should begin with a basic regimen consisting of a reduced-calorie diet and increased physical activity. The major role of medications is to help with patient compliance to a weight loss plan. Therefore, drugs should be used as part of a comprehensive weight loss program and should never be used without concomitant lifestyle modification. Drugs may be used as an adjunct to diet and physical activity for patients with a BMI that is greater than or equal to 30 kg/m² or greater than or equal to 27 kg/m² if other risk factors are present (e.g., hypertension, diabetes, dyslipidemia, sleep apnea, cardiovascular disease).^{8,9}

Sympathomimetic amine anorectic drugs have a narrow FDA labeling which reflects on the importance of prevention of inappropriate usage. The FDA approved indication for these agents is for short term treatment only. The safety of long-term anorexiant therapy has not been established conclusively beyond 12 weeks of administration. Therefore, coverage will be limited to a total of 3 months per year of each of the following: benzphetamine, diethylpropion, phendimetrazine or phentermine.

REFERENCES

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Written by: UM Development (LS)
 Date Written: 07/1997
 Revised: (GP) 6/1998, 06/2000; (JG) 07/2002; (MG) 10/2003; (NB) 11/2004, 07/2005, 06/2006; (CT) 08/2007; (MS) 07/2008; (CT) 08/2009; (KD) 06/2010; (MS) 07/2011; (CY) 06/2012; (PL/TM) 06/2013, (PL) 06/2014, 12/2014 (removed "approval of" from question #1); (MS) 07/2015, 12/2015 (updated Q5 to make trade compatible); (SE) 01/2016 (Added guidelines for approval grid); (MS) 07/2016 (removed safety question); (JG) 07/2017 (no clinical changes), (ME) 07/2018 (no clinical changes), 07/2019 (removed Suprenza)
 Reviewed: Medical Affairs 8/1997, 06/1998, 07/2002; 11/2003; (MM) 11/2004, 07/2005, 06/2006; (WF) 08/2007; 08/2008, 08/2009; (KP) 06/2010, 07/2011, 06/2012; (LMS) 10/2013; (SES) 06/2014; (DC) 07/2015, (ME) 07/2018, (CHART) 8/1/19
 External Review: 06/2000, 09/2002, 12/2003, 12/2004, 11/2005, 12/2006, 12/2007, 12/2008, 10/2009, 12/2010, 10/2011, 08/2012, 10/2013, 10/2014, 10/2015, 12/2015, 10/2016, 09/2017, 10/2018, 10/2019

CRITERIA FOR APPROVAL

- | | | | |
|---|--|-----|----|
| 1 | Has the patient received 3 months of therapy with the requested drug within the past 365 days? | Yes | No |
| <p>[Tech note: Verify PA History AND the Prescription History before approving. If the request has been approved for the requested drug in the last 365 days or the patient received a paid claim for the requested drug, forward to RPH for review even if the pop up box asked you to approve it]</p> | | | |
| 2 | Does the patient have a body mass index (BMI) greater than or equal to 30 kg per square meter?
[If yes, then skip to question 4.] | Yes | No |
| 3 | Does the patient have a body mass index (BMI) greater than or equal to 27 kg per square meter AND has additional risk factors? | Yes | No |
| 4 | Will the requested medication be used with a reduced calorie diet and increased physical activity? | Yes | No |

Guidelines for Approval

Duration of Approval		3 Months (90 days of therapy) per year	
Set 1		Set 2	
Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)
2	1	3	1
4		4	2

Mapping Instructions

	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1	Deny	Go to 2	You do not meet the requirements of your plan.

			<p>Your plan covers this drug when you have not received 3 months of therapy with the requested drug within the past year.</p> <p>Your request has been denied based on the information we have.</p> <p>[Short Description: Over max plan limit]</p>
2	Go to 4	Go to 3	
3	Go to 4	Deny	<p>You do not meet the requirements of your plan.</p> <p>Your plan covers this drug when you meet one of these conditions:</p> <ul style="list-style-type: none"> - You have a body mass index (BMI) of 30 kg per square meter or more - You have a body mass index (BMI) of 27 kg per square meter or more and you have risk factors <p>Your request has been denied based on the information we have.</p> <p>[Short Description: Not at BMI requirement]</p>
4	Approve, 3 months (90 days of therapy) per year.	Deny	<p>You do not meet the requirements of your plan.</p> <p>Your plan covers this drug when you will diet and exercise while taking this drug.</p> <p>Your request has been denied based on the information we have.</p> <p>[Short Description: Diet and exercise requirement not met]</p>

SPECIALTY GUIDELINE MANAGEMENT

APOKYN (apomorphine)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Acute, intermittent treatment of hypomobility, “off” episodes (“end-of-dose wearing off” and unpredictable “on/off” episodes) in patients with advanced Parkinson’s disease.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 6 months may be granted for the treatment of acute, intermittent treatment of hypomobility, “off” episodes (“end-of-dose wearing off” and unpredictable “on/off” episodes) for members with advanced Parkinson’s disease when all of the following criteria are met:

- A. The member experiences at least 2 hours per day of off time
- B. The member is currently being treated with carbidopa/levodopa
- C. Attempts to manage off episodes by adjusting the dosing or formulation of carbidopa/levodopa were ineffective
- D. Treatment with carbidopa/levodopa plus one of the following therapies was ineffective at managing off episodes:
 1. Dopamine agonist (e.g., pramipexole, ropinirole)
 2. Monoamine oxidase B (MAO-B) inhibitor (e.g., selegiline, rasagiline)
 3. Catechol-O-methyl transferase (COMT) inhibitor (e.g., entacapone, tolcapone)

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment of acute, intermittent treatment of hypomobility “off” episodes (“end-of-dose wearing off” and unpredictable “on/off” episodes) for members with advanced Parkinson’s disease when both of the following criteria are met:

- A. The member is currently being treated with carbidopa/levodopa
- B. The member is experiencing improvement on Apokyn therapy (e.g. reduction in daily off time, improvement in motor function post-administration)

IV. REFERENCES

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Reference number(s)
2258-A

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PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

APTIOM
(eslicarbazepine)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

Ref # 1083-A

* Drugs that are listed in the target drug box include both brand and generic and all dosages forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Aptiom is indicated for the treatment of partial-onset seizures in patients 4 years of age and older.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for partial-onset seizures in a patient 4 years of age or older

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Aptiom is indicated for the treatment of partial-onset seizures in patients 4 years of age and older.¹⁻³

REFERENCES

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Written by: UM Development (SE)
Date Written: 11/2013
Revised: (CT) 05/2014; (CF) 05/2015, 09/2015 (updated indication); (KM) 05/2016 (no clinical changes); (SF) 05/2017 (no clinical changes); (KC) 05/2018, 05/2019 (no clinical changes)
Reviewed: Medical Affairs (SES) 12/2013; (LMS) 05/2014; (DNC) 05/2015, 09/2015; (ME) 05/2018
External Review: 02/2014, 10/2014, 10/2015, 10/2016, 10/2017, 10/2018, 10/2019

CRITERIA FOR APPROVAL

- | | | | |
|---|---|-----|----|
| 1 | Is the requested drug being prescribed for partial-onset seizures in a patient 4 years of age or older? | Yes | No |
|---|---|-----|----|

Mapping Instructions			
	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Approve, 36 Months	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions:</p> <ul style="list-style-type: none"> - You have partial-onset seizures - You are 4 years of age or older <p>Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]</p>

SPECIALTY GUIDELINE MANAGEMENT

ARANESP (darbepoetin alfa)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Treatment of anemia due to chronic kidney disease (CKD), including patients on dialysis and patients not on dialysis.
2. Treatment of anemia in patients with non-myeloid malignancies where anemia is due to the effect of concomitant myelosuppressive chemotherapy, and upon initiation, there is a minimum of two additional months of planned chemotherapy.

B. Compendial Uses

1. Symptomatic anemia in patients with myelodysplastic syndromes (MDS)
2. Anemia in patients whose religious beliefs forbid blood transfusions
3. Symptomatic anemia in patients with primary myelofibrosis, post-polycythemia vera myelofibrosis, and post-essential thrombocythemia myelofibrosis
4. Cancer patients who are undergoing palliative treatment

All other indications are considered experimental/investigational and are not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Note: Requirements regarding pretreatment hemoglobin level exclude values due to a recent transfusion. All members must be assessed for iron deficiency anemia and have adequate iron stores or are receiving iron therapy before starting Aranesp. Members may not use Aranesp concomitantly with other erythropoiesis stimulating agents.

A. **Anemia Due to CKD**

Authorization of 12 weeks may be granted for members with pretreatment hemoglobin < 10 g/dL.

B. **Anemia Due to Myelosuppressive Chemotherapy**

Authorization of 12 weeks may be granted for members with nonmyeloid malignancy with pretreatment hemoglobin < 10 g/dL.

C. **Anemia in MDS**

Authorization of 12 weeks may be granted for members with pretreatment hemoglobin < 10 g/dL whose pretreatment serum EPO level is < 500 MU/ml.

D. **Anemia in Members Whose Religious Beliefs Forbid Blood Transfusions**

Authorization of 12 weeks may be granted for members with pretreatment hemoglobin < 10 g/dL.

Reference number
1616-A

E. Anemia in Primary Myelofibrosis (MF), Post-polycythemia Vera MF, and Post-Essential Thrombocythemia MF

Authorization of 12 weeks may be granted for members who meet ALL of the following criteria:

1. Pretreatment hemoglobin < 10 g/dL
2. Pretreatment serum erythropoietin level < 500 mU/mL

F. Anemia Due to Cancer

Authorization of 12 weeks may be granted for members who have cancer and are undergoing palliative treatment

III. CONTINUATION OF THERAPY

Note: Requirements regarding pretreatment hemoglobin level exclude values due to a recent transfusion. Members may not use Aranesp concomitantly with other erythropoiesis stimulating agents.

For all indications below: all members (including new members) requesting authorization for continuation of therapy after at least 12 weeks of ESA treatment must show a response with a rise in hemoglobin of ≥ 1 g/dL. Members who completed less than 12 weeks of ESA treatment and have not yet responded with a rise in hemoglobin of ≥ 1 g/dL may be granted authorization of up to 12 weeks to allow for sufficient time to demonstrate a response.

A. Anemia due to CKD

Authorization of 12 weeks may be granted for continuation of treatment when the current hemoglobin is ≤ 12 g/dL.

B. Anemia Due to Myelosuppressive Chemotherapy

Authorization of 12 weeks may be granted for continuation of treatment in members with nonmyeloid malignancy when the current hemoglobin is < 12 g/dL.

C. Anemia in MDS

Authorization of 12 weeks may be granted for continuation of treatment when the current hemoglobin is ≤ 12 g/dL.

D. Anemia in members whose religious beliefs forbid blood transfusions

Authorization of 12 weeks may be granted for continuation of treatment when the current hemoglobin is ≤ 12 g/dL.

E. Anemia in Primary Myelofibrosis, Post-polycythemia Vera Myelofibrosis, and Post-Essential Thrombocythemia Myelofibrosis

Authorization of 12 weeks may be granted for continuation of treatment when the current hemoglobin is ≤ 12 g/dL.

F. Anemia Due to Cancer

Authorization of 12 weeks may be granted for members who have cancer and are undergoing palliative treatment

IV. REFERENCES

Reference number
1616-A

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6. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Cancer- and Chemotherapy-Induced Anemia. Version 3.2018. http://www.nccn.org/professionals/physician_gls/pdf/anemia.pdf. Accessed September 18, 2018.
7. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Myelodysplastic Syndromes. Version 1.2019. http://www.nccn.org/professionals/physician_gls/pdf/mds.pdf. Accessed September 18, 2018.
8. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Myeloproliferative Neoplasms. Version 1.2019. https://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf. Accessed September 18, 2018.
9. Gabrilove J, Paquette R, Lyons R, Mushtaq C, Sekeres M, et al. Phase 2, single-arm trial to evaluate the effectiveness of darbepoetin alfa for correcting anaemia in patients with myelodysplastic syndromes. *Br J Haematol.* 2008 Aug; 142(3): 379–393.

Reference number
1800-A

SPECIALTY GUIDELINE MANAGEMENT

ARCALYST (rilonacept)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Treatment of Cryopyrin Associated Periodic Syndromes (CAPS), including Familial Cold Auto-inflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS) in adults and children 12 years of age and older.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Cryopyrin-associated periodic syndrome (CAPS)

Authorization of 12 months may be granted for treatment of CAPS when all of the following criteria are met:

- A. Member has a diagnosis of familial cold auto-inflammatory syndrome (FCAS) with classic signs and symptoms (i.e., recurrent, intermittent fever and rash that were often exacerbated by exposure to generalized cool ambient temperature) or Muckle-Wells syndrome (MWS) with classic signs and symptoms (i.e., chronic fever and rash of waxing and waning intensity, sometimes exacerbated by exposure to generalized cool ambient temperature).
- B. Member has functional impairment limiting the activities of daily living.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who are using Arcalyst for an indication outlined in Section II and who achieve or maintain positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

- A. Member has had a documented negative TB test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic DMARDs or targeted synthetic DMARDs (e.g., Olumiant, Rinvoq, Xeljanz), and repeated yearly for members with risk factors** for TB that are continuing therapy with biologics.

* If the screening testing for TB is positive, there must be documentation of further testing to confirm there is no active disease. Do not administer rilonacept to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of treatment.

Reference number
1800-A

** Risk factors for TB include: Persons with close contact to people with infectious TB disease; persons who have recently immigrated from areas of the world with high rates of TB (e.g., Africa, Asia, Eastern Europe, Latin America, Russia); children less than 5 years of age who have a positive TB test; groups with high rates of TB transmission (e.g., homeless persons, injection drug users, persons with HIV infection); persons who work or reside with people who are at an increased risk for active TB (e.g., hospitals, long-term care facilities, correctional facilities, homeless shelters).

- B. The requested drug will not be used concomitantly with any other biologic DMARD (e.g., adalimumab, anakinra, canakinumab, etanercept, infliximab, tocilizumab) or targeted synthetic DMARD (e.g. tofacitinib).

V. REFERENCES

1. Arcalyst [package insert]. Tarrytown, NY: Regeneron Pharmaceuticals, Inc.; September 2016.
2. Centers for Disease Control and Prevention. Tuberculosis (TB). TB risk factors. Available at: <https://www.cdc.gov/tb/topic/basics/risk.htm>. Accessed: August 15, 2019.

SPECIALTY GUIDELINE MANAGEMENT

ARIKAYCE (amikacin liposome inhalation suspension)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Arikayce is indicated in adults who have limited or no alternative treatment options, for the treatment of Mycobacterium avium complex (MAC) lung disease as part of a combination antibacterial drug regimen in patients who do not achieve negative sputum cultures after a minimum of 6 consecutive months of a multidrug background regimen therapy.

Limitation of Use: Arikayce has only been studied in patients with refractory MAC lung disease defined as patients who did not achieve negative sputum cultures after a minimum of 6 consecutive months of a multidrug background regimen therapy. The use of Arikayce is not recommended for patients with non-refractory MAC lung disease.

All other indications are considered experimental/investigational and are not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Mycobacterium avium complex (MAC) lung disease

Authorization of 12 months may be granted for members with mycobacterium avium complex (MAC) lung disease when the following criteria is met:

1. The patient has refractory disease with limited or no other treatment options.
2. The requested medication will be used as part of a combination antibacterial drug regimen.
3. The patient has not achieved negative sputum cultures after being treated with a multidrug background regimen therapy for a minimum of 6 consecutive months.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who are experiencing benefit from therapy as evidenced by disease stability or disease improvement (e.g., achievement and maintenance of negative sputum cultures).

IV. REFERENCES

1. Arikayce [package insert]. Bridgewater, NJ: Inmed Incorporated; September 2018
2. Griffith, DE, Aksamit, T, Brown-Elliott, BA, et al. An Official ATS/IDSA Statement: Diagnosis, Treatment, and Prevention of Nontuberculous Mycobacterial Disease. *Am J Respir Crit Care Med.* 2007;175):367-416

PRIOR AUTHORIZATION CRITERIA

**BRAND NAME
(generic)**

**ABILIFY MAINTENA
(aripiprazole extended-release injectable suspension)**

**ARISTADA
(aripiprazole lauroxil extended-release injectable suspension)**

**ARISTADA INITIO
(aripiprazole lauroxil extended-release injectable suspension)**

**Status: CVS Caremark Criteria
Type: Initial Prior Authorization**

POLICY

FDA-APPROVED INDICATIONS

Abilify Maintena

Abilify Maintena is indicated for the treatment of schizophrenia in adults and maintenance monotherapy treatment of bipolar I disorder in adults.

Aristada

Aristada is indicated for treatment of schizophrenia.

Aristada Initio

Aristada Initio, in combination with oral aripiprazole, is indicated for the initiation of Aristada when used for the treatment of schizophrenia in adults.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- Tolerability with oral aripiprazole has been established
- AND**
- The requested drug is being prescribed for the treatment of schizophrenia
- OR**
- Abilify Maintena is being prescribed for maintenance monotherapy treatment of bipolar I disorder

REFERENCES

1. Abilify Maintena [package insert]. Rockville, MD: Otsuka America Pharmaceutical, Inc.; February 2019.
2. Aristada [package insert]. Waltham, MA: Alkermes, Inc.; November 2018.
3. Aristada Initio [package insert]. Waltham, MA: Alkermes, Inc.; June 2018.
4. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed September 2019.
5. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed September 2019.
6. American Psychiatric Association. Practice guideline for the treatment of patients with schizophrenia, 2nd edition. 2010. Available at: http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/schizophrenia.pdf. Accessed September 2019.

SPECIALTY GUIDELINE MANAGEMENT

ARZERRA (ofatumumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Chronic lymphocytic leukemia (CLL):

1. Arzerra is indicated in combination with chlorambucil, for the treatment of previously untreated patients with CLL for whom fludarabine-based therapy is considered inappropriate.
2. Arzerra is indicated in combination with fludarabine and cyclophosphamide for the treatment of patients with relapsed CLL.
3. Arzerra is indicated for extended treatment of patients who are in complete or partial response after at least two lines of therapy for recurrent or progressive CLL.
4. Arzerra is indicated for the treatment of patients with CLL refractory to fludarabine and alemtuzumab.

B. Compendial Uses

1. CLL
2. Small lymphocytic lymphoma (SLL) (managed in the same manner as CLL)
3. Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma
4. Follicular lymphoma, substitute for rituximab or obinutuzumab in patients experiencing rare complications from rituximab or obinutuzumab
5. Gastric MALT lymphoma, substitute for rituximab or obinutuzumab in patients experiencing rare complications from rituximab or obinutuzumab
6. Non-gastric MALT lymphoma, substitute for rituximab substitute for rituximab or obinutuzumab in patients experiencing rare complications from rituximab or obinutuzumab
7. Nodal marginal zone lymphoma, substitute for rituximab or obinutuzumab in patients experiencing rare complications from rituximab or obinutuzumab
8. Splenic marginal zone lymphoma, substitute for rituximab or obinutuzumab in patients experiencing rare complications from rituximab or obinutuzumab
9. Histologic transformation of marginal zone lymphoma to diffuse large B-cell lymphoma, substitute for rituximab or obinutuzumab in patients experiencing rare complications from rituximab or obinutuzumab
10. Mantle cell lymphoma, substitute for rituximab or obinutuzumab in patients experiencing rare complications from rituximab or obinutuzumab
11. Diffuse large B-cell lymphoma, substitute for rituximab or obinutuzumab in patients experiencing rare complications from rituximab or obinutuzumab
12. High-grade B-cell lymphomas, substitute for rituximab or obinutuzumab in patients experiencing rare complications from rituximab or obinutuzumab
13. Burkitt lymphoma, substitute for rituximab or obinutuzumab in patients experiencing rare complications from rituximab or obinutuzumab
14. AIDS-related B-cell lymphomas, substitute for rituximab or obinutuzumab in patients experiencing rare complications from rituximab or obinutuzumab
15. Post-transplant lymphoproliferative disorders, substitute for rituximab or obinutuzumab in patients experiencing rare complications from rituximab or obinutuzumab

16. Castleman's disease, substitute for rituximab or obinutuzumab in patients experiencing rare complications from rituximab or obinutuzumab

All other indications are considered experimental/investigational and are not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Chronic Lymphocytic Leukemia (CLL) and Small Lymphocytic Lymphoma (SLL)

Authorization of 6 months may be granted for the treatment of CLL or SLL.

B. Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma (WM/LPL)

Authorization of 6 months may be granted for the treatment of Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma when all of the following criteria are met:

1. The disease is relapsed, refractory, or progressive, and
2. The member is intolerant to rituximab.

C. Follicular Lymphoma (FL), Gastric and Non-Gastric MALT Lymphoma, Nodal Marginal Zone Lymphoma, Splenic Marginal Zone Lymphoma, Histologic Transformation of Marginal Zone Lymphoma to Diffuse Large B-Cell Lymphoma, Mantle Cell Lymphoma, Diffuse Large B-Cell Lymphoma, High-Grade B-Cell Lymphomas, Burkitt Lymphoma, AIDS-Related B-Cell Lymphomas, Post-Transplant Lymphoproliferative Disorders, and Castleman's Disease

Authorization of 6 months may be granted for the treatment of follicular lymphoma (FL), gastric or non-gastric MALT lymphoma, nodal marginal zone lymphoma, splenic marginal zone lymphoma, histologic transformation of marginal zone lymphoma to diffuse large B-cell lymphoma, mantle cell lymphoma, diffuse large B-cell lymphoma, high-grade B-cell lymphomas, Burkitt lymphoma, AIDS-related B-cell lymphomas, post-transplant lymphoproliferative disorders, or Castleman's disease when the requested medication is used as a substitute for rituximab or obinutuzumab in members experiencing rare complications from rituximab or obinutuzumab such as mucocutaneous reactions including paraneoplastic pemphigus, Stevens-Johnson syndrome, lichenoid dermatitis, vesiculobullous dermatitis, and toxic epidermal necrolysis.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced disease progression or an unacceptable toxicity while on the current regimen.

IV. REFERENCES

1. Arzerra [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; August 2016.
2. National Comprehensive Cancer Network. The NCCN Drugs & Biologics Compendium. <http://www.nccn.org>. Accessed July 17, 2019.

SPECIALTY GUIDELINE MANAGEMENT

ASPARLAS (calaspargase pegol - mknl)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Asparlas is indicated as a component of a multi-agent chemotherapeutic regimen for the treatment of acute lymphoblastic leukemia in pediatric and young adult patients age 1 month to 21 years.

B. Compendial Uses

1. Lymphoblastic lymphoma (managed in the same manner as ALL)
2. Acute lymphoblastic leukemia (ALL) as a substitute for pegaspargase in patients 21 years and younger for more sustained asparaginase activity
3. Pediatric acute lymphoblastic leukemia (ALL) as a substitute for pegaspargase in patients age 1 month to 21 years for more sustained asparaginase activity

All other indications are considered experimental/investigational and are not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for the treatment of acute lymphoblastic leukemia or lymphoblastic lymphoma when all of the following criteria are met:

- A. The requested medication will be used in conjunction with multi-agent chemotherapy.
- B. The member is 21 years of age or younger.

III. CONTINUATION OF THERAPY

Authorization of 12 months total may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced disease progression or an unacceptable toxicity while on the current regimen.

IV. REFERENCES

1. Asparlas [package insert]. Boston, MA: Servier Pharmaceuticals LLC; December 2018.
2. National Comprehensive Cancer Network. The NCCN Drugs & Biologics Compendium. <http://www.nccn.org>. Accessed July 15, 2019.
3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Acute Lymphoblastic Leukemia. Version 2.2019. http://www.nccn.org/professionals/physician_gls/pdf/all.pdf. Accessed July 15, 2019.

Reference number
2833-A

4. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Pediatric Acute Lymphoblastic Leukemia. Version 1.2020.
https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf. Accessed July 15, 2019.

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS **ATYPICAL ANTIPSYCHOTICS**

BRAND NAME
(generic)

CAPLYTA
(lumateperone)

FANAPT
(iloperidone)

LATUDA
(lurasidone)

REXULTI
(brexpiprazole)

SAPHRIS
(asenapine)

SECUADO
(asenapine transdermal)

VRAYLAR
(cariprazine)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

Ref # 1340-A

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Caplyta

Caplyta is indicated for the treatment of schizophrenia in adults.

Fanapt

Fanapt tablets are indicated for the treatment of adults with schizophrenia. Efficacy was established in two short-term (4- and 6-week) placebo- and active-controlled studies of adult patients with schizophrenia. When deciding among the alternative treatments available for this condition, the prescriber should consider the finding that Fanapt is associated with prolongation of the QTc interval. Prolongation of the QTc interval is associated in some other drugs with the ability to cause torsade de pointes-type arrhythmia, a potentially fatal polymorphic ventricular tachycardia which can result in sudden death. In many cases this would lead to the conclusion that other drugs should be tried first. Whether Fanapt will cause torsade de pointes or increase the rate of sudden death is not yet known. Patients must be titrated to an effective dose of Fanapt. Thus, control of symptoms may be delayed during the first 1 to 2 weeks of treatment compared to some other antipsychotic drugs that do not require a similar titration. Prescribers should be mindful of this delay when selecting an antipsychotic drug for the treatment of schizophrenia. The effectiveness of Fanapt in long-term use, that is, for more

than 6 weeks, has not been systematically evaluated in controlled trials. Therefore, the physician who elects to use Fanapt for extended periods should periodically re-evaluate the long-term usefulness of the drug for the individual patient.

Latuda

Latuda is indicated for:

- Treatment of adult and adolescent patients age 13 to 17 years with schizophrenia
- Monotherapy treatment of adult and pediatric patients (10 to 17 years) with major depressive episodes associated with Bipolar I disorder (bipolar depression)
- Adjunctive treatment with lithium or valproate in adult patients with major depressive episodes associated with Bipolar I disorder (bipolar depression)

Rexulti

Rexulti is indicated for:

- Adjunctive treatment of major depressive disorder (MDD)
- Treatment of schizophrenia

Saphris

Saphris is indicated for:

- Schizophrenia in adults
- Bipolar I disorder
 - Acute monotherapy of manic or mixed episodes, in adults and pediatric patients 10 to 17 years of age
 - Adjunctive treatment to lithium or valproate in adults
 - Maintenance monotherapy treatment in adults

Secuado

Secuado is indicated for the treatment of adults with schizophrenia

Vraylar

- Treatment of schizophrenia in adults
- Acute treatment of manic or mixed episodes associated with bipolar I disorder in adults
- Treatment of depressive episodes associated with bipolar I disorder (bipolar depression) in adults

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- Caplyta, Fanapt or Secuado is being prescribed for the treatment of schizophrenia

OR

- Rexulti is being prescribed for any of the following: A) Adjunctive treatment of major depressive disorder (MDD), B) Treatment of schizophrenia

OR

- Saphris is being prescribed for any of the following: A) Schizophrenia, B) Acute treatment of manic or mixed episodes associated with Bipolar I disorder as monotherapy or adjunctive treatment to lithium or valproate, C) Maintenance monotherapy treatment in Bipolar I disorder

OR

- Vraylar is being prescribed for any of the following: A) Treatment of schizophrenia, B) Acute treatment of manic or mixed episodes associated with bipolar I disorder, C) Treatment of depressive episodes associated with bipolar I disorder (bipolar depression)

OR

- Latuda is being prescribed for any of the following: A) Schizophrenia, B) Adjunctive treatment with lithium or valproate for major depressive episodes associated with Bipolar I disorder (bipolar depression), C) Monotherapy treatment of major depressive episodes associated with Bipolar I disorder (bipolar depression)

AND

- The patient experienced an inadequate treatment response, intolerance, or contraindication to one of the following: A) aripiprazole, B) olanzapine, C) paliperidone, D) quetiapine, E) quetiapine extended release, F) risperidone, G) ziprasidone

RATIONALE

These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines.

Caplyta is indicated for the treatment of schizophrenia in adults. Fanapt is indicated for the treatment of adults with schizophrenia. Latuda is indicated for treatment of schizophrenia and monotherapy treatment of major depressive episodes associated with Bipolar I disorder (bipolar depression) or adjunctive treatment with lithium or valproate in adult patients with major depressive episodes associated with Bipolar I disorder (bipolar depression). Rexulti is indicated for adjunctive treatment of major depressive disorder (MDD) and treatment of schizophrenia. Saphris is indicated for schizophrenia and acute treatment of manic or mixed episodes associated with Bipolar I disorder as monotherapy or adjunctive treatment to lithium or valproate and maintenance monotherapy treatment in Bipolar I disorder. Vraylar is indicated for treatment of schizophrenia, acute treatment of manic or mixed episodes associated with Bipolar I disorder and treatment of depressive episodes associated with Bipolar I disorder (bipolar depression). Secuado is indicated for the treatment of adults with schizophrenia.

The American Psychiatric Association (APA) considers certain atypical (second-generation) antipsychotic agents (e.g., aripiprazole, olanzapine, quetiapine, risperidone, ziprasidone) first-line drugs for the management of the acute phase of schizophrenia (including first psychotic episodes), principally because of the decreased risk of adverse extrapyramidal effects and tardive dyskinesia, with the understanding that the relative advantages, disadvantages, and cost-effectiveness of conventional and atypical antipsychotic agents remain controversial. The APA states, with the possible exception of clozapine for the management of treatment-resistant symptoms, there currently is no definitive evidence that one atypical antipsychotic agent will have superior efficacy compared with another agent in the class, although meaningful differences in response may be observed in individual patients. The APA considers atypical (second-generation) antipsychotics preferred over typical antipsychotics because of their more benign side effect profile with most of the evidence supporting the use of olanzapine or risperidone with alternatives ziprasidone and quetiapine in lieu of another antipsychotic for bipolar disorder, severe manic or mixed episodes. The APA considers that second-generation antipsychotic medications (e.g., aripiprazole, olanzapine, quetiapine, risperidone) may increase the rates of response or remission of depressive symptoms in patients who typically have not responded to more than two antidepressant medication trials, even when psychotic symptoms are not present. Patient response and tolerance to antipsychotic agents are variable, and patients who do not respond to or tolerate one drug may be successfully treated with an agent from a different class or with a different adverse effect profile.¹⁰⁻¹²

Therefore, if the patient had an inadequate treatment response, intolerance, or a contraindication to one of the following: aripiprazole, olanzapine, paliperidone, quetiapine, quetiapine extended release, risperidone, or ziprasidone, the requested drug should be approved.

REFERENCES

1. Caplyta [package insert]. New York, NY: Intra-Cellular Therapies, Inc.; December 2019
2. Fanapt [package insert]. Washington, DC: Vanda Pharmaceuticals.; January 2016.
3. Latuda [package insert]. Marlborough, MA: Sunovion Pharmaceuticals Inc.; March 2018.
4. Rexulti [package insert]. Rockville, MD: Otsuka America Pharmaceutical, Inc.; February 2018.
5. Saphris [package insert]. Irvine, CA: Allergan USA Inc.; January 2017.
6. Secuado [package insert]. Miami, Florida: Noven Therapeutics, LLC.; October 2019
7. Vraylar [package insert]. Madison, NJ: Allergan USA, Inc.; May 2019.

8. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed March 2019.
9. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed March 2019.
10. American Psychiatric Association. Practice guideline for the treatment of patients with schizophrenia. *Am J Psychiatry*. 2004; 161: (Suppl) 1-56. Available at: https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/schizophrenia.pdf. Accessed March 2019.
11. American Psychiatric Association. Practice Guideline for the treatment of patients with major depressive disorder, Third Edition. October 2010. Available at: https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/mdd.pdf. Accessed March 2019.
12. American Psychiatric Association. Practice Guideline for the treatment of patients with bipolar disorder, Second Edition. April 2002. Available at: https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/bipolar.pdf. Accessed March 2019.

Written by: UM Development (SE)
 Date Written: 02/2016
 Revised: 05/2016 (no clinical changes), (SE) 06/2016 (created separate Med D), (JK) 05/2017 (added supplemental indication for Saphris), (JK) 05/2017 (annual review; removed CI), (ME) 05/2018 (extended DOA), 03/2019 (added Latuda), 06/2019 (added new FDA indication for Vraylar), 11/2019 (added Secuado), 01/2020 (added Caplyta)
 Reviewed: Medical Affairs (DHR) 02/2016, (DNC) 05/2017, (AN) 05/2017, (LMS) 03/2019, (EPA) 06/2019, (CHART) 11/14/19, (CHART) 01/16/20
 External Review: 03/2016, 08/2016, 08/2017, 08/2018, 08/2019, 12/2019 (FYI P&T), 01/2020

CRITERIA FOR APPROVAL

1	Is the request for Caplyta, Fanapt or Secuado? [If no, then skip to question 3.]	Yes	No
2	Is the requested drug being prescribed for the treatment of schizophrenia? [If yes, then skip to question 10.] [If no, then no further questions.]	Yes	No
3	Is the request for Rexulti? [If no, then skip to question 5.]	Yes	No
4	Is the requested drug being prescribed for any of the following: A) Adjunctive treatment of major depressive disorder (MDD), B) Treatment of schizophrenia? [If yes, then skip to question 10.] [If no, then no further questions.]	Yes	No
5	Is the request for Saphris? [If no, then skip to question 7.]	Yes	No
6	Is the requested drug being prescribed for any of the following: A) Schizophrenia, B) Acute treatment of manic or mixed episodes associated with Bipolar I disorder as monotherapy or adjunctive treatment to lithium or valproate, C) Maintenance monotherapy treatment in Bipolar I disorder? [If yes, then skip to question 10.] [If no, then no further questions.]	Yes	No
7	Is the request for Vraylar? [If no, then skip to question 9.]	Yes	No

- | | | | |
|----|---|-----|----|
| 8 | Is the requested drug being prescribed for any of the following: A) Treatment of schizophrenia, B) Acute treatment of manic or mixed episodes associated with bipolar I disorder, C) Treatment of depressive episodes associated with bipolar I disorder (bipolar depression)?
[If yes, then skip to question 10.] | Yes | No |
| 9 | Is the requested drug being prescribed for any of the following: A) Schizophrenia, B) Adjunctive treatment with lithium or valproate for major depressive episodes associated with Bipolar I disorder (bipolar depression), C) Monotherapy treatment of major depressive episodes associated with Bipolar I disorder (bipolar depression)?
[If no, then no further questions.] | Yes | No |
| 10 | Has the patient experienced an inadequate treatment response, intolerance, or contraindication to one of the following: A) aripiprazole, B) olanzapine, C) paliperidone, D) quetiapine, E) quetiapine extended release, F) risperidone, G) ziprasidone? | Yes | No |

Mapping Instructions

	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Go to 3	
2.	Go to 10	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you are using it for an approved use. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
3.	Go to 4	Go to 5	
4.	Go to 10	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you are using it for an approved use. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
5.	Go to 6	Go to 7	
6.	Go to 10	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you are using it for an approved use. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
7.	Go to 8	Go to 9	
8.	Go to 10	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you are using it for an approved use. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
9.	Go to 10	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you are using it for an approved use. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
10.	Approve, 36 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have tried one of the following: aripiprazole, olanzapine, paliperidone, quetiapine, quetiapine extended release, risperidone, or ziprasidone and it did not work for you or you cannot take it. Your request has been denied based on the information we have. [Short Description: No inadequate response, intolerance or contraindication to other atypical antipsychotic drugs]

SPECIALTY GUIDELINE MANAGEMENT

AUBAGIO (teriflunomide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication: Aubagio is indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Relapsing forms of multiple sclerosis

Authorization of 12 months may be granted to members who have been diagnosed with a relapsing form of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse).

B. Clinically isolated syndrome

Authorization of 12 months may be granted to members for the treatment of clinically isolated syndrome of multiple sclerosis.

III. CONTINUATION OF THERAPY

For all indications: Authorization of 12 months may be granted to members who are experiencing disease stability or improvement while receiving Aubagio.

IV. OTHER CRITERIA

Members will not use Aubagio concomitantly with other medications used for the treatment of multiple sclerosis, excluding Ampyra.

V. REFERENCE

1. Aubagio [package insert]. Cambridge, MA: Genzyme Corporation; September 2019.

SPECIALTY GUIDELINE MANAGEMENT

AUSTEDO (deutetrabenazine)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Treatment of chorea associated with Huntington's disease
2. Treatment of tardive dyskinesia in adults

B. Compendial Uses

Tourette's syndrome

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Documentation of score of items 1 to 7 of the Abnormal Involuntary Movement Scale (AIMS) for tardive dyskinesia.

III. CRITERIA FOR INITIAL APPROVAL

A. **Chorea associated with Huntington's disease**

Authorization of 6 months may be granted for treatment of chorea associated with Huntington's disease when both of the following criteria are met:

1. Member demonstrates characteristic motor examination features
2. Member meets one of the following conditions:
 - i. Laboratory results indicate an expanded *HTT* CAG repeat sequence of at least 36
 - ii. Member has a positive family history for Huntington's disease

B. **Tardive dyskinesia**

Authorization of 6 months may be granted for treatment of tardive dyskinesia when the baseline AIMS score for items 1 to 7 is obtained.

C. **Tourette's syndrome**

Authorization of 6 months may be granted for treatment of Tourette's syndrome.

IV. CONTINUATION OF THERAPY

A. Tardive Dyskinesia

Authorization of 12 months may be granted for treatment of tardive dyskinesia when the member's tardive dyskinesia symptoms have improved as indicated by a decreased AIMS score (items 1 to 7) from baseline.

B. Other Indications

Authorization of 12 months may be granted for treatment of chorea associated with Huntington's disease and Tourette's syndrome when the disease has improved or stabilized.

V. REFERENCES

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PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

AVASTIN
(bevacizumab)

MVASI
(bevacizumab-awwb)

ZIRABEV
(bevacizumab-bvzr)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

MDC
Ref # 799-A

FDA-APPROVED INDICATIONS¹⁻³

- Metastatic colorectal cancer:
 - a) In combination with IV 5-fluorouracil-based chemotherapy for first- or second-line treatment
 - b) In combination with fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatin-based chemotherapy for second-line treatment in patients who have progressed on a first-line Avastin-containing regimen
- Non-squamous non-small cell lung cancer (NSCLC), with carboplatin and paclitaxel for first line treatment of unresectable, locally advanced, recurrent or metastatic disease
- Recurrent glioblastoma in adults
- Metastatic renal cell carcinoma with interferon alfa
- Cervical cancer, in combination with paclitaxel and cisplatin or paclitaxel and topotecan in persistent, recurrent, or metastatic disease
- Avastin for epithelial ovarian, fallopian tube or primary peritoneal cancer
 - a) In combination with carboplatin and paclitaxel, followed by Avastin as a single agent, for patients with stage III or IV disease following initial surgical resection.
 - b) In combination with paclitaxel, pegylated liposomal doxorubicin or topotecan for patients with platinum-resistant disease who received no more than 2 prior chemotherapy regimens
 - c) Either in combination with carboplatin and paclitaxel or in combination with carboplatin and gemcitabine, followed by Avastin as a single agent in patients with platinum-sensitive disease

Compendial Uses⁴⁻²¹

- Breast cancer
- Central nervous system (CNS) cancers
 - Adult intracranial and spinal ependymoma
 - Anaplastic gliomas
- Malignant pleural mesothelioma
- Ovarian cancer
 - Malignant sex cord-stromal tumors
- Soft tissue sarcoma
 - AIDS-related Kaposi sarcoma
 - Angiosarcoma
 - Solitary fibrous tumor/Hemangiopericytoma
- Uterine/Endometrial cancer
- Ophthalmic-related disorders
 - Diabetic macular edema
 - Neovascular (wet) age-related macular degeneration (AMD) (includes polypoidal choroidopathy and retinal angiomatous proliferation subtypes)
 - Macular edema following retinal vein occlusion (RVO)

- Proliferative diabetic retinopathy
- Choroidal neovascularization (CNV)
- Neovascular glaucoma; adjunct
- Retinopathy of prematurity

B vs D CRITERIA FOR DETERMINATION

1	Is the requested drug being supplied from the physician and/or office stock supply and billed as part of a physician service (i.e., the drug is being furnished “incident to a physician’s service”)? [If yes, no further questions.]	Yes	No
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CRITERIA FOR APPROVAL

2	Does the patient have a diagnosis of any of the following retinal disorders: A) diabetic macular edema, B) neovascular (wet) age-related macular degeneration (includes polypoidal choroidopathy and retinal angiomatous proliferation subtypes), C) macular edema following retinal vein occlusion (RVO), D) proliferative diabetic retinopathy, E) choroidal neovascularization (CNV), F) neovascular glaucoma, or G) retinopathy of prematurity? [If yes, no further questions.]	Yes	No
3	Does the patient have any of the following diagnoses: A) breast cancer, B) malignant pleural mesothelioma, C) cervical cancer, D) renal cell carcinoma, E) uterine cancer, or F) endometrial cancer? [If yes, no further questions.]	Yes	No
4	Does the patient have a diagnosis of any of the following central nervous system cancer tumor types: A) glioblastoma, B) anaplastic gliomas, or C) adult intracranial and spinal ependymoma? [If yes, no further questions.]	Yes	No
5	Does the patient have a diagnosis of any of the following soft tissue sarcoma types: A) acquired immune deficiency syndrome (AIDS)-related Kaposi sarcoma B) angiosarcoma, or C) solitary fibrous tumor/hemangiopericytoma? [If yes, no further questions.]	Yes	No
6	Does the patient have a diagnosis of colorectal cancer (includes appendix cancer and small bowel cancer)? [If yes, no further questions.]	Yes	No
7	Does the patient have a diagnosis of non-squamous non-small cell lung cancer? [If yes, no further questions.]	Yes	No
8	Does the patient have a diagnosis of: A) epithelial ovarian cancer, B) fallopian tube cancer, or C) primary peritoneal cancer? [If yes, no further questions.]	Yes	No
9	Does the patient have a diagnosis of ovarian malignant sex cord-stromal tumor?	Yes	No

Continue to Clinical Questions if:

Guidelines for Determination	
Process through Medicare Part D	
Set 1	
Yes to question(s)	No to question(s)
None	1

For any other scenarios other than the Set above, close PA, drug is not covered as Part D

Approve if:

Guidelines for Approval							
Duration of Approval				12 months			
Set 1: Retinal disorders		Set 2: Breast cancer, RCC, Cervical cancer, Malignant pleural mesothelioma, Uterine cancer, Endometrial cancer		Set 3: CNS Cancer		Set 4: STS	
Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)
2	None	3	2	4	2	5	2
					3		3
							4
Set 5: CRC		Set 6: NSCLC		Set 7: Epithelial ovarian, fallopian tube, and primary peritoneal cancer		Set 8: Malignant sex cord-stromal tumors	
Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)
6	2	7	2	8	2	9	2
	3		3		3		3
	4		4		4		4
	5		5		5		5
			6		6		6
					7		7
							8

Mapping Instructions		
	Yes	No
1	Close PA, drug is not covered as Part D	Go to 2
2	Approve, 12 months	Go to 3
3	Approve, 12 months	Go to 4
4	Approve, 12 months	Go to 5
5	Approve, 12 months	Go to 6
6	Approve, 12 months	Go to 7
7	Approve, 12 months	Go to 8
8	Approve, 12 months	Go to 9
9	Approve, 12 months	Deny

RATIONALE

These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare-approved compendia.

The intent of the criteria is to:

1. Determine if the medication should be processed through Medicare Part D.
2. Ensure that patients follow selection elements noted in labeling and/or practice guidelines in order to decrease the potential for inappropriate utilization.

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1. Avastin [package insert]. South San Francisco, CA: Genentech, Inc.; June 2019.
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DOCUMENT HISTORY

Written: Specialty Clinical Development (KP) 01/2012
Revised: KP 09/2012 (CMS), LD 06/2013 (CMS), KF/ST 01/2014, ST 09/2014(CMS), JP 02/2015, 09/2015 (CMS), HY 01/2015, PK 02/2016 (ophthalmology), PK/HY 06/2016 (CMS), HY 01/2017 (ovarian CA), ST 01/2017 (annual), 07/2017 (CMS), TE 01/2018, TE 02/2018 (ophthalmology), TE 07/2018 (CMS), BI 07/2019 (CMS), SP 01/2020 (added Zirabev)
Reviewed: CDPR/KP 01/2012, DNC 04/2013, 01/2014, KJC 08/2014, DNC/KRU 02/2015, DHR 01/2016, SD 12/2016; MC 01/2017, AN 02/2017, ME 01/2018, AN 02/2018, LMS 02/2018, MMF 01/2020
External Review: 06/2012, 05/2013, 03/2014, 03/2015, 04/2016, 03/2017, 03/2018, 05/2018, 01/2020

SPECIALTY GUIDELINE MANAGEMENT

AVASTIN (bevacizumab) MVASI (bevacizumab-awwb) ZIRABEV (bevacizumab-bvzr)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Metastatic colorectal cancer (mCRC)
 - a. Avastin, Mvasi, or Zirabev, in combination with intravenous fluorouracil-based chemotherapy, is indicated for the first- or second-line treatment of patients with metastatic colorectal cancer.
 - b. Avastin, Mvasi, or Zirabev, in combination with fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatin-based chemotherapy, is indicated for the second-line treatment of patients with metastatic colorectal cancer who have progressed on a first-line bevacizumab-containing regimen.
2. First-line non-squamous non-small cell lung cancer (NSCLC)
Avastin, Mvasi, or Zirabev, in combination with carboplatin and paclitaxel, is indicated for the first-line treatment of patients with unresectable, locally advanced, recurrent or metastatic non-squamous non-small cell lung cancer.
3. Recurrent glioblastoma (RGM)
Avastin, Mvasi, or Zirabev, is indicated for the treatment of recurrent glioblastoma in adults.
4. Metastatic renal cell carcinoma (mRCC)
Avastin, Mvasi, or Zirabev, in combination with interferon alfa, is indicated for the treatment of metastatic renal cell carcinoma.
5. Persistent, recurrent, or metastatic cervical cancer
Avastin, Mvasi, or Zirabev, in combination with paclitaxel and cisplatin or paclitaxel and topotecan, is indicated for the treatment of patients with persistent, recurrent, or metastatic cervical cancer.
6. Epithelial ovarian, fallopian tube, or primary peritoneal cancer
 - a. Avastin, in combination with carboplatin and paclitaxel, followed by Avastin as a single agent, is indicated for the treatment of patients with stage III or IV epithelial ovarian, fallopian tube, or primary peritoneal cancer following initial surgical resection.
 - b. Avastin, in combination with paclitaxel, pegylated liposomal doxorubicin, or topotecan, is indicated for the treatment of patients with platinum-resistant recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer who received no more than 2 prior chemotherapy regimens.
 - c. Avastin, in combination with carboplatin and paclitaxel, or with carboplatin and gemcitabine, followed by Avastin as a single agent, is indicated for the treatment of patients with platinum-sensitive recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer.

B. Compendial Uses

1. Breast cancer for recurrent or stage IV (M1) human epidermal growth factor receptor 2 (HER2)-negative disease
2. Central nervous system (CNS) cancers
 - a. Low-grade (WHO Grade II) infiltrative supratentorial astrocytoma/oligodendroglioma
 - b. Intracranial and spinal ependymoma (excluding subependymoma)
 - c. Anaplastic gliomas
 - d. Medulloblastoma

- e. Primary central nervous system lymphoma
- f. Meningiomas
- g. Limited and extensive brain metastases
- h. Leptomeningeal metastases
- i. Metastatic spine tumors
- 3. Malignant pleural mesothelioma
- 4. Ovarian cancer/Fallopian tube cancer/Primary peritoneal cancer
 - a. Carcinosarcoma (malignant mixed Müllerian tumors)
 - b. Clear cell carcinoma
 - c. Mucinous carcinoma
 - d. Grade 1 endometrioid carcinoma
 - e. Low-grade serous carcinoma
 - f. Ovarian borderline epithelial tumors (low malignant potential) with invasive implants
 - g. Malignant sex cord-stromal tumors
- 5. Soft tissue sarcoma
 - a. Angiosarcoma
 - b. Solitary fibrous tumor/Hemangiopericytoma
- 6. AIDS-related Kaposi sarcoma
- 7. Uterine/Endometrial cancer
- 8. Vulvar cancer
- 9. Peritoneal mesothelioma
- 10. Pericardial mesothelioma
- 11. Tunica vaginalis testis mesothelioma
- 12. Small bowel adenocarcinoma
- 13. Appendiceal carcinoma
- 14. Anal adenocarcinoma
- 15. Ophthalmic disorders
 - a. Diabetic macular edema
 - b. Neovascular (wet) age-related macular degeneration (AMD)
 - c. Macular edema following retinal vein occlusion (RVO)
 - d. Proliferative diabetic retinopathy
 - e. Choroidal neovascularization (CNV)
 - f. Neovascular glaucoma; adjunct
 - g. Retinopathy of prematurity
 - h. Polypoidal choroidal vasculopathy

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Ophthalmic disorders

Authorization of 6 months may be granted for treatment of the following retinal disorders:

- 1. Diabetic macular edema
- 2. Neovascular (wet) age-related macular degeneration
- 3. Macular edema following retinal vein occlusion
- 4. Proliferative diabetic retinopathy
- 5. Choroidal neovascularization (including myopic choroidal neovascularization, angioid streaks, choroiditis [including choroiditis secondary to ocular histoplasmosis], idiopathic degenerative myopia, retinal dystrophies, rubeosis iridis, pseudoxanthoma elasticum, and trauma)
- 6. Neovascular glaucoma
- 7. Retinopathy of prematurity
- 8. Polypoidal choroidal vasculopathy

B. Colorectal cancer (CRC)

Authorization of 12 months may be granted for treatment of colorectal cancer, including small bowel adenocarcinoma, appendiceal carcinoma, and anal adenocarcinoma.

C. Non-small cell lung cancer (NSCLC)

Authorization of 12 months may be granted for treatment of recurrent, advanced, or metastatic non-squamous NSCLC.

D. CNS cancer

Authorization of 12 months may be granted for treatment of the following types of CNS cancer:

1. Glioblastoma
2. Intracranial and spinal ependymoma (excludes subependymoma)
3. Anaplastic gliomas
4. Low-grade (WHO Grade II) infiltrative supratentorial astrocytoma/oligodendroglioma
5. Medulloblastoma
6. Primary central nervous system lymphoma
7. Meningiomas
8. Limited and extensive brain metastases
9. Leptomeningeal metastases
10. Metastatic spine tumors

E. Ovarian cancer/Fallopian tube cancer/Primary peritoneal cancer

Authorization of 12 months may be granted for treatment of the following types of ovarian cancer, fallopian tube cancer, and primary peritoneal cancer:

1. Epithelial ovarian cancer, including:
 - i. Carcinosarcoma (malignant mixed Müllerian tumors)
 - ii. Clear cell carcinoma
 - iii. Mucinous carcinoma
 - iv. Grade 1 endometrioid carcinoma
 - v. Low-grade serous carcinoma
 - vi. Borderline epithelial tumors (low malignant potential) with invasive implants
 - vii. Malignant sex cord-stromal tumors
2. Fallopian tube cancer
3. Primary peritoneal cancer

F. Uterine/Endometrial cancer

Authorization of 12 months may be granted for treatment of progressive, advanced, or recurrent uterine cancer or endometrial cancer.

G. Cervical/Vaginal cancer

Authorization of 12 months may be granted for treatment of persistent, recurrent, or metastatic cervical or vaginal cancer.

H. Breast cancer

Authorization of 12 months may be granted for treatment of breast cancer.

I. Renal cell carcinoma

Authorization of 12 months may be granted for treatment of relapsed or metastatic renal cell carcinoma.

J. Soft tissue sarcoma

Angiosarcoma

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Authorization of 12 months may be granted for treatment of angiosarcoma, as single agent therapy.

Solitary fibrous tumor/hemangiopericytoma

Authorization of 12 months may be granted for treatment of solitary fibrous tumor or hemangiopericytoma, in combination with temozolomide.

K. Malignant pleural mesothelioma

Authorization of 12 months may be granted for treatment of malignant pleural mesothelioma, in combination with pemetrexed and either cisplatin or carboplatin, followed by single agent maintenance therapy.

L. AIDS-related Kaposi sarcoma

Authorization of 12 months may be granted for treatment of AIDS-related Kaposi sarcoma.

M. Vulvar cancer

Authorization of 12 months may be granted for treatment of unresectable locally advanced, recurrent, or metastatic vulvar cancer.

N. Peritoneal mesothelioma

Authorization of 12 months may be granted for treatment of peritoneal mesothelioma.

O. Pericardial mesothelioma

Authorization of 12 months may be granted for treatment of pericardial mesothelioma.

P. Tunica vaginalis testis mesothelioma

Authorization of 12 months may be granted for treatment of tunica vaginalis testis mesothelioma.

III. CONTINUATION OF THERAPY

A. Ophthalmic disorders

For ophthalmic disorders, authorization of 12 months may be granted for continued treatment of an indication outlined in Section II for members who have demonstrated a positive clinical response to therapy (e.g., improvement or maintenance in best corrected visual acuity [BCVA] or visual field, or a reduction in the rate of vision decline or the risk of more severe vision loss).

B. All other indications

For all other indications, authorization of 12 months may be granted for continued treatment of an indication outlined in Section II for members who are experiencing a clinical benefit to therapy or who have not experienced an unacceptable toxicity.

IV. REFERENCES

1. Avastin [package insert]. South San Francisco, CA: Genentech, Inc.; June 2019.
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SPECIALTY GUIDELINE MANAGEMENT

AVASTIN (bevacizumab) MVASI (bevacizumab-awwb) ZIRABEV (bevacizumab-bvzr)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Metastatic colorectal cancer (mCRC)
 - a. Avastin, Mvasi, or Zirabev, in combination with intravenous fluorouracil-based chemotherapy, is indicated for the first- or second-line treatment of patients with metastatic colorectal cancer.
 - b. Avastin, Mvasi, or Zirabev, in combination with fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatin-based chemotherapy, is indicated for the second-line treatment of patients with metastatic colorectal cancer who have progressed on a first-line bevacizumab-containing regimen.
2. First-line non-squamous non-small cell lung cancer (NSCLC)
Avastin, Mvasi, or Zirabev, in combination with carboplatin and paclitaxel, is indicated for the first-line treatment of patients with unresectable, locally advanced, recurrent or metastatic non-squamous non-small cell lung cancer.
3. Recurrent glioblastoma (RGM)
Avastin, Mvasi, or Zirabev, is indicated for the treatment of recurrent glioblastoma in adults.
4. Metastatic renal cell carcinoma (mRCC)
Avastin, Mvasi, or Zirabev, in combination with interferon alfa, is indicated for the treatment of metastatic renal cell carcinoma.
5. Persistent, recurrent, or metastatic cervical cancer
Avastin, Mvasi, or Zirabev, in combination with paclitaxel and cisplatin or paclitaxel and topotecan, is indicated for the treatment of patients with persistent, recurrent, or metastatic cervical cancer.
6. Epithelial ovarian, fallopian tube, or primary peritoneal cancer
 - a. Avastin, in combination with carboplatin and paclitaxel, followed by Avastin as a single agent, is indicated for the treatment of patients with stage III or IV epithelial ovarian, fallopian tube, or primary peritoneal cancer following initial surgical resection.
 - b. Avastin, in combination with paclitaxel, pegylated liposomal doxorubicin, or topotecan, is indicated for the treatment of patients with platinum-resistant recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer who received no more than 2 prior chemotherapy regimens.
 - c. Avastin, in combination with carboplatin and paclitaxel, or with carboplatin and gemcitabine, followed by Avastin as a single agent, is indicated for the treatment of patients with platinum-sensitive recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer.

B. Compendial Uses

1. Breast cancer for recurrent or stage IV (M1) human epidermal growth factor receptor 2 (HER2)-negative disease
2. Central nervous system (CNS) cancers
 - a. Low-grade (WHO Grade II) infiltrative supratentorial astrocytoma/oligodendroglioma
 - b. Intracranial and spinal ependymoma (excluding subependymoma)
 - c. Anaplastic gliomas
 - d. Medulloblastoma

- e. Primary central nervous system lymphoma
- f. Meningiomas
- g. Limited and extensive brain metastases
- h. Leptomeningeal metastases
- i. Metastatic spine tumors
- 3. Malignant pleural mesothelioma
- 4. Ovarian cancer/Fallopian tube cancer/Primary peritoneal cancer
 - a. Carcinosarcoma (malignant mixed Müllerian tumors)
 - b. Clear cell carcinoma
 - c. Mucinous carcinoma
 - d. Grade 1 endometrioid carcinoma
 - e. Low-grade serous carcinoma
 - f. Ovarian borderline epithelial tumors (low malignant potential) with invasive implants
 - g. Malignant sex cord-stromal tumors
- 5. Soft tissue sarcoma
 - a. Angiosarcoma
 - b. Solitary fibrous tumor/Hemangiopericytoma
- 6. AIDS-related Kaposi sarcoma
- 7. Uterine/Endometrial cancer
- 8. Vulvar cancer
- 9. Peritoneal mesothelioma
- 10. Pericardial mesothelioma
- 11. Tunica vaginalis testis mesothelioma
- 12. Small bowel adenocarcinoma
- 13. Appendiceal carcinoma
- 14. Anal adenocarcinoma
- 15. Hepatocellular carcinoma
- 16. Ophthalmic disorders
 - a. Diabetic macular edema
 - b. Neovascular (wet) age-related macular degeneration (AMD)
 - c. Macular edema following retinal vein occlusion (RVO)
 - d. Proliferative diabetic retinopathy
 - e. Choroidal neovascularization (CNV)
 - f. Neovascular glaucoma; adjunct
 - g. Retinopathy of prematurity
 - h. Polypoidal choroidal vasculopathy

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Ophthalmic disorders

Authorization of 6 months may be granted for treatment of the following retinal disorders:

- 1. Diabetic macular edema
- 2. Neovascular (wet) age-related macular degeneration
- 3. Macular edema following retinal vein occlusion
- 4. Proliferative diabetic retinopathy
- 5. Choroidal neovascularization (including myopic choroidal neovascularization, angioid streaks, choroiditis [including choroiditis secondary to ocular histoplasmosis], idiopathic degenerative myopia, retinal dystrophies, rubeosis iridis, pseudoxanthoma elasticum, and trauma)
- 6. Neovascular glaucoma
- 7. Retinopathy of prematurity

8. Polypoidal choroidal vasculopathy

B. Colorectal cancer (CRC)

Authorization of 12 months may be granted for treatment of colorectal cancer, including small bowel adenocarcinoma, appendiceal carcinoma, and anal adenocarcinoma.

C. Non-small cell lung cancer (NSCLC)

Authorization of 12 months may be granted for treatment of recurrent, advanced, or metastatic non-squamous NSCLC.

D. CNS cancer

Authorization of 12 months may be granted for treatment of the following types of CNS cancer:

1. Glioblastoma
2. Intracranial and spinal ependymoma (excludes subependymoma)
3. Anaplastic gliomas
4. Low-grade (WHO Grade II) infiltrative supratentorial astrocytoma/oligodendroglioma
5. Medulloblastoma
6. Primary central nervous system lymphoma
7. Meningiomas
8. Limited and extensive brain metastases
9. Leptomeningeal metastases
10. Metastatic spine tumors

E. Ovarian cancer/Fallopian tube cancer/Primary peritoneal cancer

Authorization of 12 months may be granted for treatment of the following types of ovarian cancer, fallopian tube cancer, and primary peritoneal cancer:

1. Epithelial ovarian cancer, including:
 - i. Carcinosarcoma (malignant mixed Müllerian tumors)
 - ii. Clear cell carcinoma
 - iii. Mucinous carcinoma
 - iv. Grade 1 endometrioid carcinoma
 - v. Low-grade serous carcinoma
 - vi. Borderline epithelial tumors (low malignant potential) with invasive implants
 - vii. Malignant sex cord-stromal tumors
2. Fallopian tube cancer
3. Primary peritoneal cancer

F. Uterine/Endometrial cancer

Authorization of 12 months may be granted for treatment of progressive, advanced, or recurrent uterine cancer or endometrial cancer.

G. Cervical/Vaginal cancer

Authorization of 12 months may be granted for treatment of persistent, recurrent, or metastatic cervical or vaginal cancer.

H. Breast cancer

Authorization of 12 months may be granted for treatment of breast cancer.

I. Renal cell carcinoma

Authorization of 12 months may be granted for treatment of relapsed or metastatic renal cell carcinoma.

J. Soft tissue sarcoma

Angiosarcoma

Authorization of 12 months may be granted for treatment of angiosarcoma, as single agent therapy.

Solitary fibrous tumor/hemangiopericytoma

Authorization of 12 months may be granted for treatment of solitary fibrous tumor or hemangiopericytoma, in combination with temozolomide.

K. Malignant pleural mesothelioma

Authorization of 12 months may be granted for treatment of malignant pleural mesothelioma, in combination with pemetrexed and either cisplatin or carboplatin, followed by single agent maintenance therapy.

L. AIDS-related Kaposi sarcoma

Authorization of 12 months may be granted for treatment of AIDS-related Kaposi sarcoma.

M. Vulvar cancer

Authorization of 12 months may be granted for treatment of unresectable locally advanced, recurrent, or metastatic vulvar cancer.

N. Peritoneal mesothelioma

Authorization of 12 months may be granted for treatment of peritoneal mesothelioma.

O. Pericardial mesothelioma

Authorization of 12 months may be granted for treatment of pericardial mesothelioma.

P. Tunica vaginalis testis mesothelioma

Authorization of 12 months may be granted for treatment of tunica vaginalis testis mesothelioma.

Q. Hepatocellular carcinoma

Authorization of 12 months may be granted for treatment of hepatocellular carcinoma, in combination with atezolizumab.

III. CONTINUATION OF THERAPY

A. Ophthalmic disorders

For ophthalmic disorders, authorization of 12 months may be granted for continued treatment of an indication outlined in Section II for members who have demonstrated a positive clinical response to therapy (e.g., improvement or maintenance in best corrected visual acuity [BCVA] or visual field, or a reduction in the rate of vision decline or the risk of more severe vision loss).

B. All other indications

For all other indications, authorization of 12 months may be granted for continued treatment of an indication outlined in Section II for members who are experiencing a clinical benefit to therapy or who have not experienced an unacceptable toxicity.

IV. REFERENCES

1. Avastin [package insert]. South San Francisco, CA: Genentech, Inc.; June 2019.
2. Mvasi [package insert]. Thousand Oaks, CA: Amgen Inc.; June 2019.
3. Zirabev [package insert]. New York, NY: Pfizer Inc.; June 2019.
4. The NCCN Drugs & Biologics Compendium® © 2020 National Comprehensive Cancer Network, Inc. Available at: <https://www.nccn.org>. Accessed March 30, 2020.

5. Micromedex Solutions [database online]. Truven Health Analytics, Greenwood Village, CO. Available at: <http://www.micromedexsolutions.com>. Accessed January 7, 2020.
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9. Russo V, Barone A, Conte E, et al. Bevacizumab compared with macular laser grid photocoagulation for cystoid macular edema in branch retinal vein occlusion. *Retina*. 2009;29:511-5.
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12. Yazdani S, Hendi K, Pakravan M, et al. Intravitreal bevacizumab for neovascular glaucoma: a randomized controlled trial. *J Glaucoma*. 2009;18(8):632-637.
13. Mintz-Hittner HA, Kennedy KA, Chuang AZ, et al. Efficacy of intravitreal bevacizumab for stage 3+ retinopathy of prematurity. *N Engl J Med*. 2011;364(7):603-615.
14. American Academy of Ophthalmology Retinal/Vitreous Panel. Preferred Practice Pattern® Guidelines. Age-Related Macular Degeneration. San Francisco, CA: American Academy of Ophthalmology; 2015. Available at: <https://www.aao.org/preferred-practice-pattern/age-related-macular-degeneration-ppp-2015>.
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Reference number(s)
1891-A

26. PDQ® Adult Treatment Editorial Board. PDQ Vaginal Cancer Treatment. Bethesda, MD: National Cancer Institute. Updated November 15, 2019. Available at: <https://www.cancer.gov/types/vaginal/hp/vaginal-treatment-pdq>. Accessed January 8, 2020. [PMID: 26389242]
27. PDQ® Adult Treatment Editorial Board. PDQ Cervical Cancer Treatment. Bethesda, MD: National Cancer Institute. Updated December 12, 2019. Available at: <https://www.cancer.gov/types/cervical/hp/cervical-treatment-pdq>. Accessed January 8, 2020. [PMID: 26389493]

SPECIALTY GUIDELINE MANAGEMENT

AVEED (testosterone undecanoate injection)

POLICY

I. INDICATION

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Aveed is indicated for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone.

1. Primary hypogonadism (congenital or acquired): testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy, Klinefelter's syndrome, chemotherapy, or toxic damage from alcohol or heavy metals. These men usually have low serum testosterone concentrations and gonadotropins (follicle-stimulating hormone [FSH], luteinizing hormone [LH]) above the normal range.
2. Hypogonadotropic hypogonadism (congenital or acquired): gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency, or pituitary-hypothalamic injury from tumors, trauma, or radiation. These men have low testosterone serum concentrations but have gonadotropins in the normal or low range.

Aveed should only be used in patients who require testosterone replacement therapy and in whom the benefits of the product outweigh the serious risks of pulmonary oil microembolism and anaphylaxis.

Limitations of use:

- Safety and efficacy of Aveed in men with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established.
- Safety and efficacy of Aveed in males less than 18 years old have not been established.

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review: Pretreatment morning serum total testosterone concentrations

III. EXCLUSIONS

Coverage will not be provided for members with any of the following exclusions: Use for age-related hypogonadism or late-onset hypogonadism

IV. CRITERIA FOR INITIAL APPROVAL

Reference number(s)
2432-A

Primary hypogonadism or hypogonadotropic hypogonadism

Authorization of 12 months may be granted for treatment of primary hypogonadism or hypogonadotropic hypogonadism when all of the following criteria are met:

1. Member is a biological male or a person that self identifies as male.
2. Member is at least 18 years of age.
3. Member has at least two confirmed low morning serum total testosterone concentrations based on the reference laboratory range or current practice guidelines.

V. CONTINUATION OF THERAPY

For members requesting authorization for continuation of therapy with primary hypogonadism or hypogonadotropic hypogonadism who are not currently receiving Aveed therapy through samples or a manufacturer's patient assistance program, authorization of 12 months may be granted if the member meets criteria IV.1 and IV.2 above. All other members (including new members) must meet all initial authorization criteria.

VI. REFERENCES

1. Aveed [package insert]. Malvern, PA: Endo Pharmaceuticals Solutions Inc.; January 2018.
2. Bhasin S, Cunningham G, Hayes F, et al. Testosterone Therapy in Adult Men with Androgen Deficiency Syndromes: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab.* 2010;95(6):2536-59.

SPECIALTY GUIDELINE MANAGEMENT

AVONEX (interferon beta-1a)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Avonex is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

All other indications are considered experimental/investigational and are not covered benefits.

II. CRITERIA FOR INITIAL APPROVAL

A. Relapsing forms of multiple sclerosis

Authorization of 12 months may be granted to members who have been diagnosed with a relapsing form of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse).

B. Clinically isolated syndrome

Authorization of 12 months may be granted to members for the treatment of clinically isolated syndrome of multiple sclerosis.

III. CONTINUATION OF THERAPY

For all indications: Authorization of 12 months may be granted for members who are experiencing disease stability or improvement while receiving Avonex.

IV. OTHER CRITERIA

Members will not use Avonex concomitantly with other medications used for the treatment of multiple sclerosis, excluding Ampyra.

V. REFERENCES

1. Avonex [package insert]. Cambridge, MA: Biogen Inc.; July 2019.
2. AHFS DI (Adult and Pediatric) [database online]. Hudson, OH: Lexi-Comp, Inc.; http://online.lexi.com/lco/action/index/dataset/complete_ashp [available with subscription]. Accessed (April 2019).

Reference number
3491-A

SPECIALTY GUIDELINE MANAGEMENT

AYVAKIT (avapritinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Gastrointestinal Stromal Tumor (GIST)

Ayvakit is indicated for the treatment of adults with unresectable or metastatic GIST harboring a platelet-derived growth factor receptor alpha (PDGFRA) exon 18 mutation, including PDGFRA D842V mutations.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: PDGFRA exon 18 mutation testing (e.g., polymerase chain reaction [PCR]-based assay, next-generation sequencing [NGS]-based assay) results.

III. CRITERIA FOR INITIAL APPROVAL

Gastrointestinal Stromal Tumor (GIST)

Authorization of 12 months may be granted for treatment of gastrointestinal stromal tumor (GIST) when all of the following criteria are met:

1. The member has unresectable or metastatic disease.
2. The disease harbors a platelet-derived growth factor receptor alpha (PDGFRA) exon 18 mutation, including PDGFRA D842V mutations.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for gastrointestinal stromal tumor (GIST) who have not experienced disease progression or unacceptable toxicity.

V. REFERENCES

1. Ayvakit [package insert]. Cambridge, MA: Blueprint Medicines Corporation.; January 2020.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME (generic)	AYVAKIT (avapritinib)
Status: CVS Caremark Criteria Type: Initial Prior Authorization	MDC Ref # 3495-A

FDA-APPROVED INDICATION¹

Gastrointestinal Stromal Tumor (GIST)

Ayvakit is indicated for the treatment of adults with unresectable or metastatic GIST harboring a platelet-derived growth factor receptor alpha (PDGFRA) exon 18 mutation, including PDGFRA D842V mutations.

CRITERIA FOR APPROVAL

1	Does the patient have a diagnosis of gastrointestinal stromal tumor? [If no, no further questions.]	Yes	No
2	Does the patient have unresectable or metastatic disease? [If no, no further questions.]	Yes	No
3	Does the disease harbor a platelet-derived growth factor receptor alpha (PDGFRA) exon 18 mutation, including PDGFRA D842V mutations?	Yes	No

Guidelines for Approval	
Duration of Approval	12 Months
Set 1: GIST	
Yes to question(s)	No to question(s)
1	None
2	
3	

Mapping Instructions	
	No
1. Go to 2	Deny
2. Go to 3	Deny
3. Approve, 12 months	Deny

RATIONALE

These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to ensure that patients follow selection elements noted in labeling and/or practice guidelines in order to decrease the potential for inappropriate utilization.

REFERENCES

1. Ayvakit [package insert]. Cambridge, MA: Blueprint Medicines Corporation.; January 2020.

DOCUMENT HISTORY

Created: Specialty Clinical Development (BI) 01/2020
Revised:

Ayvakit 3495-A MDC 2020.docx

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SPECIALTY GUIDELINE MANAGEMENT

VIDAZA (azacitidine) azacitidine (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Myelodysplastic syndromes (MDS): Vidaza is indicated for treatment of patients with the following French-American-British (FAB) myelodysplastic syndrome subtypes: refractory anemia (RA) or refractory anemia with ringed sideroblasts (if accompanied by neutropenia or thrombocytopenia or requiring transfusions), refractory anemia with excess blasts (RAEB), refractory anemia with excess blasts in transformation (RAEB-T), and chronic myelomonocytic leukemia (CMML).

B. Compendial Uses

1. Acute myeloid leukemia (AML)
2. Accelerated phase or blast phase myelofibrosis

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Myelodysplastic syndromes (MDS)**

Authorization of 12 months may be granted for the treatment of MDS.

B. **Acute myeloid leukemia (AML)**

Authorization of 12 months may be granted for the treatment of AML.

C. **Accelerated phase or blast phase myelofibrosis**

Authorization of 12 months may be granted for the treatment of accelerated phase or blast phase myelofibrosis.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced disease progression or an unacceptable toxicity.

IV. REFERENCES

1. Vidaza [package insert]. Summit, NJ: Celgene Corporation; July 2018.
2. National Comprehensive Cancer Network. The NCCN Drugs & Biologics Compendium. <http://www.nccn.org>. Accessed July 9, 2019.

SPECIALTY GUIDELINE MANAGEMENT

BALVERSA (erdafitinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Balversa is indicated for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma (mUC), that has:

1. susceptible FGFR3 or FGFR2 genetic alterations, and
2. progressed during or following at least one line of prior platinum-containing chemotherapy, including within 12 months of neoadjuvant or adjuvant platinum-containing chemotherapy.

Select patients for therapy based on an FDA-approved companion diagnostic for Balversa.

This indication is approved under accelerated approval based on tumor response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Fibroblast growth factor receptor (FGFR)3 or FGFR2 mutation status

III. CRITERIA FOR INITIAL APPROVAL

Urothelial carcinoma

Authorization of 12 months may be granted for treatment of locally advanced or metastatic urothelial carcinoma when both of the following criteria are met:

1. Member has a susceptible FGFR3 or FGFR2 genetic alteration.
2. Disease progressed during or following at least one line of prior platinum-containing chemotherapy, including within 12 months of neoadjuvant or adjuvant platinum-containing chemotherapy.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced disease progression or an unacceptable toxicity.

Reference number(s)
2965-A

V. REFERENCES

1. Balversa [package insert]. Horsham, PA: Janssen Products, LP; April 2019.

SPECIALTY GUIDELINE MANAGEMENT

BAVENCIO (avelumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

- A. Metastatic Merkel Cell Carcinoma
Treatment of adults and pediatric patients 12 years and older with metastatic Merkel cell carcinoma
- B. Locally Advanced or Metastatic Urothelial Carcinoma
Treatment of patients with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy or have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy
- C. Advanced Renal Cell Carcinoma
First-line treatment of patients with advanced renal cell carcinoma in combination with axitinib

Compendial Indications

- A. Bladder cancer as subsequent systemic therapy post-platinum as a single agent
- B. Metastatic upper GU tract tumors as a single agent for subsequent systemic therapy post platinum
- C. Metastatic carcinoma of the prostate as a single agent for subsequent therapy post platinum
- D. Metastatic carcinoma of the urethra as a single agent for subsequent systemic therapy post platinum
- E. Kidney cancer used in combination with axitinib as first-line therapy for relapse or stage IV disease and clear cell histology

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

Coverage will not be provided for members who have experienced disease progression while on PD-1 or PD-L1 inhibitor therapy.

III. CRITERIA FOR INITIAL APPROVAL

A. Merkel Cell Carcinoma

Authorization of 6 months may be granted for the treatment of metastatic Merkel cell carcinoma.

B. Urothelial Carcinoma – Bladder Cancer

Authorization of 6 months may be granted as a single agent for treatment of bladder cancer when any of the following criteria is met:

1. As subsequent therapy following platinum-containing chemotherapy as a single agent for locally advanced or metastatic disease.
2. Member has metastatic or local recurrence post-cystectomy.

C. Urothelial Carcinoma – Primary Carcinoma of the Urethra

Authorization of 6 months may be granted for treatment of primary carcinoma of the urethra as a single agent for recurrent, locally advanced, or metastatic disease as subsequent systemic therapy following platinum-containing chemotherapy.

D. Urothelial Carcinoma – Upper Genitourinary Tract Tumors or Urothelial Carcinoma of the Prostate

Authorization of 6 months may be granted as a single agent for the treatment of locally advanced or metastatic upper genitourinary (GU) tract tumors or urothelial carcinoma of the prostate as subsequent therapy following platinum-containing chemotherapy.

E. Kidney cancer

Authorization of 6 months may be granted for treatment of advanced, relapsed, or stage IV kidney cancer including renal cell carcinoma when Bavencio is given in combination with axitinib as first-line treatment for the disease.

IV. CONTINUATION OF THERAPY

Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES

1. Bavencio [package insert]. New York, NY: Pfizer Inc.; May 2019.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed July 17, 2019.

SPECIALTY GUIDELINE MANAGEMENT

BELEODAQ (belinostat)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Treatment of patients with relapsed or refractory peripheral T-cell lymphoma (PTCL)

B. Compendial Uses

Non-Hodgkin's Lymphoma (NHL)

1. Adult T-cell leukemia/lymphoma (ATLL)
2. Mycosis fungoides (MF)/Sezary syndrome (SS)
3. Primary cutaneous CD30+ T-cell lymphoproliferative disorders: cutaneous anaplastic large cell lymphoma
4. Extranodal NK/T-cell lymphoma, nasal type
5. Hepatosplenic gamma-delta T-cell lymphoma

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Peripheral T-cell lymphoma (PTCL)**

Authorization of 12 months may be granted for treatment of PTCL when used for relapsed or refractory disease.

B. **Adult T-cell leukemia/lymphoma (ATLL)**

Authorization of 12 months may be granted for treatment of ATLL when both of the following criteria are met:

1. Beleodaq is used as a single agent.
2. Beleodaq is used for second-line or subsequent therapy.

C. **Mycosis fungoides (MF)/Sezary syndrome (SS)**

Authorization of 12 months may be granted for treatment of mycosis fungoides (MF)/Sezary syndrome (SS).

D. **Primary cutaneous CD30+ T-cell lymphoproliferative disorders**

Authorization of 12 months may be granted for treatment of cutaneous anaplastic large cell lymphoma (ALCL) when both of the following criteria are met:

1. Beleodaq is used as a single agent, and
2. The disease is relapsed or refractory

Reference number(s)
1701-A

E. Extranodal NK/T-cell lymphoma, nasal type

Authorization of 12 months may be granted for treatment of extranodal NK/T-cell lymphoma, nasal type when all of the following criteria are met:

1. Beleodaq will be used as a single agent.
2. Patient has relapsed or refractory disease.
3. Patient has had an inadequate response or contraindication to asparaginase-based therapy (e.g., pegaspargase).

F. Hepatosplenic gamma-delta T-cell lymphoma

Authorization of 12 months may be granted for treatment of hepatosplenic gamma-delta T-cell lymphoma when both of the following are met:

1. Beleodaq will be used a single agent.
2. The patient has had two or more previous lines of chemotherapy.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced disease progression or an unacceptable toxicity.

IV. REFERENCES

1. Beleodaq [package insert]. Irvine, CA: Spectrum Pharmaceuticals, Inc. April 2017.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. Available at: <https://www.nccn.org> Accessed April 18, 2019.

SPECIALTY GUIDELINE MANAGEMENT

BENLYSTA (belimumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Treatment of patients aged 5 years and older with active, autoantibody-positive, systemic lupus erythematosus (SLE) who are receiving standard therapy.

Limitations of Use

The efficacy of Benlysta has not been evaluated in patients with severe active lupus nephritis or severe active central nervous system lupus. Benlysta has not been studied in combination with other biologics or intravenous cyclophosphamide. Use of Benlysta is not recommended in these situations.

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

Coverage will not be provided for members with any of the following exclusions:

- A. Severe active lupus nephritis
- B. Severe active central nervous system lupus (including seizures that are attributed to CNS lupus, psychosis, organic brain syndrome, cerebrovascular accident, cerebritis, or CNS vasculitis requiring therapeutic intervention within 60 days before initiation of belimumab).
- C. Member is using Benlysta in combination with other biologics or intravenous cyclophosphamide.

III. CRITERIA FOR INITIAL APPROVAL

Systemic Lupus Erythematosus (SLE)

Authorization of 12 months may be granted for treatment of active SLE when all of the following criteria are met:

- A. Prior to initiating therapy, the member is positive for autoantibodies relevant to SLE.
- B. The member is receiving standard treatment for SLE with any of the following (alone or in combination):
 - 1. Glucocorticoids (e.g., prednisone, methylprednisolone, dexamethasone)
 - 2. Antimalarials (e.g., hydroxychloroquine)
 - 3. Immunosuppressives (e.g., azathioprine, methotrexate, mycophenolate, cyclosporine, cyclophosphamide)

IV. CONTINUATION OF THERAPY

Reference number
1764-A

Authorization of 12 months may be granted for all members (including new members) who are using Benlysta for an indication outlined in section III and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition.

V. REFERENCES

1. Benlysta [package insert]. Rockville, MD: Human Genome Sciences, Inc.; April 2019.
2. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. *Arthritis Rheumatol*. 2016;68(1)1-26.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME **BEOVU**
(generic) **(brolucizumab-dbl)**

Status: CVS/Caremark Criteria
Type: Initial Prior Authorization

MDC
Ref #3347-A

FDA-APPROVED INDICATIONS¹

Beovu is indicated for the treatment of patients with neovascular (wet) age-related macular degeneration.

CRITERIA FOR APPROVAL

1	Does the patient have a diagnosis of neovascular (wet) age-related macular degeneration?	Yes	No
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Guidelines for Approval

Duration of Approval		12 Months
Set 1: AMD		
Yes to question(s)		No to question(s)
1		None

Mapping Instructions

	Yes	No
1.	Approve, 12 months	Deny

RATIONALE

These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to ensure that patients follow selection elements noted in labeling and/or practice guidelines in order to decrease the potential for inappropriate utilization.

REFERENCES

1. Beovu [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; October 2019

DOCUMENT HISTORY

Written by: Specialty Clinical Development (KF) 10/2019
Revised:
Reviewed: CDPR/AN 10/2019
External Review: 11/2019

SPECIALTY GUIDELINE MANAGEMENT

BEOVU (brolucizumab-dblI)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Neovascular (wet) age-related macular degeneration

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Neovascular (Wet) Age-Related Macular Degeneration¹

Authorization of 6 months may be granted for treatment of neovascular (wet) age-related macular degeneration.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment of an indication listed in Section II for members who have demonstrated a positive clinical response to therapy (e.g., improvement or maintenance in best corrected visual acuity [BCVA] or visual field, or a reduction in the rate of vision decline or the risk of more severe vision loss).

IV. REFERENCES

1. Beovu [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; October 2019.

SPECIALTY GUIDELINE MANAGEMENT

BERINERT (C1 esterase inhibitor [human])

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Treatment of acute abdominal, facial, or laryngeal attacks of hereditary angioedema (HAE) in adult and pediatric patients.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

- A. C4 levels and C1 inhibitor functional and antigenic protein levels
- B. F12, angiopoietin-1 or plasminogen gene mutation testing, if applicable
- C. Chart notes confirming family history of angioedema, if applicable

III. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of hereditary angioedema attacks when the medication will not be used with Firazyr, Kalbitor, or Ruconest and either of the following criteria is met:

- A. Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing:
 - 1. C1 inhibitor (C1-INH) antigenic level below the lower limit of normal as defined by the laboratory performing the test; or
 - 2. Normal C1-INH antigenic level and a low C1-INH functional level (functional C1-INH less than 50% or C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test)
- B. Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
 - 1. Member has an F12, angiopoietin-1, or plasminogen gene mutation as confirmed by genetic testing, or
 - 2. Member has a documented family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine (e.g., cetirizine) for at least one month.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy when all of the following criteria are met:

- A. Member meets the criteria for initial approval.
- B. Member has experienced reduction in severity and/or duration of attacks when they use Berinert to treat an acute attack.

V. REFERENCES

1. Berinert [package insert]. Kankakee, IL: CSL Behring LLC; September 2017.
2. Bowen T, Cicardi M, Farkas H, et al. 2010 International consensus algorithm for the diagnosis, therapy, and management of hereditary angioedema. *Allergy Asthma Clin Immunol*. 2010;6(1):24.
3. Cicardi M, Bork K, Caballero T, et al. Hereditary Angioedema International Working Group. Evidence-based recommendations for the therapeutic management of angioedema owing to hereditary C1 inhibitor deficiency: consensus report of an International Working Group. *Allergy*. 2012;67:147-157.
4. Zuraw BL, Banerji A, Bernstein JA, et al. US Hereditary Angioedema Association Medical Advisory Board 2013 recommendations for the management of hereditary angioedema due to C1 inhibitor deficiency. *J Allergy Clin Immunol: In Practice*. 2013; 1(5): 458-467.
5. Zuraw BL, Bork K, Binkley KE, et al. Hereditary angioedema with normal C1 inhibitor function: consensus of an international expert panel. *Allergy Asthma Proc*. 2012; 33(6):S145-S156.
6. Maurer M, Magerl M, Ansotegui I, et al. The international WAO/EAACI guideline for the management of hereditary angioedema – the 2017 revision and update. *Allergy*. 2018;00:1-22.
7. Lang DM, Aberer W, Bernstein JA, et al. International consensus on hereditary and acquired angioedema. *Ann Allergy Asthma Immunol*. 2012; 109:395-202.
8. Cicardi M, Aberer W, Banerji A, et al. Classification, diagnosis, and approach to treatment for angioedema: consensus report from the Hereditary Angioedema International Working Group. *Allergy*. 2014;69: 602-616.
9. Bowen T. Hereditary angioedema: beyond international consensus – circa December 2010 – The Canadian Society of Allergy and Clinical Immunology Dr. David McCourtie Lecture. *Allergy Asthma Clin Immunol*. 2011;7(1):1.
10. Bernstein J. Update on angioedema: Evaluation, diagnosis, and treatment. *Allergy and Asthma Proceedings*. 2011;32(6):408-412.
11. Longhurst H, Cicardi M. Hereditary angio-edema. *Lancet*. 2012;379:474-481.
12. Farkas H, Martinez-Saguer I, Bork K, et al. International consensus on the diagnosis and management of pediatric patients with hereditary angioedema with C1 inhibitor deficiency. *Allergy*. 2017;72(2):300-313.
13. Henao MP, Kraschnewski J, Kelbel T, Craig T. Diagnosis and screening of patients with hereditary angioedema in primary care. *Therapeutics and Clin Risk Management*. 2016; 12: 701-711.

SPECIALTY GUIDELINE MANAGEMENT

BESPONSA (inotuzumab ozogamicin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Besponsa is indicated for the treatment of adults with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL).

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Testing or analysis confirming CD22 protein on the surface of the B-cell

III. CRITERIA FOR INITIAL APPROVAL

Acute lymphoblastic leukemia (ALL)

Authorization of 12 months may be granted for treatment of relapsed or refractory ALL when all of the following criteria are met:

- A. Member has B-cell precursor ALL.
- B. The tumor is CD22-positive as confirmed by testing or analysis to identify the CD22 protein on the surface of the B-cell.
- C. Member meets one of the following:
 1. Member has Philadelphia chromosome-positive disease and is intolerant or refractory to tyrosine kinase inhibitor therapy (e.g., imatinib, dasatinib, nilotinib, bosutinib, ponatinib).
 2. Member has Philadelphia chromosome-negative disease.
- D. Member will not receive more than 6 treatment cycles of Besponsa.

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. REFERENCES

1. Besponsa [package insert]. Philadelphia, PA: Wyeth Pharmaceuticals, Inc.; March 2018.
2. Kantarjian Hagop M, DeAngelo Daniel J., Stelljes Matthias, et al. Inotuzumab Ozogamicin versus Standard Therapy for Acute Lymphoblastic Leukemia. *N Engl J Med*. 2016; 375: 740-53.

Reference number(s)
2261-A

3. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed April 17, 2019.
4. The NCCN Clinical Practice Guidelines in Oncology® Acute Lymphoblastic Leukemia (Version 1.2019). © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed April 17, 2019.

QUANTITY LIMIT CRITERIA

DRUG CLASS **LONG ACTING BETA2-ADRENERGIC AGONIST, COMBINATIONS
ORAL INHALATION**

BRAND NAME*
(generic)

LONG-ACTING BETA2-ADRENERGIC AGONISTS:

ARCAPTA NEOHALER
(indacaterol)

BROVANA
(arformoterol tartrate)

PERFOROMIST
(formoterol)

SEREVENT DISKUS
(salmeterol)

STRIVERDI RESPIMAT
(olodaterol)

LONG-ACTING BETA2-ADRENERGIC AGONIST / ANTICHOLINERGIC:

ANORO ELLIPTA
(umeclidinium/vilanterol)

BEVESPI AEROSPHERE
(glycopyrrolate/formoterol)

DUAKLIR PRESSAIR
(aclidinium/formoterol)

STIOLTO RESPIMAT
(tiotropium bromide/olodaterol)

UTIBRON NEOHALER
(glycopyrrolate/indacaterol)

LONG-ACTING BETA2-ADRENERGIC AGONIST / CORTICOSTEROID:

ADVAIR DISKUS
(fluticasone propionate/salmeterol)

ADVAIR HFA
(fluticasone propionate/salmeterol)

AIRDUO RESPICLICK

(fluticasone propionate/salmeterol)

BREO ELLIPTA
(fluticasone furoate/vilanterol)

DULERA
(mometasone/formoterol)

SYMBICORT
(budesonide/formoterol)

LONG-ACTING BETA2-ADRENERGIC AGONIST / ANTICHOLINERGIC / CORTICOSTEROID:
TRELEGY ELLIPTA
(fluticasone furoate/umeclidinium/vilanterol)

Status: CVS Caremark Criteria

Type: Quantity Limit

Ref # 34-H

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Long-Acting Beta2-Adrenergic Agonists:

Arcapta Neohaler

Arcapta Neohaler is a long-acting beta -agonist indicated for long-term, once-daily maintenance bronchodilator treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema.

Arcapta Neohaler is not indicated to treat asthma. The safety and effectiveness of Arcapta Neohaler in asthma have not been established.

Brovana

Brovana (arformoterol tartrate) Inhalation Solution is indicated for the long-term, twice daily (morning and evening) maintenance treatment of bronchoconstriction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema. Brovana Inhalation Solution is for use by nebulization only.

Brovana Inhalation Solution is not indicated to treat asthma. The safety and effectiveness of Brovana Inhalation Solution in asthma have not been established.

Perforomist

Perforomist (formoterol fumarate) Inhalation Solution is indicated for the long-term, twice daily (morning and evening) administration in the maintenance treatment of bronchoconstriction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema.

Perforomist Inhalation Solution is not indicated to treat asthma. The safety and effectiveness of Perforomist Inhalation Solution in asthma have not been established.

Serevent Diskus

Treatment of Asthma

Serevent Diskus is indicated for the treatment of asthma and in the prevention of bronchospasm only as concomitant therapy with an inhaled corticosteroid (ICS) in patients aged 4 years and older with reversible obstructive airway disease, including patients with symptoms of nocturnal asthma. LABA, such as salmeterol, the active ingredient in Serevent Diskus, as monotherapy (without ICS) increase the risk of asthma related death. Use of Serevent Diskus for the treatment of asthma without concomitant use of an ICS is contraindicated. Use Serevent Diskus only as additional therapy for patients with asthma who are currently taking but are inadequately controlled on an ICS. Do not use Serevent Diskus for patients whose asthma is adequately controlled on low- or medium-dose ICS.

Available data from controlled clinical trials suggest that LABA as monotherapy increase the risk of asthma-related hospitalization in pediatric and adolescent patients. For pediatric and adolescent patients with asthma who require

addition of a LABA to an ICS, a fixed-dose combination product containing both an ICS and a LABA should ordinarily be used to ensure adherence with both drugs. In cases where use of a separate ICS and a LABA is clinically indicated, appropriate steps must be taken to ensure adherence with both treatment components. If adherence cannot be assured, a fixed-dose combination product containing both an ICS and a LABA is recommended.

Prevention of Exercise-Induced Bronchospasm

Serevent Diskus is also indicated for prevention of exercise-induced bronchospasm (EIB) in patients aged 4 years and older. Use of Serevent Diskus as a single agent for the prevention of EIB may be clinically indicated in patients who do not have persistent asthma. In patients with persistent asthma, use of Serevent Diskus for the prevention of EIB may be clinically indicated, but the treatment of asthma should include an ICS.

Maintenance Treatment of Chronic Obstructive Pulmonary Disease

Serevent Diskus is indicated for the long-term twice-daily administration in the maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease (COPD) (including emphysema and chronic bronchitis).

Striverdi Respimat

Striverdi Respimat is a long-acting beta2-agonist indicated for long-term, once-daily maintenance bronchodilator treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema.

Striverdi Respimat is not indicated to treat asthma. The safety and effectiveness of Striverdi Respimat in asthma have not been established.

Long-Acting Beta2-Adrenergic Agonist / Anticholinergic:

Anoro Ellipta

Anoro Ellipta is indicated for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD). Anoro Ellipta is NOT indicated for the treatment of asthma. The safety and efficacy of Anoro Ellipta in asthma have not been established.

Bevespi Aerosphere

Bevespi Aerosphere is a combination of glycopyrrolate and formoterol fumarate indicated for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema.

Bevespi Aerosphere is not indicated for the treatment of asthma.

Duaklir Pressair

Duaklir Pressair is a combination of aclidinium bromide (an anticholinergic) and formoterol fumarate (a LABA) indicated for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD).

Duaklir Pressair is not indicated for the relief of acute bronchospasm or for the treatment of asthma.

Stiolto Respimat

Stiolto Respimat is a combination of tiotropium and olodaterol indicated for long-term, once daily maintenance treatment of patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema.

Stiolto Respimat is not indicated to treat asthma. The safety and effectiveness of Stiolto Respimat in asthma have not been established.

Utibron Neohaler

Utibron Neohaler is a combination of indacaterol and glycopyrrolate indicated for the long-term, maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema.

Utibron Neohaler is NOT indicated for the treatment of asthma.

Long-Acting Beta2-Adrenergic Agonist / Corticosteroids:

Advair Diskus

Treatment of Asthma

Advair Diskus is indicated for the twice-daily treatment of asthma in patients aged 4 years and older. Advair Diskus should be used for patients not adequately controlled on a long-term asthma control medication such as an inhaled corticosteroid (ICS) or whose disease warrants initiation of treatment with both an ICS and long-acting beta-adrenergic agonist (LABA).

Maintenance Treatment of Chronic Obstructive Pulmonary Disease

Advair Diskus 250/50 is indicated for the twice-daily maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema. Advair Diskus 250/50 is also indicated to reduce exacerbations of COPD in patients with a history of exacerbations. Advair Diskus 250/50 twice daily is the only approved dosage for the treatment of COPD because an efficacy advantage of the higher strength Advair Diskus 500/50 over Advair Diskus 250/50 has not been demonstrated.

Advair HFA

Advair HFA is indicated for the twice-daily treatment of asthma in patients aged 12 years and older. Advair HFA should be used for patients not adequately controlled on a long-term asthma control medication such as an inhaled corticosteroid (ICS) or whose disease warrants initiation of treatment with both an ICS and long-acting beta -adrenergic agonist (LABA). AirDuo Respiclick

AirDuo Respiclick is indicated for the treatment of asthma in patients aged 12 years and older. AirDuo Respiclick should be used for patients not adequately controlled on a long term asthma control medication such as an inhaled corticosteroid or whose disease warrants initiation of treatment with both an inhaled corticosteroid and long acting beta adrenergic agonist (LABA).

Breo Ellipta

Maintenance Treatment of Chronic Obstructive Pulmonary Disease

Breo Ellipta 100/25 is indicated for the long-term, once-daily, maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema. Breo Ellipta 100/25 is also indicated to reduce exacerbations of COPD in patients with a history of exacerbations. Breo Ellipta 100/25 once daily is the only strength indicated for the treatment of COPD.

Treatment of Asthma

Breo Ellipta is indicated for the once-daily treatment of asthma in patients aged 18 years and older. Breo Ellipta should be used for patients not adequately controlled on a long-term asthma control medication such as an inhaled corticosteroid (ICS) or whose disease warrants initiation of treatment with both an ICS and long-acting beta -adrenergic agonist (LABA).

Dulera

Dulera is indicated for the twice-daily treatment of asthma in patients 5 years of age and older. Dulera should be used for patients not adequately controlled on a long-term asthma-control medication such as an inhaled corticosteroid (ICS) or whose disease warrants initiation of treatment with both an ICS and long-acting beta2-adrenergic agonist (LABA).

Symbicort

Treatment of Asthma

Symbicort is indicated for the treatment of asthma in patients 6 years of age and older. Symbicort should be used for patients not adequately controlled on a long-term asthma-control medication such as an inhaled corticosteroid (ICS) or whose disease warrants initiation of treatment with both an inhaled corticosteroid and long-acting beta -adrenergic agonist (LABA).

Maintenance Treatment of Chronic Obstructive Pulmonary Disease (COPD)

Symbicort 160/4.5 is indicated for the maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD) including chronic bronchitis and/or emphysema.

Symbicort 160/4.5 is also indicated to reduce exacerbations of COPD. Symbicort 160/4.5 is the only strength indicated for the treatment of COPD.

Long-Acting Beta2-Adrenergic Agonist / Anticholinergic / Corticosteroids:

Trelegy Ellipta

Trelegy Ellipta is indicated for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD). Trelegy Ellipta is NOT indicated for the treatment of asthma.

Important Limitations of Use

LABAs are NOT indicated for the relief of acute bronchospasm.

LABAs are NOT indicated to treat acute deteriorations of chronic obstructive pulmonary disease.

RATIONALE

The 1 month limit is a quantity sufficient for 30 day supply and the 3 months limit is 3 times the 1 month limit. If the patient is requesting more than the initial quantity limit the claim will reject with a message indicating quantity limits are exceeded.

More frequent administration or a greater number of inhalations of the prescribed strength of LABA Inhalers, or combination product containing both an inhaled corticosteroid and LABA is not recommended as some patients are more likely to experience adverse effects with higher doses of LABA.

Long-Acting Beta2-Adrenergic Agonists:

Arcapta Neohaler

The recommended dosage of Arcapta Neohaler is the once-daily inhalation of the contents of one 75 mcg Arcapta capsule using the Neohaler inhaler. Do not use Arcapta Neohaler more than one time every 24 hours.

Arcapta Neohaler is available as a box with one inhaler and 30 Arcapta capsules.

Brovana

The recommended dose of Brovana (arformoterol tartrate) Inhalation Solution is one 15mcg unit dose vial administered twice daily by nebulization. A total daily dose of greater than 30mcg (15 mcg twice daily) is not recommended. Brovana Inhalation Solution is supplied as 2mL unit-dose vials in a carton containing 30 vials or 60 vials.

Perforomist

The recommended dose of Perforomist (formoterol fumarate) Inhalation Solution is one 20mcg unit-dose vial administered twice daily by nebulization. A total daily dose greater than 40mcg is not recommended.

Perforomist Inhalation Solution is supplied as a 2mL solution for nebulization in unit dose vials in cartons of 30 vials and 60 vials.

Serevent Diskus

For bronchodilatation and prevention of symptoms of asthma, including the symptoms of nocturnal asthma, the usual dosage for adults and children aged 4 years and older is 1 inhalation (50 mcg) twice daily, approximately 12 hours apart. One inhalation of Serevent Diskus at least 30 minutes before exercise has been shown to protect patients against exercise-induced bronchospasm (EIB). When used intermittently as needed for prevention of EIB, this protection may last up to 9 hours in adults and adolescents and up to 12 hours in patients aged 4 to 11 years. Additional doses of Serevent should not be used for 12 hours after the administration of this drug.

For maintenance treatment of bronchospasm associated with COPD (including chronic bronchitis and emphysema), the dosage for adults is 1 inhalation (50 mcg) twice daily approximately 12 hours apart.

More frequent administration or a greater number of inhalations (more than 1 inhalation twice daily) is not recommended.

Serevent Diskus is supplied as an inhaler containing 60 blisters.

Serevent Diskus is also available as an institutional pack containing 28 blisters. However, this package size will not be included in the criteria.

Striverdi Respimat

The recommended dose of Striverdi Respimat is two inhalations once-daily at the same time of the day. Do not use Striverdi Respimat more than two inhalations every 24 hours.

Striverdi Respimat Inhalation Spray is available as a cartridge with inhaler, net fill weight of at least 4 grams, containing 60 metered actuations.

Long-Acting Beta2-Adrenergic Agonist / Anticholinergic:

Anoro Ellipta

Anoro Ellipta (umeclidinium/vilanterol 62.5 mcg/25 mcg) should be administered as 1 inhalation once daily by the orally inhaled route only. Do not use Anoro Ellipta more than 1 time every 24 hours.

Anoro Ellipta is supplied as an inhaler containing 2 strips with 30 blisters each (60 blisters). One strip contains umeclidinium and the other strip contains vilanterol. A blister from each strip is used to create 30 doses.

Anoro Ellipta is also available as an institutional pack containing 7 blisters per strip (14 doses). However, this package size will not be included in the criteria.

Bevespi Aerosphere

Bevespi Aerosphere (9mcg/4.8mcg) should be administered as two inhalations taken twice daily by the orally inhaled route only. Do not take more than two inhalations twice daily.

Bevespi Aerosphere is supplied as a 120 inhalation canister with a net fill weight of 10.7 grams.

Bevespi Aerosphere is also available as an institutional pack as a 28 inhalation canister with a net fill weight of 5.9 grams. However, this package size will not be included in the criteria.

Duaklir Pressair

The recommended dose of Duaklir Pressair is one oral inhalation of 400 mcg/12 mcg, twice daily. Do not take more than one inhalation twice daily.

Duaklir Pressair 400 mcg/12 mcg (aclidinium bromide and formoterol fumarate inhalation powder) is available in 60 and 30 metered doses.

Stiolto Respimat

The recommended dose of Stiolto Respimat is two inhalations once-daily at the same time of the day. Do not use Stiolto Respimat more than two inhalations every 24 hours.

Stiolto Respimat Inhalation Spray is available as a cartridge and an inhaler, with a net fill weight of at least 4 grams, containing 60 metered actuations.

Stiolto Respimat Inhalation Spray is also available as an institutional pack containing 10 or 28 metered actuations. However, these package sizes will not be included in the criteria.

Utibron Neohaler

The recommended dosage of Utibron Neohaler is the inhalation of the contents of one Utibron capsule twice-daily using the Neohaler device. More frequent administration or a greater number of inhalations (more than 1 capsule twice-daily) of Utibron Neohaler is not recommended.

Utibron Neohaler is available as a box containing a Neohaler device and 60 Utibron capsules.

Utibron capsules are also available in a box of 6. However, this package size will not be included in the criteria.

Long-Acting Beta2-Adrenergic Agonist / Corticosteroids:

Advair Diskus

For patients with asthma aged 4 to 11 years who are not controlled on an inhaled corticosteroid, the dosage is 1 inhalation of Advair Diskus 100/50 twice daily.

For patients aged 12 years and older, the dosage is 1 inhalation twice daily. The recommended starting dosages for Advair Diskus for patients aged 12 years and older are based upon patients' asthma severity. The maximum recommended dosage is Advair Diskus 500/50 twice daily.

The recommended dosage for patients with COPD is 1 inhalation of Advair Diskus 250/50 twice daily.

Advair Diskus 100/50, 250/50, 500/50 are supplied as an inhaler containing 60 blisters.

Advair Diskus is also available as an institutional pack containing 14 blisters. However, this package size will not be included in the criteria.

Advair HFA

For patients aged 12 years and older, the dosage is 2 inhalations twice daily, approximately 12 hours apart.

The recommended starting dosages for Advair HFA for patients aged 12 years and older are based upon patients' asthma severity. The maximum recommended dosage is 2 inhalations of Advair HFA 230/21 twice daily.

Advair HFA 45/21, 115/21, and 230/21 are supplied in 12g canister containing 120 metered actuations in boxes of 1.

Advair HFA is also available as an institutional pack 8gm canister containing 60 inhalations. However, this package size will not be included in the criteria.

AirDuo Respiclick

AirDuo Respiclick should be administered as one inhalation twice daily (approximately 12 hours apart) by the orally inhaled route. Do not use AirDuo Respiclick more than 2 times every 24 hours.

The usual recommended starting dose for patients not on inhaled corticosteroids is 55/14mcg twice daily. For other patients, the starting dose should be based on previous asthma drug therapy and disease severity. For patients switching to AirDuo Respiclick from another inhaled corticosteroid or combination product, select the low (55/14mcg), medium (113/14mcg) or high (232/14mcg) dose strength of AirDuo Respiclick based on the strength of the previous inhaled corticosteroid product or the strength of the inhaled corticosteroid from a combination product and disease severity. For patients who do not respond to AirDuo Respiclick 55/14 mcg after 2 weeks of therapy, increasing the dose may provide additional asthma control. If a dosage regimen of AirDuo Respiclick fails to provide adequate control of asthma, the therapeutic regimen should be re-evaluated and additional therapeutic options (e.g., replacing the current strength of AirDuo Respiclick with a higher strength, or adding additional controller therapies) should be considered. The highest recommended dose of AirDuo Respiclick is 232/14mcg twice daily.

AirDuo Respiclick is supplied in three strengths 55/14mcg, 113/14mcg or 232/14mcg and each inhaler provides 60 actuations.

Breo Ellipta

For chronic obstructive pulmonary disease, Breo Ellipta 100/25 should be administered as 1 inhalation once daily. The maximum recommended dosage is 1 inhalation of Breo Ellipta 100/25 once daily, the only strength indicated for the treatment of COPD.

For asthma, the recommended starting dosage is Breo Ellipta 100/25 or Breo Ellipta 200/25 administered as 1 inhalation once daily. The maximum recommended dosage is 1 inhalation of Breo Ellipta 200/25 once daily. The starting dosage is based on patients' asthma severity. For patients who do not respond adequately to Breo Ellipta 100/25, increasing the dose to Breo Ellipta 200/25 may provide additional improvement in asthma control.

Breo Ellipta 100/25 and 200/25 is supplied as an inhaler containing 2 strips, each with 30 blisters (60 blisters). One strip contains fluticasone furoate and the other strip contains vilanterol. A blister from each strip is used to create 30 doses. Breo Ellipta is also available as an institutional pack containing 14 blisters per strip. However, this package size will not be included in the criteria.

Dulera

For patients 12 years and older, the dosage is either 2 inhalations twice daily of Dulera 100mcg/5mcg or Dulera 200mcg/5mcg. When choosing the starting dosage strength of Dulera, consider the patients' disease severity, based on their previous asthma therapy, including the inhaled corticosteroid dosage, as well as the patients' current control of asthma symptoms and risk of future exacerbation.. For patients who do not respond adequately after 2 weeks of therapy with two inhalations of Dulera 100 mcg/5 mcg twice daily, increasing the dosage to two inhalations of Dulera 200 mcg/5 mcg twice daily may provide additional asthma control. The maximum recommended dosage is two inhalations of Dulera 200mcg/5mcg twice daily (maximum daily dosage 800mcg/20mcg).

For patients aged 5 to less than 12 years, the dosage is 2 inhalations of Dulera 50mcg/5mcg twice daily. The maximum daily dosage is 200mcg/20mcg.

Dulera 50mcg/5mcg, 100mcg/5mcg and 200mcg/5mcg are available in 13gm net fill weight canister with 120 inhalations. Dulera is also available as an institutional pack 8.8gm net fill weight canister with 60 inhalations. However, this package size will not be included in the criteria

Symbicort

For asthma patients 6 to less than 12 years of age, the dosage is 2 inhalations of Symbicort 80/4.5 twice daily.

For asthma, in patients 12 years of age and older, the dosage is 2 inhalations of Symbicort 80/4.5 or 160/4.5 twice daily. The recommended starting dosages for Symbicort for patients 12 years of age and older are based upon patients' asthma severity or level of control of asthma symptoms, and risk of exacerbations on current inhaled corticosteroids. The maximum recommended dosage in adult and adolescent patients 12 years and older is Symbicort 160/4.5, two inhalations twice daily.

For patients with COPD the recommended dose is Symbicort 160/4.5, two inhalations twice daily.

Symbicort 80/4.5 and 160/4.5 are available in a 10.2gm net fill weight canister containing 120 actuations.

Symbicort 80/4.5 and 160/4.5 are also available in institutional pack 6.9gm and 6gm, respectively, containing 60 inhalations. However, this package size will not be included in the criteria.

Long-Acting Beta2-Adrenergic Agonist / Anticholinergic / Corticosteroids:

Trelegy Ellipta

Trelegy Ellipta should be administered as 1 inhalation once daily. Do not use Trelegy Ellipta more than 1 time every 24 hours.

Trelegy Ellipta is supplied as an inhaler containing 2 strips, each with 30 blisters (60 blisters). One strip contains fluticasone furoate and the other strip contains a blend of umeclidinium and vilanterol. A blister from each strip is used to create 1 dose, for 30 inhalations

Trelegy Ellipta is also available as an institutional pack containing 14 blisters per strip. However, this package size will not be included in the criteria.

REFERENCES

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2. Advair HFA [package insert]. Research Triangle Park, NC: GlaxoSmithKline; February 2019.
3. AirDuo Respiclick [package insert]. Frazer, PA: Teva Respiratory, LLC; November 2018.
4. Anoro Ellipta [package insert]. Research Triangle Park, NC: GlaxoSmithKline; July 2019.
5. Arcapta Neohaler [package insert]. Marlborough MA: Sunovion Pharmaceuticals Inc.; May, 2019.
6. Bevespi Aerosphere [package insert]. Wilmington, DE: AstraZeneca; May 2019.
7. Breo Ellipta [package insert]. Research Triangle Park, NC: GlaxoSmithKline; January 2019.
8. Brovana [package insert]. Marlborough, MA: Sunovion Pharmaceuticals, Inc.; May 2019.
9. Duaklir Pressair [package insert]. Morrisville, NC: Circassia Pharmaceuticals Inc.; March 2019.
10. Dulera [package insert]. Whitehouse Station, NJ: Schering Corp/MSD; August 2019.
11. Perforomist [package insert]. Morgantown, WV: Mylan Specialty L.P.; May 2019.
12. Serevent Diskus [package insert]. Research Triangle Park, NC: GlaxoSmithKline; July 2019.
13. Stiolto Respimat [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; May 2019.
14. Striverdi Respimat [package insert.] Ridgefield, CT; Boehringer Ingelheim Pharmaceuticals, Inc.: May 2019.

15. Symbicort [package insert]. Wilmington, DE: AstraZeneca. July 2019.
 16. Trelegy Ellipta [package insert]. Research Triangle Park, NC: GlaxoSmithKline; May 2019.
 17. Utibron Neohaler [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; May 2019.

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Reviewed: (MG) 06/2003, 11/2004, 03/2005 (Xopenex HFA and Albuterol HFA added); (NB) 03/2006, 09/2006 (Advair HFA added); (CT) 03/2007(2) (Perforomist added), 02/2008, 02/2009, 09/2009 (updated Xopenex soln limit 02/2009(2)), (MS) 01/2010; (RP) 02/2011, 07/2011 (Arcapta Neohaler added), 06/2012, (TM) 02/2013, 05/2013 (add Breo Ellipta), (TM) 11/2013 (separate short & long acting), 12/2013 (add Anoro Ellipta), 07/2014 (add Striverdi Respimat), 11/2013, 11/2014, 05/2015 (add Stiolto Respimat), 11/2015 (add Utibron); (MS) 11/2015 (no clinical changes), 04/2016 (added Bevespi Aerosphere), (TM) 11/2016 (no clinical changes), (TM) 01/2017 (update Symbicort indication&dosing)(no clinical changes), (TM) 01/2017 (add Airduo), (TM) 09/2017 (add Trelegy Ellipta), 11/2017 (removed Foradil d/c, no clinical changes), 02/2018 (update combo indication), (TM) 11/2018 (no clinical changes), (TM) 04/2019 (added Duaklir), (TM) 11/2019 (no clinical changes)

Reviewed: CRC 06/2003; CDPR/Medical Affairs (MM) 11/2004, 03/2005, 03/2006; (WF) 03/2007(2), 02/2008, 02/2009, 09/2009, 02/2010; (KP) 02/2011; (KP) 07/2011, 06/2012, (LS) 02/2013, (LB) 05/2013, (DC) 11/2013, (LS) 12/2013, (MM) 08/2014, (DNC) 11/2014, (DNC) 05/2015, (ME) 04/2016, (ME) 02/2017, (AM) 09/2017, (GD) 04/2019, (CHART) 11/27/19

External Review: 08/2003, 12/2004, 11/2005, 06/2006, 06/2007, 06/2008, 06/2009, 06/2011, 10/2011, 10/2012, 06/2013, 01/2014, 08/2014, 02/2015, 02/2016, 06/2016, 02/2017, 10/2017, 02/2018, 02/2019, 06/2019 (FYI), 02/2020

LIMIT CRITERIA LONG-ACTING BETA2-ADRENERGIC AGONISTS:

Medication*	Maintenance Dose	Maximum Daily Dose	Package Size	1 Month Limit* 3 Months Limit*
Arcapta Neohaler	inhalation of the powder contents of 1 capsule once daily	1 capsule	30 capsules per box	1 package (30 capsules) / 25 days 3 packages (30 capsules each) / 75 days
Brovana	nebulization of 1 vial (2mL) twice daily	2 vials (2mL each)	30 vials (2mL each) per carton	2 packages (60 vials x 2mL) / 25 days 6 packages (180 vials x 2mL) / 75 days
			60 vials (2mL each) per carton	1 package (60 vials x 2mL) / 25 days 3 packages (180 vials x 2mL) / 75 days
Perforomist	nebulization of 1 vial (2 mL) twice daily	2 vials (2mL each)	30 vials (2mL each) per carton	2 packages (60 vials x 2mL) / 25 days 6 packages (180 vials x 2mL) / 75 days
			60 vials (2mL each) per carton	1 package (60 vials x 2mL) / 25 days 3 packages (180 vials x 2mL) / 75 days
Serevent Diskus	1 inhalation twice daily	2 inhalations	60 blisters per inhaler	1 package (60 blisters) / 25 days 3 packages (60 blisters each) / 75 days
Striverdi Respimat	2 inhalations once daily	2 inhalations	60 inhalations per 4gm cartridge	1 package (4gm) / 25 days 3 packages (4gm each) / 75 days

LIMIT CRITERIA LONG-ACTING BETA2-ADRENERGIC AGONIST / ANTICHOLINERGIC:

Medication*	Maintenance Dose	Maximum Daily Dose	Package Size	1 Month Limit* 3 Months Limit*
Anoro Ellipta	1 inhalation once daily	1 inhalation	30 inhalations/60 blisters per inhaler	1 package (60 blisters) / 25 days 3 packages (60 blisters each) / 75 days
Bevespi Aerosphere	2 inhalations twice daily	4 inhalations	120 inhalations per 10.7gm canister	1 package (10.7gm) / 25 days 3 packages (10.7gm each) / 75 days
Duaklir Pressair	1 inhalation twice daily	2 inhalations	30 inhalations per inhaler	2 packages (30 inh each) / 25 days 6 packages (30 inh each) / 75 days
			60 inhalations per inhaler	1 package (60 inh) / 25 days 3 packages (60 inh each) / 75 days
Stiolto Respimat	2 inhalations once daily	2 inhalations	60 inhalations per 4gm cartridge	1 package (4gm) / 25 days 3 packages(4gm each) / 75 days
Utibron Neohaler	1 inhalation twice daily	2 inhalations	60 capsules per box	1 package (60 capsules) / 25 days 3 packages (60 capsules each) / 75 days

LIMIT CRITERIA LONG-ACTING BETA2-ADRENERGIC AGONIST / CORTICOSTEROIDS:

Medication*	Maintenance Dose	Maximum Daily Dose	Package Size	1 Month Limit* 3 Months Limit*
Advair Diskus	1 inhalation twice daily	2 inhalations	60 blisters per inhaler	1 package (60 blisters) / 25 days 3 packages (60 blisters each) / 75 days
Advair HFA	2 inhalations twice daily	4 inhalations	120 inhalations per 12gm canister	1 package (12gm) / 25 days 3 packages (12gm each) / 75 days
Airduo Respiclick	1 inhalation twice daily	2 inhalations	60 inhalations per inhaler	1 package / 25 days 3 packages / 75 days
Breo Ellipta	1 inhalation once daily	1 inhalation	30 inhalations/60 blisters per inhaler	1 package (60 blisters) / 25 days 3 packages (60 blisters each) / 75 days
Dulera	2 inhalations twice daily	4 inhalations	120 inhalations per 13gm canister	1 package (13gm) / 25 days 3 packages (13gm each) / 75 days
Symbicort	2 inhalations twice daily	4 inhalations	120 inhalations per 10.2gm canister	1 package (10.2gm) / 25 days 3 packages (10.2gm each) / 75 days

LIMIT CRITERIA LONG-ACTING BETA2-ADRENERGIC AGONIST / ANTICHOLINERGIC / CORTICOSTEROIDS:

Medication*	Maintenance Dose	Maximum Daily Dose	Package Size	1 Month Limit* 3 Months Limit*
Trelegy Ellipta	1 inhalation once daily	1 inhalation	30 inhalations/60 blisters per inhaler	1 package (60 blisters) / 25 days 3 packages (60 blisters each) / 75 days

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

**The limit criteria apply to both brand and generic, if available.*

SPECIALTY GUIDELINE MANAGEMENT

BETASERON (interferon beta-1b) EXTAVIA (interferon beta-1b)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications: Betaseron and Extavia are indicated for the treatment of relapsing forms of multiple sclerosis to reduce the frequency of clinical exacerbations. Patients with multiple sclerosis in whom efficacy has been demonstrated include patients who have experienced a first clinical episode and have MRI features consistent with multiple sclerosis.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Relapsing forms of multiple sclerosis

Authorization of 12 months may be granted to members who have been diagnosed with a relapsing form of multiple sclerosis.

B. First clinical episode of multiple sclerosis

Authorization of 12 months may be granted to members for the treatment of a first clinical episode of multiple sclerosis.

III. CONTINUATION OF THERAPY

For all indications: Authorization of 12 months may be granted for members who are experiencing disease stability or improvement while receiving Betaseron or Extavia.

IV. OTHER CRITERIA

Members will not use Betaseron or Extavia concomitantly with other medications used for the treatment of multiple sclerosis, excluding Ampyra.

V. REFERENCES

1. Betaseron [package insert]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc.; August 2018.
2. Extavia [package insert]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc.; December 2018.

Reference number(s)
1840-A

3. AHFS DI (Adult and Pediatric) [database online]. Hudson, OH: Lexi-Comp, Inc.; http://online.lexi.com/lco/action/index/dataset/complete_ashp [available with subscription]. Accessed (April 2019).

SPECIALTY GUIDELINE MANAGEMENT

Targretin (bexarotene) capsules bexarotene capsules (generic) Targretin (bexarotene) gel 1%

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Targretin/bexarotene capsules are indicated for the treatment of cutaneous manifestations of cutaneous T-cell lymphoma (CTCL) in patients who are refractory to at least one prior systemic therapy.
2. Targretin gel is indicated for the topical treatment of cutaneous lesions in patients with CTCL (Stage IA and IB) who have refractory or persistent disease after other therapies or who have not tolerated other therapies.

B. Compendial Uses

1. Targretin/bexarotene capsules
 - a. Mycosis fungoides (MF)
 - b. Sezary syndrome (SS)
 - c. Primary cutaneous CD30+ T-cell lymphoproliferative disorders:
 - a. Primary cutaneous anaplastic large cell lymphoma (ALCL)
 - b. Lymphomatoid papulosis (LyP)
2. Targretin gel
 - a. Mycosis fungoides (MF)
 - b. Chronic or smoldering adult T-cell leukemia/lymphoma (ATLL)
 - c. Primary cutaneous B-cell lymphoma:
 - a. Primary cutaneous marginal zone lymphoma
 - b. Primary cutaneous follicle center lymphoma

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Targretin/bexarotene Capsules

1. Mycosis Fungoides (MF)/Sézary Syndrome (SS)

Authorization of 12 months may be granted for the treatment of MF or SS.

2. Primary Cutaneous Anaplastic Large Cell Lymphoma (ALCL)/Lymphomatoid Papulosis (LyP)

Authorization of 12 months may be granted for the treatment of primary cutaneous ALCL or LyP.

B. Targretin Gel

1. Cutaneous T-cell Lymphoma (CTCL): Mycosis Fungoides (MF) (excluding Sézary syndrome)

Authorization of 12 months may be granted for the treatment of MF.

2. Adult T-cell Leukemia/Lymphoma (ATLL)

Authorization of 12 months may be granted for the treatment of chronic or smoldering ATLL.

3. Primary Cutaneous B-cell Lymphoma

Authorization of 12 months may be granted for the treatment of primary cutaneous marginal zone lymphoma or primary cutaneous follicle center lymphoma.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced disease progression or an unacceptable toxicity.

IV. REFERENCES

1. Targretin capsules [package insert]. St. Petersburg, FL: Catalent Pharma Solutions LLC; June 2016. .
2. Targretin gel [package insert]. San Antonio, TX: DPT Laboratories, Ltd.; October 2015.
3. Bexarotene capsules [package insert]. Morgantown, WV: Mylan Pharmaceuticals Inc.; June 2018.
4. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed January 27, 2019.
5. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Primary Cutaneous Lymphomas (Version 2.2019). <https://www.nccn.org>. Accessed January 27, 2019.
6. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: T-Cell Lymphomas (Version 2.2019). <https://www.nccn.org>. Accessed January 27, 2019.

SPECIALTY GUIDELINE MANAGEMENT

BLINCYTO (blinatumomab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

1. Blincyto is indicated for the treatment of B-cell precursor acute lymphoblastic leukemia (ALL) in first or second complete remission with minimal residual disease (MRD) greater than or equal to 0.1% in adults and children.
2. Blincyto is indicated for the treatment of relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL) in adults and children.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

- A. Documentation of Philadelphia chromosome testing
- B. Testing or analysis confirming CD19 protein on the surface of the B cell

III. CRITERIA FOR INITIAL APPROVAL

B-cell Precursor Acute Lymphoblastic Leukemia

Authorization of 9 months may be granted for treatment of B-cell precursor acute lymphoblastic leukemia (ALL) when all of the following criteria are met:

- A. The member meets one of the following:
 1. The member has relapsed or refractory Philadelphia chromosome positive disease and had an inadequate response or intolerance to a tyrosine kinase inhibitor (TKI) (e.g., imatinib, dasatinib).
 2. The member has Philadelphia chromosome negative disease and meets one of the following:
 - a. Member has relapsed or refractory disease
 - b. Blincyto will be used as consolidation therapy for minimal residual disease positive (MRD+) following a complete response to induction therapy.
- B. Blincyto will be used as monotherapy with corticosteroids as premedication prior to infusion
- C. The B-cells must be CD19-positive as confirmed by testing or analysis

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced unacceptable toxicity or disease progression while on the current regimen.

Reference number(s)
2228-A

V. REFERENCES

1. Blincyto [package insert]. Thousand Oaks, CA: Amgen Inc.; May 2018.
2. The NCCN Drugs & Biologics Compendium 2018 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 25, 2019.
3. The NCCN Clinical Practice Guidelines in Oncology Acute Lymphoblastic Leukemia (Version 1.2018) 2018 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed March 25, 2019.

SPECIALTY GUIDELINE MANAGEMENT

VELCADE (bortezomib) bortezomib

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Multiple myeloma
2. Mantle cell lymphoma

B. Compendial Uses

1. Systemic light chain amyloidosis
2. Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma
3. Multicentric Castleman's disease
4. Adult T-cell leukemia/lymphoma
5. Angioimmunoblastic T-cell lymphoma
6. Peripheral T-cell lymphoma NOS
7. Anaplastic large cell lymphoma
8. Enteropathy-associated T-cell lymphoma
9. Monomorphic epitheliotropic intestinal T-cell lymphoma
10. Nodal peripheral T-cell lymphoma with TFH phenotype
11. Follicular T-cell lymphoma
12. Antibody mediated rejection of solid organ
13. Primary cutaneous anaplastic large cell lymphoma

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Multiple myeloma**

Authorization of 12 months may be granted for the treatment of multiple myeloma.

B. **Mantle cell lymphoma**

Authorization of 12 months may be granted for the treatment of mantle cell lymphoma.

C. **Multicentric Castleman's disease**

Authorization of 12 months may be granted for the treatment of relapsed, refractory or progressive multicentric Castleman's disease.

D. **Systemic light chain amyloidosis**

Authorization of 12 months may be granted for the treatment of systemic light chain amyloidosis when the requested medication will be used in any of the following regimens:

1. In combination with melphalan and dexamethasone
2. In combination with cyclophosphamide and dexamethasone

Reference number(s)
2233-A

3. In combination with dexamethasone
4. As a single agent

E. Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma

Authorization of 12 months may be granted for the treatment of Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma when the requested medication will be used in any of the following regimens:

1. In combination with rituximab
2. In combination with dexamethasone
3. In combination with rituximab and dexamethasone
4. As a single agent

F. Adult T-cell Leukemia/Lymphoma

Authorization of 12 months may be granted for the treatment of adult T-cell leukemia/lymphoma when the requested medication will be used as a single agent for second-line or subsequent therapy.

G. Peripheral T-cell lymphoma

Authorization of 12 months may be granted for the treatment of angioimmunoblastic T-cell lymphoma, peripheral T-cell lymphoma not otherwise specified, anaplastic large cell lymphoma, enteropathy-associated T-cell lymphoma, monomorphic epitheliotropic intestinal T-cell lymphoma, nodal peripheral T-cell lymphoma with TFH phenotype, or follicular T-cell lymphoma when all of the following criteria are met:

1. The disease is relapsed or refractory
2. The requested medication is used as a single agent for second-line and subsequent therapy
3. The member is not a candidate for autologous stem cell transplantation

H. Antibody mediated rejection of solid organ

Authorization of 12 months may be granted for the treatment of antibody mediated rejection of solid organ.

I. Primary cutaneous anaplastic large cell lymphoma

Authorization of 12 months may be granted for the treatment of relapsed or refractory primary cutaneous anaplastic large cell lymphoma (ALCL) when the requested medication is used as a single agent.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced an unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Velcade [package insert]. Cambridge, MA: Millenium Pharmaceuticals, Inc.; June 2017.
2. bortezomib [package insert]. Lake Zurich, IL: Fresenius Kabi; July 2018
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5. The NCCN Clinical Practice Guidelines in Oncology® B-cell Lymphomas (Version 5.2018) © 2018 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed March 29, 2019.
6. The NCCN Clinical Practice Guidelines in Oncology® Systemic Light Chain Amyloidosis (Version 1.2018) © 2018 National Comprehensive Cancer Network, Inc. Available at: www.nccn.org. Accessed March 4, 2018.

Reference number(s)
2233-A

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8. The NCCN Clinical Practice Guidelines in Oncology® T-Cell Lymphomas (Version 5.2018) © 2018 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed March 21, 2019.
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SPECIALTY GUIDELINE MANAGEMENT

TRACLEER (bosentan) bosentan

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Indicated for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group 1):

- A. In adults to improve exercise ability and to decrease clinical worsening.
- B. In pediatric patients aged 3 years and older with idiopathic or congenital PAH to improve pulmonary vascular resistance (PVR), which is expected to result in an improvement in exercise ability.

All other indications are considered experimental/investigational and not medically necessary.

Compendial Use

Eisenmenger's syndrome, WHO functional class III PAH

II. CRITERIA FOR INITIAL APPROVAL

A. Pulmonary Arterial Hypertension (PAH)

Authorization of 12 months may be granted for treatment of PAH when ALL of the following criteria are met:

1. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
2. PAH was confirmed by either criterion (1) or criterion (2) below:
 - a. Pretreatment right heart catheterization with all of the following results:
 - i. mPAP \geq 25 mmHg
 - ii. PCWP \leq 15 mmHg
 - iii. PVR $>$ 3 Wood units
 - b. For infants less than one year of age with any of the following conditions, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed:
 - i. Post cardiac surgery
 - ii. Chronic heart disease
 - iii. Chronic lung disease associated with prematurity
 - iv. Congenital diaphragmatic hernia

B. Eisenmenger's Syndrome

Authorization of 12 months may be granted for treatment of members with WHO functional class III Eisenmenger's syndrome (refer to Appendix).

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with an indication listed in Section II who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

IV. APPENDIX

WHO Classification of Pulmonary Hypertension

1 PAH

- 1.1 Idiopathic (PAH)
- 1.2 Heritable PAH
- 1.3 Drug- and toxin-induced PAH
- 1.4. PAH associated with:
 - 1.4.1 Connective tissue diseases
 - 1.4.2 HIV infection
 - 1.4.3 Portal hypertension
 - 1.4.4 Congenital heart diseases
 - 1.4.5 Schistosomiasis
- 1.5 PAH long-term responders to calcium channel blockers
- 1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement
- 1.7 Persistent PH of the newborn syndrome

2 PH due to left heart disease

- 2.1 PH due to heart failure with preserved LVEF
- 2.2 PH due to heart failure with reduced LVEF
- 2.3 Valvular heart disease
- 2.4 Congenital/acquired cardiovascular conditions leading to post-capillary PH

3 PH due to lung diseases and/or hypoxia

- 3.1 Obstructive lung disease
- 3.2 Restrictive lung disease
- 3.3 Other lung disease with mixed restrictive/obstructive pattern
- 3.4 Hypoxia without lung disease
- 3.5 Developmental lung disorders

4 PH due to pulmonary artery obstruction

- 4.1 Chronic thromboembolic PH
- 4.2 Other pulmonary artery obstructions
 - 4.2.1 Sarcoma (high or intermediate grade) or angiosarcoma
 - 4.2.2 Other malignant tumors
 - Renal carcinoma
 - Uterine carcinoma
 - Germ cell tumours of the testis
 - Other tumours
 - 4.2.3 Non-malignant tumours
 - Uterine leiomyoma
 - 4.2.4 Arteritis without connective tissue disease
 - 4.2.5 Congenital pulmonary artery stenosis
 - 4.2.6 Parasites
 - Hydatidosis

5 PH with unclear and/or multifactorial mechanisms

Reference number(s)
1649-A

- 5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders
- 5.2 Systemic and metabolic disorders: Pulmonary Langerhans cell histiocytosis, Gaucher disease, glycogen storage disease, neurofibromatosis, sarcoidosis
- 5.3 Others: chronic renal failure with or without hemodialysis, fibrosing mediastinitis
- 5.4 Complex congenital heart disease

WHO Functional Assessment for Pulmonary Hypertension

Class I

Patients with pulmonary hypertension but without resulting limitation of physical activity. Ordinary physical activity does not cause undue dyspnea or fatigue, chest pain or near syncope.

Class II

Patients with pulmonary hypertension resulting in a slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity causes undue dyspnea or fatigue, chest pain or near syncope.

Class III

Patients with pulmonary hypertension resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes undue dyspnea or fatigue, chest pain or near syncope.

Class IV

Patients with pulmonary hypertension with inability to carry out any physical activity without symptoms. These patients manifest signs of right heart failure. Dyspnea and/or fatigue may even be present at rest. Discomfort is increased by any physical activity.

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Reference number(s)
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SPECIALTY GUIDELINE MANAGEMENT

BOSULIF (bosutinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Adult patients with:

1. Newly-diagnosed chronic phase (CP) Philadelphia chromosome-positive chronic myelogenous leukemia (Ph+ CML)
2. Chronic phase, accelerated phase (AP), or blast phase (BP) Ph+ CML with resistance or intolerance to prior therapy

B. Compendial Uses

1. Primary treatment of patients with advanced phase CML (accelerated phase or blast phase)
2. Follow-up therapy for CML patients after hematopoietic stem cell transplant (HSCT)
3. Therapy for relapsed or refractory Ph+ acute lymphoblastic leukemia (ALL)

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review:

- A. Prior to initiation of therapy: results of cytogenetic and/or molecular testing for detection of the Ph chromosome or the BCR-ABL gene
- B. For members requesting initiation of Bosulif therapy for treatment of CML or ALL after experiencing resistance to prior tyrosine kinase inhibitor (TKI) therapy: results of T315I mutation testing

III. CRITERIA FOR INITIAL APPROVAL

A. **Chronic Myeloid Leukemia (CML)**

Authorization of 6 months may be granted for treatment of CML that has been confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing when any of the following criteria are met:

1. Member has not received prior therapy with a TKI (e.g., dasatinib, imatinib, nilotinib, ponatinib)
2. Member experienced toxicity or intolerance to prior therapy with a TKI
3. Member experienced resistance to prior therapy with a TKI and results of mutational testing are negative for T315I mutation
4. Member has received HSCT for CML

B. **Ph+ Acute Lymphoblastic Leukemia (ALL)/Lymphoblastic Lymphoma (LL)**

Reference number(s)
2171-A

Authorization of 12 months may be granted for treatment of relapsed or refractory Ph+ ALL or LL that has been confirmed by detection of Ph chromosome or BCR-ABL gene by cytogenetic and/ or molecular testing when results of mutational testing are negative for T315I mutation.

IV. CONTINUATION OF THERAPY

A. CML

Authorization of 12 months may be granted for continued treatment of CML that has been confirmed by detection of Ph chromosome or BCR-ABL gene by cytogenetic and/ or molecular testing when either of the following criteria are met:

1. BCR-ABL1 \leq 10% for members who have been receiving Bosulif for \leq 12 months
2. No evidence of disease progression for members who have been receiving Bosulif for $>$ 12 months
3. Member has received HSCT

B. Ph+ ALL/LL

Authorization of 12 months may be granted for continued treatment of Ph+ ALL or LL that has been confirmed by detection of Ph chromosome or BCR-ABL gene by cytogenetic and/ or molecular testing in members who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES

1. Bosulif [package insert]. New York, NJ: Pfizer Inc.; October 2018.
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4. NCCN Clinical Practice Guidelines in Oncology® Acute Lymphoblastic Leukemia (Version 1.2019). © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed April 17, 2019.

SPECIALTY GUIDELINE MANAGEMENT

BOTOX (onabotulinumtoxin A)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Overactive bladder with symptoms of urge urinary incontinence, urgency, and frequency, in adults who have an inadequate response to or are intolerant of an anticholinergic medication
2. Urinary incontinence due to detrusor over activity associated with a neurologic condition (e.g., spinal cord injury, multiple sclerosis) in adults who have an inadequate response to or are intolerant of an anticholinergic medication
3. Prophylaxis of headaches in adult patients with chronic migraine (≥ 15 days per month with headache lasting 4 hours a day or longer)
4. Treatment of upper limb spasticity in adult patients
5. Treatment of lower limb spasticity in adult patients
6. Treatment of upper limb spasticity in pediatric patients 2 to 17 years of age
7. Treatment of lower limb spasticity in pediatric patients 2 to 17 years of age, excluding spasticity caused by cerebral palsy
8. Cervical dystonia in adults, to reduce the severity of abnormal head position and neck pain
9. Severe primary axillary hyperhidrosis that is inadequately managed with topical agents in adult patients
10. Strabismus and blepharospasm associated with dystonia, including benign essential blepharospasm or VII nerve disorders in patients 12 years of age and older

B. Compendial Uses

1. Achalasia
2. Chronic anal fissures
3. Essential tremor
4. Excessive salivation
5. Hemifacial spasm
6. Spasmodic dysphonia (laryngeal dystonia)
7. Oromandibular dystonia
8. Myofascial pain syndrome
9. Focal hand dystonia
10. Facial myokymia
11. Hirschsprung disease with internal sphincter achalasia
12. Orofacial tardive dyskinesia
13. Painful bruxism
14. Palatal myoclonus
15. First bite syndrome
16. Palmar or gustatory (Frey's syndrome) hyperhidrosis

17. Myofascial pain syndrome

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

Coverage will not be provided for cosmetic use.

III. CRITERIA FOR INITIAL APPROVAL

A. Blepharospasm

Authorization of 12 months may be granted for treatment of blepharospasm.

B. Cervical dystonia

Authorization of 12 months may be granted for treatment of cervical dystonia (e.g., torticollis) when there is sustained head torsion and/or tilt with limited range of motion.

C. Chronic migraine prophylaxis

Authorization of 6 months (two injection cycles) may be granted for treatment of chronic migraine prophylaxis when all of the following criteria are met:

1. Member experiences headaches \geq 15 days per month with headaches lasting longer than 4 hours,
2. Member completed an adequate trial of three oral migraine preventative therapies coming from at least 2 of the following classes with a trial of each medication at least 60 days in duration:
 - i. Antidepressants (e.g., amitriptyline, nortriptyline, venlafaxine)
 - ii. Antiepileptic drugs (AEDs) (e.g., divalproex sodium, topiramate, valproate sodium)
 - iii. Beta-adrenergic blocking agents (e.g., metoprolol, propranolol, timolol, atenolol, nadolol)
 - iv. Calcium channel blockers (e.g., amlodipine, diltiazem, felodipine).
3. Member must not use any CGRP-inhibitors and Botox together
4. Members headache has at least two of the following:
 - i. Aggravated by routine movement
 - ii. Moderate to severe pain intensity
 - iii. Pulsating
 - iv. Unilateral
5. Members headache has at least one of the following:
 - i. Nausea/vomiting
 - ii. Sensitivity to light
 - iii. Sensitivity to sound

D. Overactive bladder with urinary incontinence

Authorization of 12 months may be granted for treatment of overactive bladder with urinary incontinence, urgency, and frequency when all of the following criteria are met:

1. The member has tried and failed behavioral therapy.
2. The member has had an inadequate response or experienced intolerance to two anticholinergic medications (e.g., Vesicare [solifenacin], Enablex [darifenacin], Toviaz [fesoterodine], Detrol/Detrol LA [tolterodine], Sanctura/Sanctura XR [trospium], Ditropan XL [oxybutynin]).

E. Primary axillary, palmar, and gustatory (Frey's syndrome) hyperhidrosis

Authorization of 12 months may be granted for treatment of primary axillary, palmar, or gustatory (Frey's syndrome) hyperhidrosis when all of the following criteria are met:

1. Member is unresponsive or unable to tolerate pharmacotherapy prescribed for excessive sweating (e.g., anticholinergics, beta-blockers, or benzodiazepines); and
2. Significant disruption of professional and/or social life has occurred because of excessive sweating; and
3. Topical aluminum chloride or other extra-strength antiperspirants are ineffective or result in a severe rash.

F. Strabismus

Authorization of 12 months may be granted for treatment of strabismus when interference with normal visual system development is likely to occur and spontaneous recovery is unlikely.

Note: Strabismus repair is considered cosmetic in adults with uncorrected congenital strabismus and no binocular fusion.

G. Upper limb spasticity

Authorization of 12 months may be granted for treatment of upper limb spasticity.

H. Lower limb spasticity

Authorization of 12 months may be granted for treatment of lower limb spasticity.

I. Urinary incontinence associated with a neurologic condition (e.g., spinal cord injury, multiple sclerosis)

Authorization of 12 months may be granted for treatment of urinary incontinence associated with a neurologic condition (e.g., spinal cord injury, multiple sclerosis) when all of the following criteria are met;

1. The member has tried and failed behavioral therapy
2. The member has had an inadequate response or experienced intolerance to an anticholinergic medication (e.g., Vesicare [solifenacin], Enablex [darifenacin], Toviaz [fesoterodine], Detrol/Detrol LA [tolterodine], Sanctura/Sanctura XR [trospium], Ditropan XL [oxybutynin]).

J. Achalasia

Authorization of 12 months may be granted for treatment of achalasia when the member has tried and failed conventional therapy such as pneumatic dilation and surgical myotomy.

K. Chronic anal fissures

Authorization of 12 months may be granted for treatment of chronic anal fissures when the member has not responded to first line therapy such as topical calcium channel blockers or topical nitrates.

L. Essential tremor

Authorization of 12 months may be granted for treatment of essential tremor.

M. Excessive salivation

Authorization of 12 months may be granted for treatment of excessive salivation (chronic sialorrhea) when the member has been refractory to pharmacotherapy (e.g., anticholinergics).

N. Hemifacial Spasm

Authorization of 12 months may be granted for treatment of hemifacial spasm.

O. Spasmodic dysphonia (laryngeal dystonia)

Authorization of 12 months may be granted for treatment of spasmodic dysphonia (laryngeal dystonia).

P. Oromandibular dystonia

Authorization of 12 months may be granted for treatment of oromandibular dystonia.

Q. Myofascial Pain Syndrome

Authorization of 12 months may be granted for treatment of myofascial pain syndrome when the member has tried and failed all of the following:

1. Physical therapy
2. Injection of local anesthetics into trigger points
3. Injection of corticosteroids into trigger points

R. Focal hand dystonia

Authorization of 12 months may be granted for the treatment of focal hand dystonias.

S. Facial myokymia

Authorization of 12 months may be granted for the treatment of facial myokymia.

T. Hirschsprung disease with internal sphincter achalasia

Authorization of 12 months may be granted for the treatment of Hirschsprung's disease with internal sphincter achalasia following endorectal pull through and the member is refractory to laxative therapy.

U. Orofacial tardive dyskinesia

Authorization of 12 months may be granted for the treatment of orofacial tardive dyskinesia when conventional therapies have been tried and failed (e.g., benzodiazepines, clozapine, or tetrabenazine).

V. Painful bruxism

Authorization of 12 months may be granted for the treatment of painful bruxism when the member has had an inadequate response to a night guard and has had an inadequate response to pharmacologic therapy such as diazepam.

W. Palatal myoclonus

Authorization of 12 months may be granted for the treatment of palatal myoclonus when the member has disabling symptoms (e.g., intrusive clicking tinnitus) who had an inadequate response to clonazepam, lamotrigine, carbamazepine or valproate.

X. First bite syndrome

Authorization of 12 months may be granted for the treatment of first bite syndrome when the member has failed relief from analgesics, antidepressants or anticonvulsants.

IV. CONTINUATION OF THERAPY

- A. All members (including new members) requesting authorization for continuation of therapy must meet ALL initial authorization criteria for all approvable conditions other than chronic migraine prophylaxis.
- B. Authorization of 12 months may be granted for treatment of chronic migraine prophylaxis when the member has achieved or maintained a reduction in monthly headache frequency since starting therapy with Botox.

V. REFERENCES

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SPECIALTY GUIDELINE MANAGEMENT

BRAFTOVI (encorafenib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Braftovi is indicated, in combination with binimetinib, for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation, as detected by an FDA-approved test.

Limitations of use: Braftovi is not indicated for treatment of patients with wild-type BRAF melanoma.

B. Compendial Uses

1. Glioma, BRAF V600 activating mutation-positive
2. Meningioma, BRAF V600 activating mutation-positive
3. Astrocytoma, BRAF V600 activating mutation-positive
4. Colorectal cancer, BRAF V600E activating mutation-positive

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of BRAF mutation documentation is necessary to initiate the prior authorization review.

III. CRITERIA FOR INITIAL APPROVAL

A. **Melanoma**

Authorization of 12 months may be granted for treatment of unresectable or metastatic melanoma when all of the following criteria are met:

1. Braftovi is used in combination with binimetinib (Mektovi)
2. Tumor is positive for BRAF V600E or V600K mutation.

B. **Central Nervous System Cancer**

Authorization of 12 months may be granted for treatment of BRAF V600 mutation-positive gliomas, meningiomas, or astrocytomas.

C. **Colorectal Cancer**

Authorization of 12 months may be granted for treatment of unresectable advanced or metastatic colorectal cancer when the following criteria are met:

1. Braftovi is used in combination with binimetinib (Mektovi) and either cetuximab or panitumumab
2. Tumor is positive for BRAF V600E mutation.
3. Will be used as subsequent therapy

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy for an indication outlined in section III when there is no evidence of unacceptable toxicity or disease progression on the current regimen.

V. REFERENCES

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SPECIALTY GUIDELINE MANAGEMENT

BRINEURA (cerliponase alfa)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Brineura is indicated to slow the loss of ambulation in symptomatic pediatric patients 3 years of age and older with late infantile neuronal ceroid lipofuscinosis type 2 (CLN2), also known as tripeptidyl peptidase 1 (TPP1) deficiency.

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: tripeptidyl peptidase 1 (TPP1) enzyme assay or genetic testing results supporting diagnosis.

III. CRITERIA FOR INITIAL APPROVAL

Late infantile neuronal ceroid lipofuscinosis type 2 (CLN2)

Authorization of 12 months may be granted for members with CLN2 when all of the following criteria are met:

1. Diagnosis of CLN2 was confirmed by enzyme assay demonstrating a deficiency of tripeptidyl peptidase 1 (TPP1) enzyme activity or by genetic testing; and
2. Member is 3 years of age or older; and
3. Brineura will be administered by, or under the direction of a physician knowledgeable in intraventricular administration; and
4. Dosage of Brineura will not exceed 300 mg once every other week ; and
5. Member does not have acute intraventricular access device-related complications (e.g., leakage, device failure, or device-related infection) or a ventriculoperitoneal shunt.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for late infantile neuronal ceroid lipofuscinosis type 2 (CLN2) when the following criteria are met:

- A. Member has experienced a slowed loss of ambulation from baseline; and
- B. Member does not have acute intraventricular access device-related complications (e.g., leakage, device failure, or device-related infection) or ventriculoperitoneal shunts.

Reference number
1831-A

V. REFERENCES

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SPECIALTY GUIDELINE MANAGEMENT

BRUKINSA (zanubrutinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Brukina is a kinase inhibitor indicated for the treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Mantle Cell Lymphoma

Authorization of 12 months may be granted for treatment of mantle cell lymphoma when the member has received at least one prior therapy.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Brukina [package insert]. San Mateo, CA: BeiGene USA, Inc.; November 2019.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME **BRUKINSA**
(generic) (zanubrutinib)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

MDC
Ref # 3414-A

FDA-APPROVED INDICATIONS

Brukina is a kinase inhibitor indicated for the treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy.

CRITERIA FOR APPROVAL

1	Does the patient have a diagnosis of mantle cell lymphoma? [If no, no further questions.]	Yes	No
2	Has the patient received at least one prior therapy?	Yes	No

Guidelines for Approval	
Duration of Approval	12 months
Set 1: Mantle Cell Lymphoma	
Yes to question(s)	No to question(s)
1	None
2	

Mapping Instructions	
	Yes
1.	Go to 2
2.	Approve, 12 months
	No
	Deny
	Deny

RATIONALE

These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to ensure that patients follow selection elements noted in labeling and/or practice guidelines in order to decrease the potential for inappropriate utilization.

REFERENCES

1. Brukina [package insert]. San Mateo, CA: BeiGene USA, Inc.; November 2019.

DOCUMENT HISTORY

Created: Specialty Clinical Development (AS) 11/2019
Revised:
Reviewed: CDPR / MF 11/2019
External Review: 12/2019

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS **GLUCAGON-LIKE PEPTIDE 1 (GLP-1) RECEPTOR AGONIST**

BRAND NAME*
(generic)

BYDUREON
(exenatide extended-release)

BYDUREON BCISE
(exenatide extended-release)

Status: CVS Caremark Criteria

Type: Initial Prior Authorization with Quantity Limit

Ref # 751-C

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Bydureon/Bydureon BCISE is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use

- Bydureon/Bydureon BCISE is not recommended as first-line therapy for patients who have inadequate glycemic control on diet and exercise because of the uncertain relevance of the rat thyroid C-cell tumor findings to humans.
- Bydureon/Bydureon BCISE is not a substitute for insulin. Bydureon/Bydureon BCISE should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis, as it would not be effective in these settings.
- The concurrent use of Bydureon/Bydureon BCISE with insulin has not been studied and cannot be recommended.
- Bydureon/Bydureon BCISE is an extended-release formulation of exenatide. Bydureon/Bydureon BCISE should not be used with other products containing the active ingredient exenatide.
- Bydureon/Bydureon BCISE has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has been receiving GLP-1 Agonist therapy for at least 3 months and has demonstrated a reduction in A1c (hemoglobin A1c) since starting GLP-1 Agonist therapy
[Note: Examples of GLP-1 Agonists are Adlyxin, Bydureon, Byetta, Ozempic, Tanzeum, Trulicity, Victoza]

OR

- The patient has a diagnosis of type 2 diabetes mellitus

AND

- The patient has experienced an inadequate treatment response, intolerance, or contraindication to metformin

OR

- The patient requires combination therapy AND has an A1c (hemoglobin A1c) of 7.5 percent or greater

Quantity Limits apply.

Bydureon 751-C 07-2019.doc

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RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Bydureon/Bydureon BCISE is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Bydureon/Bydureon BCISE (2 mg per dose) should be administered once every seven days (weekly). The dose can be administered at any time of day, with or without meals.¹⁻⁴

Clinical guidelines from the American Diabetes Association and the American Association of Clinical Endocrinologists and American College of Endocrinology for the management of hyperglycemia in type 2 diabetes indicate that metformin monotherapy should be started at diagnosis of type 2 diabetes unless there are contraindications. Metformin is effective and safe, is inexpensive, and may reduce risk of cardiovascular events and death. In patients with contraindications or intolerance of metformin, initial therapy should be based on patient factors; consider a drug from another class.^{5,6}

The clinical guidelines also state that the A1c test is the major tool for assessing glycemic control and has strong predictive value for diabetes complications. Thus, A1c testing should be performed routinely in all patients with diabetes at initial assessment and as part of continuing care. The guidelines set goals for therapeutic effectiveness which must be evaluated frequently (e.g., every 3 months) until stable, using multiple criteria, including A1c. Less frequent monitoring is acceptable once targets are achieved.^{5,6} Therefore; continued use of any GLP-1 Agonist (e.g., Adlyxin, Byetta, Bydureon, Ozempic, Tanzeum, Trulicity, and Victoza) will be approved for patients who have demonstrated a reduction in A1c since starting GLP-1 Agonist therapy for at least three months.

If the A1c target is not achieved after approximately 3 months and patient does not have atherosclerotic cardiovascular disease (ASCVD) or chronic kidney disease (CKD), consider a combination of metformin and one of the preferred six treatment options: sulfonylurea, thiazolidinedione, dipeptidyl peptidase 4 (DPP-4) inhibitors, sodium-glucose cotransporter 2 (SGLT2) inhibitors, glucagon-like peptide 1 (GLP-1) receptor agonists, or basal insulin; the choice of which agent to add is based on drug-specific effects and patient factors. For patients in whom ASCVD, Heart Failure, or CKD predominates, the best choice for a second agent is a GLP-1 receptor agonist or SGLT2 inhibitor with demonstrated cardiovascular risk reduction, after consideration of drug-specific and patient factors.⁵⁻⁶

In patients with an initial A1c of 7.5% or greater, or in patients who are unable to achieve their glycemic goals with monotherapy, combination therapy is recommended⁶

Exenatide slows gastric emptying, which reduces the rate at which meal-derived glucose appears in the circulation, reduces food intake, and is associated with weight loss.¹⁻³ A quantity limit is in place to aid proper utilization of Bydureon/Bydureon BCISE. At maximum approved dosing for Bydureon/Bydureon BCISE, four (4) units will be allowed for a 28 day supply (12 units per 84 day supply).

REFERENCES

1. Bydureon [package insert]. West Chester, OH: Amylin Pharmaceuticals, Inc.; February 2019.
2. Bydureon BCise [package insert]. West Chester, OH: Amylin Pharmaceuticals, Inc.; February 2019.
3. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed July 2019.
4. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed July 2019.
5. American Diabetes Association (ADA) Standards of Medical Care in Diabetes-2019—*Diabetes Care*. 2019; 42(Supplement 1).
6. Garber AJ, et al. AACE/ACE Consensus Statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the Comprehensive Type 2 Diabetes Management Algorithm 2019, *Endocr Pract*. 2019; 25 (No 1); 69-100.

Written by: UM Development (SE)
 Date Written: 02/2012
 Revised: 08/2012 (MDC-2 created), (PL) 10/2012 (extended duration on commercial version), (PL) 07/2013, (PL) 07/2014; (CF) 07/2015, (SF) 07/2016, 07/2017, 07/2018 (no clinical change), 07/2019 (no clinical changes), (CHART) 08/01/2019
 Reviewed: Medical Affairs (KP) 02/2012, (DHR) 08/2012, 10/2012; (DNC) 07/2013, 07/2014, 07/2015; (MES) 07/2016, 07/2017
 External Review: 02/2012, 03/2012, 10/2012, 10/2013, 10/2014, 10/2015, 10/2016, 10/2017, 10/2018, 10/2019

CRITERIA FOR APPROVAL

- | | | | |
|---|--|-----|----|
| 1 | Has the patient been receiving GLP-1 Agonist therapy for at least 3 months?
[Note: Examples of GLP-1 Agonists are Adlyxin, Bydureon, Byetta, Ozempic, Tanzeum, Trulicity, Victoza]
[If no, then skip to question 3.] | Yes | No |
| 2 | Has the patient demonstrated a reduction in A1c (hemoglobin A1c) since starting GLP-1 Agonist therapy?
[If yes, then skip to question 6.] | Yes | No |
| 3 | Does the patient have a diagnosis of type 2 diabetes mellitus? | Yes | No |
| 4 | Has the patient experienced an inadequate treatment response, intolerance, or contraindication to metformin?
[If yes, then skip to question 6.] | Yes | No |
| 5 | Does the patient require combination therapy AND have an A1c (hemoglobin A1c) of 7.5 percent or greater? | Yes | No |
| 6 | Does the patient require more than 4 pens or auto-injectors per 28 days (or 12 pens or auto-injectors per 84 days)?
[Rph Note: If yes, then deny and enter a partial approval for 4 pens or auto-injectors (4 units) per 21 days (or 12 pens or auto-injectors (12 units) per 63 days)] | Yes | No |

Mapping Instructions

	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Go to 3	
2.	Go to 6	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions: - You have been receiving this drug or another drug in the same class for at least 3 months - You had a reduction in A1c (hemoglobin A1c) since starting therapy Your request has been denied based on the information we have. [Short Description: No response to treatment]
3.	Go to 4	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have type 2 diabetes mellitus. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
4.	Go to 6	Go to 5	
5.	Go to 6	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet one of these conditions: - You have tried metformin and it did not work for you, or you cannot use it

			<p>- You require combination therapy and you have an A1c (hemoglobin A1c) of 7.5 percent or greater</p> <p>Your request has been denied based on the information we have.</p> <p>[Short description: No inadequate treatment response, intolerance or contraindication to metformin, no requirement for combination therapy]</p>
6.	Deny	Approve, 36 months, 4 pens or auto-injectors per 21 days* (12 pens or auto-injectors per 63 days*)	<p>You do not meet the requirements of your plan. You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 4 pens or auto-injectors per 28 days (or 12 pens or auto-injectors per 84 days). You have been approved for the maximum quantity that your plan covers for a duration of 36 months. Your request for additional quantities of the requested drug and strength has been denied.</p> <p>[Short description: Over max quantity]</p>

**The duration of 21 days is used for a 28-day fill period and 63 days is used for an 84-day fill period to allow time for refill processing.*

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	GLUCAGON-LIKE PEPTIDE 1 (GLP-1) RECEPTOR AGONIST
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BRAND NAME* (generic)
--

BYDUREON (exenatide extended-release)
--

BYDUREON BCISE (exenatide extended-release)
--

Status: CVS Caremark Criteria Type: Initial Prior Authorization
--

Ref # 796-A

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Bydureon/Bydureon BCISE is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use

- Bydureon/Bydureon BCISE is not recommended as first-line therapy for patients who have inadequate glycemic control on diet and exercise because of the uncertain relevance of the rat thyroid C-cell tumor findings to humans.
- Bydureon/Bydureon BCISE is not a substitute for insulin. Bydureon/Bydureon BCISE should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis, as it would not be effective in these settings.
- The concurrent use of Bydureon/Bydureon BCISE with insulin has not been studied and cannot be recommended.
- Bydureon/Bydureon BCISE is an extended-release formulation of exenatide. Bydureon/Bydureon BCISE should not be used with other products containing the active ingredient exenatide.
- Bydureon/Bydureon BCISE has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- Patient has been receiving GLP-1 Agonist therapy for at least 3 months and has demonstrated a reduction in A1c (hemoglobin A1c) since starting GLP-1 Agonist therapy
[Note: Examples of GLP-1 Agonists are Adlyxin, Bydureon, Byetta, Ozempic, Tanzeum, Trulicity, Victoza]

OR

- The patient has a diagnosis of Type 2 diabetes mellitus

AND

- The patient has experienced an inadequate treatment response, intolerance, or contraindication to metformin

OR

- The patient requires combination therapy AND has an A1c (hemoglobin A1c) of 7.5 percent or greater

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Bydureon/Bydureon BCISE is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Clinical guidelines from the American Diabetes Association and the American Association of Clinical Endocrinologists and American College of Endocrinology for the management of hyperglycemia in type 2 diabetes indicate that metformin monotherapy should be started at diagnosis of type 2 diabetes unless there are contraindications. Metformin is effective and safe, is inexpensive, and may reduce risk of cardiovascular events and death. In patients with contraindications or intolerance of metformin, initial therapy should be based on patient factors; consider a drug from another class.^{5,6}

The clinical guidelines also state that the A1c test is the major tool for assessing glycemic control and has strong predictive value for diabetes complications. Thus, A1c testing should be performed routinely in all patients with diabetes at initial assessment and as part of continuing care. The guidelines set goals for therapeutic effectiveness which must be evaluated frequently (e.g., every 3 months) until stable, using multiple criteria, including A1c. Less frequent monitoring is acceptable once targets are achieved.^{5,6} Therefore, continued use of any GLP-1 Agonist (e.g., Adlyxin, Byetta, Bydureon, Ozempic, Tanzeum, Trulicity, and Victoza) will be approved for patients who have demonstrated a reduction in A1c since starting GLP-1 Agonist therapy for at least three months.

If the A1c target is not achieved after approximately 3 months and patient does not have atherosclerotic cardiovascular disease (ASCVD) or chronic kidney disease (CKD), consider a combination of metformin and one of the preferred six treatment options: sulfonylurea, thiazolidinedione, dipeptidyl peptidase 4 (DPP-4) inhibitors, sodium-glucose cotransporter 2 (SGLT2) inhibitors, glucagon-like peptide 1 (GLP-1) receptor agonists, or basal insulin; the choice of which agent to add is based on drug-specific effects and patient factors. For patients in whom ASCVD, Heart Failure, or CKD predominates, the best choice for a second agent is a GLP-1 receptor agonist or SGLT2 inhibitor with demonstrated cardiovascular risk reduction, after consideration of drug-specific and patient factors.⁵⁻⁶

In patients with an initial A1c of 7.5% or greater, or in patients who are unable to achieve their glycemic goals with monotherapy, combination therapy is recommended⁶

REFERENCES

1. Bydureon [package insert]. West Chester, OH: Amylin Pharmaceuticals, Inc.; February 2019.
2. Bydureon BCise [package insert]. West Chester, OH: Amylin Pharmaceuticals, Inc.; February 2019.
3. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed July 2019.
4. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed July 2019.
5. American Diabetes Association (ADA) Standards of Medical Care in Diabetes-2019—*Diabetes Care*. 2019; 42(Supplement 1).
6. Garber AJ, et al. AACE/ACE Consensus Statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the Comprehensive Type 2 Diabetes Management Algorithm 2019, *Endocr Pract*. 2019; 25 (No 1); 69-100

Written by: UM Development (SE)
Date Written: 02/2012
Revised: 08/2012 (MDC-2 created), (PL) 10/2012 (extended duration on commercial version), (PL) 07/2013, (PL) 12/2013 (clarified Q#2), (PL) 07/2014; (CF) 07/2015, (SF) 07/2016, 07/2017, 07/2018 (no clinical changes), 07/2019 (no clinical changes, removed MDC designation)
Reviewed: Medical Affairs (KP) 02/2012, (DHR) 08/2012, 10/2012; (DNC) 07/2013, 07/2014, 07/2015; (MES) 07/2016, 07/2017, (CHART) 08/01/2019
External Review: 02/2012, 03/2012, 10/2012, 10/2013, 10/2014, 10/2015, 10/2016, 10/2017, 10/2018, 10/2019

CRITERIA FOR APPROVAL

1	Has the patient been receiving GLP-1 Agonist therapy for at least 3 months? [Note: Examples of GLP-1 Agonists are Adlyxin, Bydureon, Byetta, Ozempic, Tanzeum, Trulicity, Victoza] [If no, then skip to question 3.]	Yes	No
2	Has the patient demonstrated a reduction in A1c (hemoglobin A1c) since starting GLP-1 Agonist therapy? [No further questions.]	Yes	No
3	Does the patient have a diagnosis of type 2 diabetes mellitus?	Yes	No
4	Has the patient experienced an inadequate treatment response, intolerance or contraindication to metformin? [If yes, then no further questions.]	Yes	No
5	Does the patient require combination therapy AND have an A1c (hemoglobin A1c) of 7.5 percent or greater?	Yes	No

Guidelines for Approval

Duration of Approval 12 Months

Set 1		Set 2		Set 3	
Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)
1	None	3	1	3	1
2		4		5	4

Mapping Instructions

	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Go to 3	
2.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions: - You have been receiving this drug or another drug in the same class for at least 3 months - You had a reduction in A1c (hemoglobin A1c) since starting therapy Your request has been denied based on the information we have. [Short Description: No response to treatment]
3.	Go to 4	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have type 2 diabetes mellitus. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
4.	Approve, 12 months	Go to 5	
5.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet one of these conditions:

			<ul style="list-style-type: none"> - You have tried metformin and it did not work for you, or you cannot use it - You require combination therapy and you have an A1c (hemoglobin A1c) of 7.5 percent or greater <p>Your request has been denied based on the information we have. [Short description: No inadequate treatment response, intolerance or contraindication to metformin, no requirement for combination therapy]</p>
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PRIOR AUTHORIZATION CRITERIA

DRUG CLASS **GLUCAGON-LIKE PEPTIDE 1 (GLP-1) RECEPTOR AGONIST**

BRAND NAME*
(generic)

BYETTA
(exenatide)

Status: CVS Caremark Criteria

Type: Initial Prior Authorization with Quantity Limit

Ref # 39-C

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Byetta is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use

- Byetta is not a substitute for insulin. Byetta should not be used for the treatment of type 1 diabetes or diabetic ketoacidosis, as it would not be effective in these settings.
- The concurrent use of Byetta with prandial insulin has not been studied and cannot be recommended.
- Based on postmarketing data Byetta has been associated with acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis. Byetta has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at increased risk for pancreatitis while using Byetta. Other antidiabetic therapies should be considered in patients with a history of pancreatitis.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has been receiving GLP-1 Agonist therapy for at least 3 months and has demonstrated a reduction in A1c (hemoglobin A1c) since starting GLP-1 Agonist therapy

[Note: Examples of GLP-1 Agonists are Adlyxin, Bydureon, Byetta, Ozempic, Tanzeum, Trulicity, Victoza]

OR

- The patient has a diagnosis of type 2 diabetes mellitus

AND

- The patient has experienced an inadequate treatment response, intolerance, or contraindication to metformin

OR

- The patient requires combination therapy AND has an A1c (hemoglobin A1c) of 7.5 percent or greater

Quantity Limits apply.

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Byetta is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Byetta should be initiated 5 mcg administered twice daily at any time within the 60-minute period before the morning and evening meals (or before the two main meals of the day, approximately 6 hours or more apart). Byetta should not be administered after a meal. Based on clinical response, the dose of Byetta may be increased to 10 mcg twice daily after 1 month of therapy.

Clinical guidelines from the American Diabetes Association and the American Association of Clinical Endocrinologists and American College of Endocrinology for the management of hyperglycemia in type 2 diabetes indicate that metformin monotherapy should be started at diagnosis of type 2 diabetes unless there are contraindications. Metformin is effective and safe, is inexpensive, and may reduce risk of cardiovascular events and death. In patients with contraindications or intolerance of metformin, initial therapy should be based on patient factors; consider a drug from another class.⁴⁻⁵

The clinical guidelines also state that the A1c test is the major tool for assessing glycemic control and has strong predictive value for diabetes complications. Thus, A1c testing should be performed routinely in all patients with diabetes at initial assessment and as part of continuing care. The guidelines set goals for therapeutic effectiveness which must be evaluated frequently (e.g., every 3 months) until stable, using multiple criteria, including A1c. Less frequent monitoring is acceptable once targets are achieved.⁴⁻⁵ Therefore; continued use of any GLP-1 Agonist (e.g., Adlyxin, Byetta, Bydureon, Ozempic, Tanzeum, Trulicity, and Victoza) will be approved for patients who have demonstrated a reduction in A1c since starting GLP-1 Agonist therapy for at least three months.

If the A1c target is not achieved after approximately 3 months and patient does not have atherosclerotic cardiovascular disease (ASCVD) or chronic kidney disease (CKD), consider a combination of metformin and one of the preferred six treatment options: sulfonylurea, thiazolidinedione, dipeptidyl peptidase 4 (DPP-4) inhibitors, sodium-glucose cotransporter 2 (SGLT2) inhibitors, glucagon-like peptide 1 (GLP-1) receptor agonists, or basal insulin; the choice of which agent to add is based on drug-specific effects and patient factors. For patients in whom ASCVD, Heart Failure, or CKD predominates, the best choice for a second agent is a GLP-1 receptor agonist or SGLT2 inhibitor with demonstrated cardiovascular risk reduction, after consideration of drug-specific and patient factors.⁴⁻⁵

In patients with an initial A1c of 7.5% or greater, or in patients who are unable to achieve their glycemic goals with monotherapy, combination therapy is recommended.⁴⁻⁵

Exenatide slows gastric emptying, which reduces the rate at which meal-derived glucose appears in the circulation, reduces food intake, and is associated with weight loss.¹⁻³ A quantity limit is in place to aid proper utilization of Byetta. At maximum approved dosing for Byetta, 1 pen containing 60 doses will be allowed for a 30 day supply (3 pens per 90 day supply).

REFERENCES

1. Byetta [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; December 2018.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed July 2019.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed July 2019.
4. American Diabetes Association (ADA) Standards of Medical Care in Diabetes-2019—*Diabetes Care*. 2019; 42(Supplement 1).
5. Garber AJ, et al. AACE/ACE Consensus Statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the Comprehensive Type 2 Diabetes Management Algorithm 2019, *Endocr Pract*. 2019; 25 (No 1); 69-100.

Written by: UM Development (SE)
Date Written: 02/2012
Revised: 08/2012 (MDC-2 created), (PL) 10/2012 (extended duration on commercial version), (PL) 07/2013, (PL) 07/2014; (CF) 07/2015, (SF) 07/2016, 07/2017, 07/2018 (no clinical changes), 07/2019 (no clinical changes)
Reviewed: Medical Affairs (KP) 02/2012, (DHR) 08/2012, 10/2012; (DNC) 07/2013, 07/2014, 07/2015; (MES) 07/2016, 07/2017, (CHART) 08/01/2019
External Review: 02/2012, 03/2012, 10/2012, 10/2013, 10/2014, 10/2015, 10/2016, 10/2017, 10/2018, 10/2019

CRITERIA FOR APPROVAL

1	Has the patient been receiving GLP-1 Agonist therapy for at least 3 months? [Note: Examples of GLP-1 Agonists are Adlyxin, Bydureon, Byetta, Ozempic, Tanzeum, Trulicity, Victoza] [If no, then skip to question 3.]	Yes	No
2	Has the patient demonstrated a reduction in A1c (hemoglobin A1c) since starting GLP-1 Agonist therapy? [If yes, then skip to question 6.]	Yes	No
3	Does the patient have a diagnosis of type 2 diabetes mellitus?	Yes	No
4	Has the patient experienced an inadequate treatment response, intolerance, or contraindication to metformin? [If yes, then skip to question 6.]	Yes	No
5	Does the patient require combination therapy AND have an A1c (hemoglobin A1c) of 7.5 percent or greater?	Yes	No
6	Does the patient require more than 1 prefilled pen per month (or 3 prefilled pens per 3 months)? [RPh Note: If yes, then deny and enter a partial approval for 1 prefilled pen (1.2mL for 5 mcg dose, 60 doses per prefilled pen, or 2.4mL for 10mcg dose, 60 doses per prefilled pen) per 25 days (3 prefilled pens (3.6mL for 5mcg dose, 60 doses per prefilled pen, 7.2mL for 10mcg dose, 60 doses per prefilled pen) per 75 days)]	Yes	No

Mapping Instructions

DENIAL REASONS – DO NOT USE FOR MEDICARE PART D

	Yes	No	
1.	Go to 2	Go to 3	
2.	Go to 6	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions: - You have been receiving this drug or another drug in the same class for at least 3 months - You had a reduction in A1c (hemoglobin A1c) since starting therapy Your request has been denied based on the information we have. [Short Description: No response to treatment]
3.	Go to 4	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have type 2 diabetes mellitus. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
4.	Go to 6	Go to 5	
5.	Go to 6	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet one of these conditions: - You have tried metformin it did not work for you, or you cannot use it - You require combination therapy and you have an A1c (hemoglobin A1c) of 7.5 percent or greater Your request has been denied based on the information we have. [Short description: No inadequate treatment response, intolerance or contraindication to metformin, no requirement for combination therapy]
6.	Deny	Approve, 36 months, 1.2mL for 5 mcg	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 1 prefilled pen per month (or 3

		dose, 60 doses per prefilled pen, or 2.4mL for 10mcg dose, 60 doses per prefilled pen/ 25 days* (3 prefilled pens (3.6mL for 5mcg dose, 60 doses per prefilled pen, 7.2mL for 10mcg dose, 60 doses per prefilled pen) /75 days*)	prefilled pens per 3 months) of the requested drug and strength. You have been approved for the maximum quantity that your plan covers for a duration of 36 months. Your request for additional quantities of the requested drug and strength has been denied. [Short description: Over max quantity]
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**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS **GLUCAGON-LIKE PEPTIDE 1 (GLP-1) RECEPTOR AGONIST**

BRAND NAME*
(generic)

BYETTA
(exenatide)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

Ref # 520-A

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Byetta is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use

- Byetta is not a substitute for insulin. Byetta should not be used for the treatment of type 1 diabetes or diabetic ketoacidosis, as it would not be effective in these settings.
- The concurrent use of Byetta with prandial insulin has not been studied and cannot be recommended.
- Based on postmarketing data Byetta has been associated with acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis. Byetta has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at increased risk for pancreatitis while using Byetta. Other antidiabetic therapies should be considered in patients with a history of pancreatitis.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has been receiving GLP-1 Agonist therapy for at least 3 months and has demonstrated a reduction in A1c (hemoglobin A1c) since starting GLP-1 Agonist therapy
[Note: Examples of GLP-1 Agonists are Adlyxin, Bydureon, Byetta, Ozempic, Tanzeum, Trulicity, Victoza]

OR

- The patient has a diagnosis of type 2 diabetes mellitus

AND

- The patient has experienced an inadequate treatment response, intolerance, or contraindication to metformin
- OR**
- The patient requires combination therapy AND has an A1c (hemoglobin A1c) of 7.5 percent or greater

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Byetta is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Clinical guidelines from the American Diabetes Association and the American Association of Clinical Endocrinologists and American College of Endocrinology for the management of hyperglycemia in type 2 diabetes indicate that metformin monotherapy should be started at diagnosis of type 2 diabetes unless there are contraindications. Metformin is effective and safe, is inexpensive, and may reduce risk of cardiovascular events and death. In patients with contraindications or intolerance of metformin, initial therapy should be based on patient factors; consider a drug from another class.⁴⁻⁵

The clinical guidelines also state that the A1c test is the major tool for assessing glycemic control and has strong predictive value for diabetes complications. Thus, A1c testing should be performed routinely in all patients with diabetes at initial assessment and as part of continuing care. The guidelines set goals for therapeutic effectiveness which must be

evaluated frequently (e.g., every 3 months) until stable, using multiple criteria, including A1c. Less frequent monitoring is acceptable once targets are achieved.⁴⁻⁵ Therefore; continued use of any GLP-1 Agonist (e.g., Adlyxin, Byetta, Bydureon, Ozempic, Tanzeum, Trulicity, and Victoza) will be approved for patients who have demonstrated a reduction in A1c since starting GLP-1 Agonist therapy for at least three months.

If the A1c target is not achieved after approximately 3 months and patient does not have atherosclerotic cardiovascular disease (ASCVD) or chronic kidney disease (CKD), consider a combination of metformin and one of the preferred six treatment options: sulfonylurea, thiazolidinedione, dipeptidyl peptidase 4 (DPP-4) inhibitors, sodium-glucose cotransporter 2 (SGLT2) inhibitors, glucagon-like peptide 1 (GLP-1) receptor agonists, or basal insulin; the choice of which agent to add is based on drug-specific effects and patient factors. For patients in whom ASCVD, Heart Failure, or CKD predominates, the best choice for a second agent is a GLP-1 receptor agonist or SGLT2 inhibitor with demonstrated cardiovascular risk reduction, after consideration of drug-specific and patient factors.⁴⁻⁵

In patients with an initial A1c of 7.5% or greater, or in patients who are unable to achieve their glycemic goals with monotherapy, combination therapy is recommended.⁴⁻⁵

REFERENCES

1. Byetta [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; December 2018.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed July 2019.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed July 2019.
4. American Diabetes Association (ADA) Standards of Medical Care in Diabetes-2019—*Diabetes Care*. 2019; 42(Supplement 1).
5. Garber AJ, et al. AACE/ACE Consensus Statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the Comprehensive Type 2 Diabetes Management Algorithm 2019, *Endocr Pract*. 2019; 25 (No 1); 69-100.

Written by: UM Development (SE)
 Date Written: 02/2012
 Revised: 08/2012 (MDC-2 created), (PL) 10/2012 (extended duration on commercial version), (PL) 07/2013, (PL) 12/2013 (clarified Q#2), (PL) 07/2014; (CF) 07/2015, (SF) 07/2016, 07/2017, 07/2018 (no clinical changes), 07/2019 (no clinical changes; removed MDC designation)
 Reviewed: Medical Affairs (KP) 02/2012, (DHR) 08/2012, 10/2012; (DNC) 07/2013, 07/2014, 07/2015; (MES) 07/2016, 07/2017, (CHART) 08/01/2019
 External Review: 02/2012, 03/2012, 10/2012, 10/2013, 10/2014, 10/2015, 10/2016, 10/2017, 10/2018, 10/2019

CRITERIA FOR APPROVAL

1	Has the patient been receiving GLP-1 Agonist therapy for at least 3 months? [Note: Examples of GLP-1 Agonists are Adlyxin, Bydureon, Byetta, Ozempic, Tanzeum, Trulicity, Victoza] [If no, then skip to question 3.]	Yes	No
2	Has the patient demonstrated a reduction in A1c (hemoglobin A1c) since starting GLP-1 Agonist therapy? [No further questions.]	Yes	No
3	Does the patient have a diagnosis of type 2 diabetes mellitus?	Yes	No
4	Has the patient experienced an inadequate treatment response, intolerance, or contraindication to metformin?	Yes	No

[If yes, then no further questions.]

5 Does the patient require combination therapy AND have an A1c (hemoglobin A1c) of 7.5 percent or greater? Yes No

Guidelines for Approval

Duration of Approval 12 Months

Set 1		Set 2		Set 3	
Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)
1	None	3	1	3	1
2		4		5	4

Mapping Instructions

DENIAL REASONS – DO NOT USE FOR MEDICARE PART D			
	Yes	No	
1.	Go to 2	Go to 3	
2.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions: - You have been receiving this drug or another drug in the same class for at least 3 months - You had a reduction in A1c (hemoglobin A1c) since starting therapy Your request has been denied based on the information we have. [Short Description: No response to treatment]
3.	Go to 4	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have type 2 diabetes mellitus. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
4.	Approve, 12 months	Go to 5	
5.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet one of these conditions: - You have tried metformin and it did not work for you, or you cannot use it - You require combination therapy and you have an A1c (hemoglobin A1c) of 7.5 percent or greater Your request has been denied based on the information we have. [Short description: No inadequate treatment response, intolerance or contraindication to metformin, no requirement for combination therapy]

SPECIALTY GUIDELINE MANAGEMENT

CABLIVI (caplacizumab-yhdp)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Cablivi is indicated for the treatment of adult patients with acquired thrombotic thrombocytopenic purpura (aTTP), in combination with plasma exchange and immunosuppressive therapy.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
For continuation of therapy: medical record documentation of signs of persistent underlying aTTP

III. CRITERIA FOR INITIAL APPROVAL

Acquired thrombotic thrombocytopenic purpura (aTTP)

Authorization of 30 days may be granted for treatment of acquired thrombotic thrombocytopenic purpura (aTTP) after the plasma exchange period in the inpatient setting when all of the following criteria are met:

- A. The member received the requested medication with plasma exchange.
- B. The requested medication will be given in combination with immunosuppressive therapy.
- C. The member will not receive the requested medication beyond 30 days from the cessation of plasma exchange unless the member has documented persistent aTTP.
- D. The member has not experienced more than 2 recurrences of aTTP while on the requested medication. (A recurrence is when the patient needs to reinstitute plasma exchange. A 28 day extension of therapy does not count as a recurrence.)

IV. CONTINUATION OF THERAPY

Authorization of 28 days may be granted for continuation of therapy for aTTP when all of the following criteria are met:

- A. The request for continuation of therapy is for extension of therapy after the initial course of the requested medication (initial course: treatment with the requested medication during and 30 days after plasma exchange).
- B. The member has either of the following documented signs of persistent underlying aTTP:
 1. ADAMTS13 activity level less than 10% or

Reference number(s)
2871-A

2. All of the following:
 - a. Microangiopathic hemolytic anemia (MAHA) documented by the presence of schistocytes on peripheral smear
 - b. Thrombocytopenia (platelet count below normal per laboratory reference range), and
 - c. Elevated lactate dehydrogenase (LDH) level (LDH level above normal per laboratory reference range)
- C. The requested medication will be given in combination with immunosuppressive therapy.
- D. The member has not received a prior 28 day extension of therapy after the initial course of the requested medication for this course of treatment.
- E. The member has not experienced more than 2 recurrences of aTTP while on the requested medication. (A recurrence is when the patient needs to reinstitute plasma exchange. A 28 day extension of therapy does not count as a recurrence.)

V. REFERENCES

1. Cablivi [package insert]. Cambridge, MA: Genzyme Corporation; February 2019.
2. Scully M, Cataland SR, Peyvandi F; et al. Caplacizumab treatment for acquired thrombotic thrombocytopenic purpura. *N Engl J Med*. 2019;380(4):335-346.
3. Sadler JE. Pathophysiology of thrombotic thrombocytopenic purpura. *Blood*. 2017;130(10):1181-1188.
4. Scully M, Cataland S, Coppo P, et al. Consensus on the standardization of terminology in thrombotic thrombocytopenic purpura and related thrombotic microangiopathies. *J Thromb Haemost*. 2017; 15(2):312-322.
5. Scully M, Hunt BJ, Benjamin S, et al. Guidelines on the diagnosis and management of thrombotic thrombocytopenic purpura and other thrombotic microangiopathies. *Br J Haematol*. 2012;158(3):323-335.
6. Westwood JP, Thomas M, Alwan F, et al. Rituximab prophylaxis to prevent thrombotic thrombocytopenic purpura relapse: outcome and evaluation of dosing regimens. *Blood Adv*. 2017; 1(15):1159-1166.

SPECIALTY GUIDELINE MANAGEMENT

CABOMETYX (cabozantinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Cabometyx is indicated for the treatment of patients with:

1. Advanced renal cell carcinoma (RCC)
2. Hepatocellular carcinoma (HCC) who have been previously treated with sorafenib

B. Compendial Uses

1. Relapsed or surgically unresectable stage IV kidney cancer
2. Non-small cell lung cancer
3. Hepatocellular carcinoma (HCC) who have been previously treated with lenvatinib

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of RET gene rearrangement documentation is necessary to initiate the prior authorization review for the indication of non-small cell lung cancer.

III. CRITERIA FOR INITIAL APPROVAL

A. **Renal Cell Carcinoma**

Authorization of 12 months may be granted for treatment of relapsed, unresectable, or metastatic renal cell carcinoma.

B. **Hepatocellular carcinoma (HCC)**

Authorization of 12 months may be granted for treatment of hepatocellular carcinoma (HCC) who have been previously treated with sorafenib (Nexavar) or lenvatinib (Lenvima).

C. **Non-small Cell Lung Cancer**

Authorization of 12 months may be granted for treatment of RET (rearranged during transfection) positive non-small cell lung cancer.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy for an indication outlined in Section III when there is no evidence of unacceptable toxicity or disease progression on the current regimen.

V. REFERENCES

1. Cabometyx [package insert]. South San Francisco, CA: Exelixis, Inc.; January 2019.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed May 24, 2019.
3. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Kidney Cancer. Version 4.2019. Accessed May 24, 2019. https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf.
4. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Hepatobiliary Cancer. Version 2.2019. Accessed May 24, 2019.
5. Clinical Consult: CVS Caremark Clinical Programs Review. Focus on Genitourinary Cancer Clinical Programs. July 2018.

SPECIALTY GUIDELINE MANAGEMENT

CALQUENCE (acalabrutinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

A. Mantle Cell Lymphoma

Calquence is indicated for the treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy.

B. Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma

Calquence is indicated for the treatment of adult patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL).

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Mantle cell lymphoma

Authorization of 12 months may be granted for treatment of mantle cell lymphoma when the member has received at least one prior therapy.

B. Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL)

Authorization of 12 months may be granted for treatment of CLL/SLL.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced disease progression or an unacceptable toxicity.

IV. REFERENCES

1. Calquence [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; November 2019.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed November 11, 2019.
3. The NCCN Clinical Practice Guidelines in Oncology® B-Cell Lymphomas Version 2.2019. National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 7, 2019.
4. The NCCN Clinical Practice Guidelines in Oncology® Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Version 2.2020. National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed November 21, 2019.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

INVOKANA
(canagliflozin)

INVOKAMET
(canagliflozin / metformin)

INVOKAMET XR
(canagliflozin / metformin extended-release)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

Ref # 973-A

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Invokana

Invokana (canagliflozin) is indicated:

- as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
- to reduce the risk of major adverse cardiovascular events (cardiovascular death, nonfatal myocardial infarction and nonfatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease (CVD).
- to reduce the risk of end-stage kidney disease (ESKD), doubling of serum creatinine, cardiovascular (CV) death, and hospitalization for heart failure in adults with type 2 diabetes mellitus and diabetic nephropathy with albuminuria > 300 mg/day.

Limitations of Use

Invokana is not recommended in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis.

Invokamet, Invokamet XR

Invokamet and Invokamet XR are a combination of canagliflozin and metformin hydrochloride (HCl) indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both canagliflozin and metformin HCl is appropriate.

Canagliflozin is indicated to reduce the risk of major adverse cardiovascular events (cardiovascular death, nonfatal myocardial infarction and nonfatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease (CVD). However, the effectiveness of Invokamet/Invokamet XR on reducing the risk of major cardiovascular events in adults with type 2 diabetes and cardiovascular disease has not been established.

Limitations of Use

Not recommended in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has been receiving the requested drug for at least 3 months

AND

- The patient has demonstrated a reduction in A1c (hemoglobin A1c) since starting this therapy

OR

- The request is for Invokana (canagliflozin) **AND**
 - The patient has established cardiovascular disease**OR**
 - The patient has diabetic nephropathy with albuminuria greater than 300 mg per day

OR

- Patient has the diagnosis of type 2 diabetes mellitus

AND

- The patient has experienced an inadequate treatment response, intolerance, or contraindication to metformin
- OR**
- The patient requires combination therapy **AND** has an A1c (hemoglobin A1c) of 7.5 percent or greater
- OR**
- The request is for Invokana (canagliflozin) **AND**
 - The patient has established cardiovascular disease**OR**
 - The patient has diabetic nephropathy with albuminuria greater than 300 mg per day

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Invokana (canagliflozin), Invokamet (canagliflozin/metformin) and Invokamet XR (canagliflozin/metformin extended-release) are indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Invokana is also indicated to reduce the risk of major adverse cardiovascular events (cardiovascular death, nonfatal myocardial infarction and nonfatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease (CVD); and to reduce the risk of end-stage kidney disease (ESKD), doubling of serum creatinine, cardiovascular (CV) death, and hospitalization for heart failure in adults with type 2 diabetes mellitus and diabetic nephropathy with albuminuria > 300 mg/day. However, the effectiveness of canagliflozin combination products such as Invokamet and Invokamet XR for these indications has not been established.

Clinical guidelines from the American Diabetes Association and the American Association of Clinical Endocrinologists and American College of Endocrinology for the management of hyperglycemia in type 2 diabetes indicate that metformin monotherapy should be started at diagnosis of type 2 diabetes unless there are contraindications. Metformin is effective and safe, is inexpensive, and may reduce risk of cardiovascular events and death. In patients with contraindications or intolerance of metformin, initial therapy should be based on patient factors; consider a drug from another class.^{5,6}

The clinical guidelines also state that the A1c test is the major tool for assessing glycemic control and has strong predictive value for diabetes complications. Thus, A1c testing should be performed routinely in all patients with diabetes at initial assessment and as part of continuing care. The guidelines set goals for therapeutic effectiveness which must be evaluated frequently (e.g., every 3 months) until stable, using multiple criteria, including A1c. Less frequent monitoring is acceptable once targets are achieved.^{5,6} Therefore, continued use of Invokana, Invokamet, or Invokamet XR will be approved for patients who have demonstrated a reduction in A1c (hemoglobin A1c) since starting Invokana, Invokamet, or Invokamet XR therapy for at least three months.

If the A1c target is not achieved after approximately 3 months and patient does not have atherosclerotic cardiovascular disease (ASCVD) or chronic kidney disease (CKD), consider a combination of metformin and one of the preferred six treatment options: sulfonylurea, thiazolidinedione, dipeptidyl peptidase 4 (DPP-4) inhibitors, sodium-glucose cotransporter 2 (SGLT2) inhibitors, glucagon-like peptide 1 (GLP-1) receptor agonists, or basal insulin; the choice of which agent to add is based on drug-specific effects and patient factors. For patients in whom ASCVD, Heart Failure or CKD predominates,

the best choice for a second agent is a GLP-1 receptor agonist or SGLT2 inhibitor with demonstrated cardiovascular risk reduction, after consideration of drug-specific and patient factors.⁵

In patients with an initial A1c of 7.5% or greater, or in patients who are unable to achieve their glycemic goals with monotherapy, combination therapy is recommended.⁶

The CANVAS and CANVAS-R trials compared the risk of Major Adverse Cardiovascular Event (MACE) between canagliflozin and placebo when these were added to and used concomitantly with standard of care treatments for diabetes and atherosclerotic cardiovascular disease. Concomitant antidiabetic and atherosclerotic therapies could be adjusted, at the discretion of investigators, to ensure participants were treated according to standard of care for these diseases.² Therefore, Invokana will be approved for initial therapy and continuation of therapy for patients who have established cardiovascular disease.

The CREDENCE trial compared canagliflozin with placebo in patients with type 2 diabetes mellitus, an estimated glomerular filtration rate ≥ 30 to < 90 mL/min/1.73 m² and albuminuria (urine albumin/creatinine > 300 to ≤ 5000 mg/g) who were receiving standard of care, including a maximum-tolerated, labeled daily dose of an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker. Patients were randomized to receive canagliflozin 100 mg or placebo and treatment was continued until the initiation of dialysis or renal transplantation.² The use of other background therapy for glycemic management and control of cardiovascular risk factors was recommended in accordance with local guidelines.⁷ Therefore, Invokana will be approved for initial therapy and continuation of therapy for patients who have diabetic nephropathy with albuminuria greater than 300 mg/day.

REFERENCES

1. Invokamet, Invokamet XR [package insert]. Titusville, New Jersey: Janssen Pharmaceuticals, Inc.; October 2018.
2. Invokana [package insert]. Titusville, New Jersey: Janssen Pharmaceuticals, Inc.; September 2019.
3. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed June 2019.
4. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed June 2019.
5. American Diabetes Association. Standards of Medical Care in Diabetes-2019: *Diabetes Care* January 2019;42(Supplement1).
6. Garber AJ, Abrahamson MJ, Barzilay JI, et al. Consensus Statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the Comprehensive Type 2 Diabetes Management Algorithm 2019, *Endocr Pract*. January 2019; 25 (No 1):69-100
7. Perkovic V, Jardine MJ, Neal B, et al. Canagliflozin and Renal Outcomes in Type 2 Diabetes and Nephropathy. *N Engl J Med* 2019; 380:2295-306.

Written by: UM Development (PL)
Date Written: 04/2013
Revised: (PL) 12/2013; (MS) 07/2014, 08/2014 (added Invokamet), (DN/SE) 07/2015; (KM) 07/2016 (updated Invokamet contraindication), 09/2016 (added Invokamet XR), 07/2017, 07/2018 (no clinical changes), 11/2018 (updated indications); (DFW) 07/2019 (no clinical changes), 10/2019 (updated Invokana indication/questions)
Reviewed: Medical Affairs (KP) 04/2013; (LCB) 12/2013, (SS) 07/2014, (MM) 08/2014, (DNC) 07/2015; (ME) 07/2016, 07/2017, 11/2018, (CHART) 8/1/19, (CHART) 10/03/19
External Review: 06/2013, 02/2014, 08/2014, 10/2015, 10/2016, 10/2017, 10/2018, 12/2018, 10/2019

CRITERIA FOR APPROVAL

1	Has the patient been receiving the requested drug for at least 3 months? [If no, then skip to question 4.]	Yes	No
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2	Has the patient demonstrated a reduction in A1c (hemoglobin A1c) since starting this therapy? [If yes, then no further questions.]	Yes	No
3	Is this request for Invokana (canagliflozin)? [If yes, then skip to question 8.] [If no, then no further questions.]	Yes	No
4	Does the patient have a diagnosis of type 2 diabetes mellitus?	Yes	No
5	Has the patient experienced an inadequate treatment response, intolerance, or contraindication to metformin? [If yes, then no further questions.]	Yes	No
6	Does the patient require combination therapy AND have an A1c (hemoglobin A1c) of 7.5 percent or greater? [If yes, then no further questions.]	Yes	No
7	Is this request for Invokana (canagliflozin)?	Yes	No
8	Does the patient have established cardiovascular disease? [If yes, then no further questions.]	Yes	No
9	Does the patient have diabetic nephropathy with albuminuria greater than 300 mg per day?	Yes	No

Mapping Instructions			
	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Go to 4	
2.	Approve, 36 months	Go to 3	
3.	Go to 8	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet these conditions: - You have been receiving the requested drug for at least 3 months - You had a reduction in A1c (hemoglobin A1c) since starting this therapy. Your request has been denied based on the information we have. [Short Description: No response to treatment]
4.	Go to 5	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have type 2 diabetes mellitus. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
5.	Approve, 36 months	Go to 6	
6.	Approve, 36 months	Go to 7	
7.	Go to 8	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet any of these conditions: - You have tried metformin and it did not work for you, or you cannot use it

			<p>- You require combination therapy and you have an A1c (hemoglobin A1c) of 7.5 percent or greater</p> <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No inadequate response, intolerance or contraindication to metformin, no confirmation of combination therapy requirement]</p>
8.	Approve, 36 months	Go to 9	
9.	Approve, 36 months	Deny	<p>You do not meet the requirements of your plan.</p> <p>Your plan covers this drug when you meet any of these conditions:</p> <ul style="list-style-type: none"> - You have tried metformin and it did not work for you, or you cannot use it - You require combination therapy and you have an A1c (hemoglobin A1c) of 7.5 percent or greater - You have cardiovascular (heart) disease - You have diabetic nephropathy (kidney disease) with albuminuria greater than 300 mg per day - You have been taking the requested drug for at least 3 months and you had a reduction in A1c (hemoglobin A1c) since starting this therapy <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No inadequate response, intolerance or contraindication to metformin, No confirmation of combination therapy requirement, No established cardiovascular disease or diabetic nephropathy with albuminuria greater than 300 mg per day for Invokana]</p>

SPECIALTY GUIDELINE MANAGEMENT

CAPRELSA (vandetanib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Treatment of symptomatic or progressive medullary thyroid cancer in patients with unresectable locally advanced or metastatic disease

Use Caprelsa in patients with indolent, asymptomatic or slowly progressing disease only after careful consideration of the treatment related risks of Caprelsa.

B. Compendial Uses

1. Follicular, Hurthle cell, and papillary thyroid carcinoma
2. Non-small cell lung cancer with RET gene rearrangements

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of RET gene rearrangement documentation is necessary to initiate the prior authorization review for the indication of non-small cell lung cancer.

III. CRITERIA FOR INITIAL APPROVAL

A. **Thyroid carcinoma (follicular, Hürthle cell, papillary)**

Authorization of 12 months may be granted for the treatment of radioiodine refractory follicular, Hürthle cell, or papillary thyroid carcinoma.

B. **Medullary thyroid carcinoma**

Authorization of 12 months may be granted for the treatment of medullary thyroid carcinoma.

C. **Non-small cell lung cancer (NSCLC)**

Authorization of 12 months may be granted for the treatment of NSCLC with RET gene rearrangements.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy for an indication outlined in Section III when there is no evidence of unacceptable toxicity or disease progression on the current regimen.

V. REFERENCES

Reference number
1783-A

1. Caprelsa [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals; October 2018.
2. The NCCN Drugs & Biologics Compendium™ © 2018 National Comprehensive Cancer Network, Inc. <https://www.nccn.org> Accessed October 24, 2018.
3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology® Thyroid Carcinoma (Version 1.2018). <https://www.nccn.org> Accessed October 24, 2018.
4. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology® Non-Small Cell Lung Cancer (Version 1.2019). <https://www.nccn.org>. Accessed October 24, 2018.

SPECIALTY GUIDELINE MANAGEMENT

CARBAGLU (carglumic acid)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. **Acute hyperammonemia in patients with NAGS deficiency**
Carbaglu is indicated as an adjunctive therapy in pediatric and adult patients for the treatment of acute hyperammonemia due to the deficiency of the hepatic enzyme N-acetylglutamate synthase (NAGS). During acute hyperammonemic episodes, concomitant administration of Carbaglu with other ammonia lowering therapies such as alternate pathway medications, hemodialysis, and dietary protein restriction is recommended.
2. **Maintenance therapy for chronic hyperammonemia in patients with NAGS deficiency**
Carbaglu is indicated for maintenance therapy in pediatric and adult patients for chronic hyperammonemia due to the deficiency of the hepatic enzyme NAGS. During maintenance therapy, the concomitant use of other ammonia lowering therapies and protein restriction may be needed based on plasma ammonia levels.

B. Compendial Uses

1. Methylmalonic acidemia
2. Propionic acidemia

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: enzyme assay or genetic testing results supporting diagnosis of NAGS deficiency.

III. CRITERIA FOR INITIAL APPROVAL

A. **N-acetylglutamate synthase (NAGS) Deficiency**

Authorization of 12 months may be granted for members with diagnosis of NAGS deficiency confirmed by enzymatic or genetic testing.

B. **Methylmalonic Acidemia**

Authorization of 12 months may be granted for members who have a diagnosis of methylmalonic acidemia.

C. **Propionic Acidemia**

Reference number(s)
2122-A

Authorization of 12 months may be granted for members who have a diagnosis of propionic acidemia.

IV. CONTINUATION OF THERAPY

A. N-acetylglutamate synthase (NAGS) Deficiency

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for NAGS deficiency who are experiencing benefit from therapy as evidenced by a decrease in ammonia levels from baseline.

B. Methylmalonic Acidemia or Propionic Acidemia

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for methylmalonic acidemia or propionic acidemia who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

V. REFERENCES

1. Carbaglu [package insert]. Lebanon, NJ: Recordati Rare Diseases, Inc.; November 2017.
2. Filippi L, Gozzini E, Fiorini P, et al. N-carbamylglutamate in emergency management of hyperammonemia in neonatal acute onset propionic and methylmalonic aciduria. *Neonatology*. 2010;97(3):286-290.
3. Levrat V, Forest I, Fouilhoux A, et al. Carglumic acid: an additional therapy in the treatment of organic acidurias with hyperammonemia. *Orphanet J Rare Dis*. 2008;3:2.
4. Gebhardt B, Vlaho S, Fischer D, et al. N-carbamylglutamate enhances ammonia detoxification in a patient with decompensated methylmalonic aciduria. *Mol Genet Metab*. 2003;79(4):303-304.
5. Gebhardt B, Dittrich S, Parbel S, et al. N-carbamylglutamate protects patients with decompensated propionic aciduria from hyperammonaemia. *J Inher Metab Dis*. 2005;28(2):241-244.
6. Schwahn BC, Pleterse L, Bisset WM, et al. Biochemical efficacy of N-carbamylglutamate in neonatal severe hyperammonaemia due to propionic acidemia. *Eur J Pediatr*. 2010;169(1):133-134.
7. Valayannopoulos V, Baruteau J, Delgado MB, et al. Carglumic acid enhances rapid ammonia detoxification in classical organic acidurias with a favourable risk-benefit profile: a retrospective observational study. *Orphanet J Rare Dis*. 2016;11:32.
8. Baumgartner MR, Hörster F, Dionisi-Vici C, et al. Proposed guidelines for the diagnosis and management of methylmalonic and propionic acidemia. *Orphanet J Rare Dis*. 2014; 9:130.

Reference number(s)
1880-A

SPECIALTY GUIDELINE MANAGEMENT

CAYSTON (aztreonam for inhalation solution)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Cayston is indicated to improve respiratory symptoms in cystic fibrosis patients with *Pseudomonas aeruginosa*.

All other indications are considered experimental/investigational and are not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Cystic Fibrosis

Authorization of 12 months may be granted for members with cystic fibrosis when *Pseudomonas aeruginosa* is present in airway cultures OR the member has a history of *Pseudomonas aeruginosa* infection or colonization in the airways.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

IV. REFERENCES

1. Cayston [package insert]. Foster City, CA: Gilead Sciences, Inc.; February 2019.
2. Mogayzel PJ, Naureckas ET, Robinson KA, et al. Cystic fibrosis pulmonary guidelines. Chronic medications for maintenance of lung health. *Am J Respir Crit Care Med*. 2013; 187:680-689.

SPECIALTY GUIDELINE MANAGEMENT

CERDELGA (eliglustat)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Cerdelga is indicated for the long-term treatment of adult patients with Gaucher disease type 1 who are CYP2D6 extensive metabolizers, intermediate metabolizers, or poor metabolizers as detected by an FDA-cleared test.

Limitations of use: Patients who are CYP2D6 ultra-rapid metabolizers may not achieve adequate concentrations of Cerdelga to achieve a therapeutic effect. A specific dosage cannot be recommended for those patients whose CYP2D6 genotype cannot be determined (indeterminate metabolizers).

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: beta-glucocerebrosidase enzyme assay or genetic testing results supporting diagnosis and the results of the CYP2D6 test

III. CRITERIA FOR INITIAL APPROVAL

Gaucher disease type 1

Authorization of 12 months may be granted for treatment of Gaucher disease type 1 when all of the following criteria are met:

1. Diagnosis of Gaucher disease was confirmed by enzyme assay demonstrating a deficiency of beta-glucocerebrosidase (glucosidase) enzyme activity or by genetic testing
2. Member is a CYP2D6 extensive metabolizer, an intermediate metabolizer, or a poor metabolizer as detected by an FDA-cleared test

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for Gaucher disease type 1 who are not experiencing an inadequate response or any intolerable adverse events from therapy.

V. REFERENCES

Reference number
2050-A

1. Cerdelga [package insert]. Cambridge, MA: Genzyme Corporation; August 2018.

SPECIALTY GUIDELINE MANAGEMENT

CEREZYME (imiglucerase)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Cerezyme is indicated for long-term enzyme replacement therapy (ERT) for pediatric and adult patients with a confirmed diagnosis of type 1 Gaucher disease that results in one or more of the following conditions: anemia, thrombocytopenia, bone disease, hepatomegaly, or splenomegaly.

B. Compendial Uses

Gaucher disease type 3

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: beta-glucocerebrosidase enzyme assay or genetic testing results supporting diagnosis.

III. CRITERIA FOR INITIAL APPROVAL

A. Gaucher disease type 1

Authorization of 12 months may be granted for treatment of Gaucher disease type 1 when the diagnosis of Gaucher disease was confirmed by enzyme assay demonstrating a deficiency of beta-glucocerebrosidase (glucosidase) enzyme activity or by genetic testing.

B. Gaucher disease type 3

Authorization of 12 months may be granted for treatment of Gaucher disease type 3 when the diagnosis of Gaucher disease was confirmed by enzyme assay demonstrating a deficiency of beta-glucocerebrosidase (glucosidase) enzyme activity or by genetic testing, and the patient is experiencing neurological symptoms.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for Gaucher disease type 1 or type 3 who are not experiencing an inadequate response or any intolerable adverse events from therapy.

Reference number
2051-A

V. REFERENCES

1. Cerezyme [package insert]. Cambridge, MA: Genzyme Corporation; April 2018.
2. Altarescu G, Hill S, Wiggs E, et al. The efficacy of enzyme replacement therapy in patients with chronic neuronopathic Gaucher's disease. *J Pediatr*. 2001;138:539-547.
3. Erikson A, Forsberg H, Nilsson M, Astrom M, Mansson JE. Ten years' experience of enzyme infusion therapy of Norrbottnian (type 3) Gaucher disease. *Acta Paediatr*. 2006;95:312-317.
4. Pastores GM, Hughes DA. Gaucher Disease. [Updated February 26, 2015]. In: Pagon RA, Adam MP, Ardinger HH, et al, editors. GeneReviews® [Internet]. Seattle, WA: University of Washington, Seattle; 1993-2016.
5. Kaplan P, Baris H, De Meirleir L, et al. Revised recommendations for the management of Gaucher disease in children. *Eur J Pediatr*. 2013;172:447-458.

Reference number(s)
1912-A, 1913-A

SPECIALTY GUIDELINE MANAGEMENT

CETROTIDE (cetorelix acetate) ganirelix acetate

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Cetrotide and ganirelix are indicated for the inhibition of premature luteinizing hormone (LH) surges in women undergoing controlled ovarian stimulation.

All other indications are considered experimental/investigational and not medically necessary.

II. MEDICAL BENEFIT ALIGNMENT

Specialty Guideline Management coverage review will be bypassed for drug(s) being requested for a procedure that has been approved under a member's medical benefit plan. Such members will be exempt from the requirements in Sections III and IV. A medical authorization number and confirmation of the approved procedure(s) will be required.

NOTE: Some plans may opt-out of medical benefit alignment. Members receiving coverage under such plans must meet the requirements in Sections III and IV.

III. CRITERIA FOR INITIAL APPROVAL

Inhibition of premature LH surges

Authorization of 12 months may be granted for the inhibition of premature LH surges in members undergoing ovulation induction or assisted reproductive technology (ART).

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. REFERENCES

1. Cetrotide [package insert]. Rockland, MA: EMD Serono; May 2018.
2. Ganirelix [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; February 2019.
3. Bakas P, Konidaris S, Liapis A, et al. Role of gonadotropin-releasing hormone antagonist in the management of subfertile couples with intrauterine insemination and controlled ovarian stimulation. *Fertil Steril*. 2011;95:2024-2028.

STEP THERAPY CRITERIA

DRUG CLASS	ORAL CALCITONIN GENE-RELATED PEPTIDE (CGRP) RECEPTOR ANTAGONISTS	
BRAND NAME* (generic)	NURTEC ODT (rimegepant)	
	UBRELVY (ubrogepant)	
Status: CVS Caremark Criteria		
Type: Initial Step Therapy with Quantity Limit;		
Post Step Therapy Prior Authorization with Quantity Limit		Ref # 3481-E

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Nurtec ODT

Nurtec ODT is indicated for the acute treatment of migraine with or without aura in adults.

Limitations of Use

Nurtec ODT is not indicated for the preventive treatment of migraine.

Ubrelvy

Ubrelvy is indicated for the acute treatment of migraine with or without aura in adults.

Limitations of Use

Ubrelvy is not indicated for the preventive treatment of migraine.

INITIAL STEP THERAPY with QUANTITY LIMIT*

*Include Rx and OTC products unless otherwise stated.

If the patient has filled a prescription for at least a 30 day supply of two triptan 5-HT₁ receptor agonists (include combinations) within the past 180 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.** If the patient does not meet the initial step therapy criteria, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

**If the patient meets the initial step therapy criteria, then the initial limit criteria will apply. If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that quantity limits are exceeded.

****INITIAL LIMIT CRITERIA**

Limits do not accumulate together, patient is allowed the maximum limit for each drug and strength.

PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

Drug	1 Month Limit*	3 Month Limit*
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Nurtec ODT (rimegepant)	16 orally disintegrating tablets / 25 days	48 orally disintegrating tablets / 75 days
Ubrelevy 50mg (ubrogepant)	16 tablets / 25 days	48 tablets / 75 days
Ubrelevy 100mg (ubrogepant)	16 tablets / 25 days	48 tablets / 75 days

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the acute treatment of migraine in an adult patient
- AND**
- The patient experienced an inadequate response or an intolerance to two triptan 5-HT₁ receptor agonists
- OR**
- The patient has a contraindication that would prohibit a trial of triptan 5-HT₁ receptor agonists

Quantity Limits apply.

RATIONALE

If the patient has filled a prescription for at least a 30 day supply of two triptan medications within the past 180 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit. If the patient meets the initial step therapy criteria, then the initial limit criteria will apply. The quantity is set at 16 tablets per 1 month or 48 tablets per 3 months.

If the patient does not meet the initial step therapy criteria, then prior authorization is required. If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that quantity limits are exceeded.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Nurtec ODT and Ubrelevy are indicated for the acute treatment of migraine with or without aura in adults. Nurtec ODT and Ubrelevy are not indicated for the preventive treatment of migraine.^{1,7}

The American Headache Society Position Statement on Integrating New Migraine Treatments into Clinical Practice (2019) recommends that all patients with migraine should be offered a trial of acute treatment. Effective acute treatment can reduce the pain, associated symptoms, and disability associated with attacks. Treat at the first sign of pain to improve the probability of achieving freedom from pain and reduce attack-related disability.⁴ Acute treatments that the American Headache Society Position Statement considered effective or probably effective are based on a 2015 American Headache Society expert review of evidence from controlled trials.⁴

The American Headache Society Evidence Assessment of Migraine Pharmacotherapies (2015) recommends specific medications within the following classes deemed effective for migraine acute therapy: triptans, ergotamine derivatives, nonsteroidal anti-inflammatory drugs (NSAIDs), opioids, and combination medications.⁵ The American Headache Society Evidence Assessment states that the specific medications – triptans (almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan [oral, nasal spray, injectable, transcutaneous patch], zolmitriptan [oral and nasal spray]) and dihydroergotamine (nasal spray, inhaler) are effective. Effective nonspecific medications include acetaminophen, nonsteroidal anti-inflammatory drugs (aspirin, diclofenac, ibuprofen, and naproxen), opioids (butorphanol nasal spray), sumatriptan/naproxen, and the combination of acetaminophen/aspirin/caffeine.⁵ The American Headache Society Evidence Assessment, states that although opioids, such as butorphanol, codeine/acetaminophen, and tramadol/acetaminophen, are probably effective, they are not recommended for regular use.⁵ Per the American Headache Society Evidence Assessment, there are many acute migraine treatments for which evidence supports efficacy. Clinicians must

consider medication efficacy, potential side effects, and potential medication-related adverse events when prescribing acute medications for migraine.⁵

The American Headache Society Position Statement on Integrating New Migraine Treatments into Clinical Practice (2019) recommends the use of NSAIDs (including aspirin), nonopioid analgesics, acetaminophen, or caffeinated analgesic combinations (e.g., aspirin + acetaminophen + caffeine) for mild-to-moderate attacks and migraine-specific agents (triptans, dihydroergotamine [DHE]) for moderate or severe attacks and mild-to-moderate attacks that respond poorly to NSAIDs or caffeinated combinations.⁴ Several different triptans are available on the market with different strengths, dosage forms and routes of administration.^{2,3} The American Headache Society Position Statement recommends choosing a nonoral formulation in patients whose attacks are associated with severe nausea or vomiting or who have trouble swallowing orally administered medications. This includes sumatriptan 3, 4, or 6 mg SC and intranasal and inhaled powder formulations and ketorolac in intranasal and intramuscular (IM) formulations. Dihydroergotamine SC and intranasal spray are alternatives. Nonoral routes of administration should also be considered in patients who do not respond well to traditional oral treatments or experience significant nausea or vomiting early during attacks.⁴

The American Academy of Neurology and the American Headache Society Practice Guideline Update Summary: Acute Treatment of Migraine in Children and Adolescents (2019) states that patients respond differently to the same medication. In adults, failure to respond to 1 triptan does not preclude response to an alternate triptan.⁶ Per the American Academy of Neurology and the American Headache Society Practice Guideline Update Summary, in adults who respond to a triptan but have recurrence of their headache within 24 hours, taking a second dose is effective.⁶ Also, the American Academy of Neurology and the American Headache Society Practice Guideline Update Summary states that migraine features (severity, associated symptoms, disability, and most bothersome symptoms) differ among individuals and among different attacks in the same individual. For migraines that rapidly peak in severity or are associated with nausea and vomiting, nonoral forms of treatment may be more effective.⁶

The American Headache Society Position Statement on Integrating New Migraine Treatments into Clinical Practice (2019) states that emerging agents with novel mechanisms of action that have demonstrated efficacy for the acute treatment of migraine include the small molecule CGRP receptor antagonists, ubrogepant and rimegepant, and lasmiditan, a selective serotonin (5-HT_{1F}) receptor agonist. The American Headache Society Position Statement states that unlike triptans and ergotamine derivatives, these novel treatment options do not result in constriction of blood vessels and may have a special role in patients with cardiovascular contraindications to triptans. Patients who have contraindications to the use of triptans or who have failed to respond to or tolerate at least 2 oral triptans, as determined by either a validated acute treatment patient reported outcome questionnaire (e.g., Migraine Treatment Optimization Questionnaire [mTOQ], Migraine Assessment of Current Therapy [Migraine-ACT], Patient Perception of Migraine Questionnaire-Revised [PPMQ-R], Functional Impairment Scale [FIS], Patient Global Impression of Change [PGIC]) or healthcare provider attestation), are eligible for ubrogepant, rimegepant, lasmiditan, or a neuromodulation device.⁴

Due to the high evidence of triptan efficacy in the acute treatment of migraine headaches, patients will be required to experience an inadequate treatment response or intolerance to at least two different triptan medications unless the patient has a contraindication that would prohibit a trial of these drugs.

The recommended dose of Nurtec ODT is 75 mg taken orally. The maximum dose in a 24-hour period is 75 mg. The safety of treating more than 15 migraines in a 30-day period has not been established. Nurtec ODT 75 mg orally disintegrating tablets are supplied in cartons containing a blister pack of 8 orally disintegrating tablets.⁷ Therefore, the limit is set at 16 tablets per month and 48 tablets per 3 months, allowing for 15 headaches and accommodating the package size of two packs of 8 tablets.

The recommended dose of Ubrelvy is 50 mg or 100 mg taken orally. If needed, a second dose may be taken at least 2 hours after the initial dose. The maximum dose in a 24-hour period is 200 mg. The safety of treating more than 8 migraines in a 30-day period has not been established. Dosing modifications should be made for concomitant use of specific drugs and for patients with hepatic or renal impairment. Therefore, the limit is set per each strength at 16 tablets per month and 48 tablets per 3 months, not to accumulate, allowing for dosing modifications. Ubrelvy is supplied in unit-dose packets (each packet contains 1 tablet) in boxes containing 6 packets, 8 packets, 10 packets, 12 packets, or 30 packets. It is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

REFERENCES

1. Ubrelvy [package insert]. Madison, NJ: Allergan USA, Inc.; December 2019.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed January 2020.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed January 2020.
4. American Headache Society. The American Headache Society Position Statement on Integrating New Migraine Treatments into Clinical Practice. *Headache* 2019; 59:1-18.
5. Marmura M, Silberstein S, Schwedt T. The Acute Treatment of Migraine in Adults: The American Headache Society Evidence Assessment of Migraine Pharmacotherapies. *Headache* 2015;55:3-20.
6. Oskoui M, Pringsheim T, Holler-Managan Y, et al. Practice guideline update summary: Acute Treatment of Migraine in Children and Adolescents. Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology and the American Headache Society. *Neurology* 2019;93:487-499.
7. Nurtec ODT [package insert]. New Haven, CT: Biohaven Pharmaceuticals, Inc; February 2020..

Written by: UM Development (TM)
 Date Written: 12/2019
 Revised: (TM) 02/2020 (added Nurtec ODT)
 Reviewed: Medical Affairs (CHART) 01/16/20, (CHART) 03/12/20
 External Review: 01/2020, 03/2020

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for the acute treatment of migraine in an adult patient?	Yes	No
2	Has the patient experienced an inadequate treatment response or an intolerance to two triptan 5-HT ₁ receptor agonists? [If yes, then skip to question 4.]	Yes	No
3	Does the patient have a contraindication that would prohibit a trial of triptan 5-HT ₁ receptor agonists?	Yes	No
4	Does the patient require more than the plan allowance of 16 tablets per month? [Note: Coverage is provided up to an amount sufficient for treating at the maximum recommended dose.]	Yes	No

[RPh Note: If yes, then deny and enter a partial approval for 16 tablets/25 days or 48 tablets/75 days.]

Mapping Instructions

	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions: - You use this drug for acute treatment of migraine - You are an adult [Short Description: No approvable diagnosis]
2.	Go to 4	Go to 3	
3.	Go to 4	Deny	You do not meet the requirements of your plan.

			<p>Your plan covers this drug when you have tried two triptan drugs and they did not work for you, or you cannot use them.</p> <p>[Short Description: No inadequate response, intolerance or contraindication to prerequisite drug]</p>
4.	<p>Deny</p> <p>RPh Note: For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage</p>	<p>Approve, 12 months, 16 tabs/25 days* or 48 tabs/75 days* See Quantity Limit Chart</p>	<p>You have requested more than the maximum quantity allowed by your plan.</p> <p>Current plan approved criteria cover up to:</p> <ul style="list-style-type: none"> - 16 tablets/month of Nurtec ODT 75mg - 16 tablets/month of Ubrelvy 50mg - 16 tablets/month of Ubrelvy100mg <p>You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied.</p> <p>[Short Description: Over max quantity]</p>

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

QUANTITY LIMIT

Limits do not accumulate together, patient is allowed the maximum limit for each drug and strength

PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

Drug	1 Month Limit*	3 Month Limit*
Nurtec ODT (rimegepant)	16 orally disintegrating tablets / 25 days	48 orally disintegrating tablets / 75 days
Ubrelvy 50mg (ubrogepant)	16 tablets / 25 days	48 tablets / 75 days
Ubrelvy 100mg (ubrogepant)	16 tablets / 25 days	48 tablets / 75 days

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

STEP THERAPY CRITERIA

DRUG CLASS	ORAL CALCITONIN GENE-RELATED PEPTIDE (CGRP) RECEPTOR ANTAGONISTS	
BRAND NAME* (generic)	NURTEC ODT (rimegepant)	
	UBRELVY (ubrogepant)	
Status: CVS Caremark Criteria		
Type: Initial Step Therapy with Quantity Limit;		
Post Step Therapy Prior Authorization with Quantity Limit		Ref # 3481-E

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Nurtec ODT

Nurtec ODT is indicated for the acute treatment of migraine with or without aura in adults.

Limitations of Use

Nurtec ODT is not indicated for the preventive treatment of migraine.

Ubrelvy

Ubrelvy is indicated for the acute treatment of migraine with or without aura in adults.

Limitations of Use

Ubrelvy is not indicated for the preventive treatment of migraine.

INITIAL STEP THERAPY with QUANTITY LIMIT*

*Include Rx and OTC products unless otherwise stated.

If the patient has filled a prescription for at least a 30 day supply of two triptan 5-HT₁ receptor agonists (include combinations) within the past 180 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.** If the patient does not meet the initial step therapy criteria, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

**If the patient meets the initial step therapy criteria, then the initial limit criteria will apply. If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that quantity limits are exceeded.

****INITIAL LIMIT CRITERIA**

Limits do not accumulate together, patient is allowed the maximum limit for each drug and strength.

PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

Drug	1 Month Limit*	3 Month Limit*
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Nurtec ODT (rimegepant)	16 orally disintegrating tablets / 25 days	48 orally disintegrating tablets / 75 days
Ubrovelvy 50mg (ubrogepant)	16 tablets / 25 days	48 tablets / 75 days
Ubrovelvy 100mg (ubrogepant)	16 tablets / 25 days	48 tablets / 75 days

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the acute treatment of migraine in an adult patient
- AND**
- The patient experienced an inadequate response or an intolerance to two triptan 5-HT₁ receptor agonists
- OR**
- The patient has a contraindication that would prohibit a trial of triptan 5-HT₁ receptor agonists

Quantity Limits apply.

RATIONALE

If the patient has filled a prescription for at least a 30 day supply of two triptan medications within the past 180 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit. If the patient meets the initial step therapy criteria, then the initial limit criteria will apply. The quantity is set at 16 tablets per 1 month or 48 tablets per 3 months.

If the patient does not meet the initial step therapy criteria, then prior authorization is required. If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that quantity limits are exceeded.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Nurtec ODT and Ubrovelvy are indicated for the acute treatment of migraine with or without aura in adults. Nurtec ODT and Ubrovelvy are not indicated for the preventive treatment of migraine.^{1,7}

The American Headache Society Position Statement on Integrating New Migraine Treatments into Clinical Practice (2019) recommends that all patients with migraine should be offered a trial of acute treatment. Effective acute treatment can reduce the pain, associated symptoms, and disability associated with attacks. Treat at the first sign of pain to improve the probability of achieving freedom from pain and reduce attack-related disability.⁴ Acute treatments that the American Headache Society Position Statement considered effective or probably effective are based on a 2015 American Headache Society expert review of evidence from controlled trials.⁴

The American Headache Society Evidence Assessment of Migraine Pharmacotherapies (2015) recommends specific medications within the following classes deemed effective for migraine acute therapy: triptans, ergotamine derivatives, nonsteroidal anti-inflammatory drugs (NSAIDs), opioids, and combination medications.⁵ The American Headache Society Evidence Assessment states that the specific medications – triptans (almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan [oral, nasal spray, injectable, transcutaneous patch], zolmitriptan [oral and nasal spray]) and dihydroergotamine (nasal spray, inhaler) are effective. Effective nonspecific medications include acetaminophen, nonsteroidal anti-inflammatory drugs (aspirin, diclofenac, ibuprofen, and naproxen), opioids (butorphanol nasal spray), sumatriptan/naproxen, and the combination of acetaminophen/aspirin/caffeine.⁵ The American Headache Society Evidence Assessment, states that although opioids, such as butorphanol, codeine/acetaminophen, and tramadol/acetaminophen, are probably effective, they are not recommended for regular use.⁵ Per the American Headache Society Evidence Assessment, there are many acute migraine treatments for which evidence supports efficacy. Clinicians must

consider medication efficacy, potential side effects, and potential medication-related adverse events when prescribing acute medications for migraine.⁵

The American Headache Society Position Statement on Integrating New Migraine Treatments into Clinical Practice (2019) recommends the use of NSAIDs (including aspirin), nonopioid analgesics, acetaminophen, or caffeinated analgesic combinations (e.g., aspirin + acetaminophen + caffeine) for mild-to-moderate attacks and migraine-specific agents (triptans, dihydroergotamine [DHE]) for moderate or severe attacks and mild-to-moderate attacks that respond poorly to NSAIDs or caffeinated combinations.⁴ Several different triptans are available on the market with different strengths, dosage forms and routes of administration.^{2,3} The American Headache Society Position Statement recommends choosing a nonoral formulation in patients whose attacks are associated with severe nausea or vomiting or who have trouble swallowing orally administered medications. This includes sumatriptan 3, 4, or 6 mg SC and intranasal and inhaled powder formulations and ketorolac in intranasal and intramuscular (IM) formulations. Dihydroergotamine SC and intranasal spray are alternatives. Nonoral routes of administration should also be considered in patients who do not respond well to traditional oral treatments or experience significant nausea or vomiting early during attacks.⁴

The American Academy of Neurology and the American Headache Society Practice Guideline Update Summary: Acute Treatment of Migraine in Children and Adolescents (2019) states that patients respond differently to the same medication. In adults, failure to respond to 1 triptan does not preclude response to an alternate triptan.⁶ Per the American Academy of Neurology and the American Headache Society Practice Guideline Update Summary, in adults who respond to a triptan but have recurrence of their headache within 24 hours, taking a second dose is effective.⁶ Also, the American Academy of Neurology and the American Headache Society Practice Guideline Update Summary states that migraine features (severity, associated symptoms, disability, and most bothersome symptoms) differ among individuals and among different attacks in the same individual. For migraines that rapidly peak in severity or are associated with nausea and vomiting, nonoral forms of treatment may be more effective.⁶

The American Headache Society Position Statement on Integrating New Migraine Treatments into Clinical Practice (2019) states that emerging agents with novel mechanisms of action that have demonstrated efficacy for the acute treatment of migraine include the small molecule CGRP receptor antagonists, ubrogepant and rimegepant, and lasmiditan, a selective serotonin (5-HT_{1F}) receptor agonist. The American Headache Society Position Statement states that unlike triptans and ergotamine derivatives, these novel treatment options do not result in constriction of blood vessels and may have a special role in patients with cardiovascular contraindications to triptans. Patients who have contraindications to the use of triptans or who have failed to respond to or tolerate at least 2 oral triptans, as determined by either a validated acute treatment patient reported outcome questionnaire (e.g., Migraine Treatment Optimization Questionnaire [mTOQ], Migraine Assessment of Current Therapy [Migraine-ACT], Patient Perception of Migraine Questionnaire-Revised [PPMQ-R], Functional Impairment Scale [FIS], Patient Global Impression of Change [PGIC]) or healthcare provider attestation), are eligible for ubrogepant, rimegepant, lasmiditan, or a neuromodulation device.⁴

Due to the high evidence of triptan efficacy in the acute treatment of migraine headaches, patients will be required to experience an inadequate treatment response or intolerance to at least two different triptan medications unless the patient has a contraindication that would prohibit a trial of these drugs.

The recommended dose of Nurtec ODT is 75 mg taken orally. The maximum dose in a 24-hour period is 75 mg. The safety of treating more than 15 migraines in a 30-day period has not been established. Nurtec ODT 75 mg orally disintegrating tablets are supplied in cartons containing a blister pack of 8 orally disintegrating tablets.⁷ Therefore, the limit is set at 16 tablets per month and 48 tablets per 3 months, allowing for 15 headaches and accommodating the package size of two packs of 8 tablets.

The recommended dose of Ubrelvy is 50 mg or 100 mg taken orally. If needed, a second dose may be taken at least 2 hours after the initial dose. The maximum dose in a 24-hour period is 200 mg. The safety of treating more than 8 migraines in a 30-day period has not been established. Dosing modifications should be made for concomitant use of specific drugs and for patients with hepatic or renal impairment. Therefore, the limit is set per each strength at 16 tablets per month and 48 tablets per 3 months, not to accumulate, allowing for dosing modifications. Ubrelvy is supplied in unit-dose packets (each packet contains 1 tablet) in boxes containing 6 packets, 8 packets, 10 packets, 12 packets, or 30 packets. It is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

REFERENCES

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Written by: UM Development (TM)
 Date Written: 12/2019
 Revised: (TM) 02/2020 (added Nurtec ODT)
 Reviewed: Medical Affairs (CHART) 01/16/20, (CHART) 03/12/20
 External Review: 01/2020, 03/2020

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for the acute treatment of migraine in an adult patient?	Yes	No
2	Has the patient experienced an inadequate treatment response or an intolerance to two triptan 5-HT ₁ receptor agonists? [If yes, then skip to question 4.]	Yes	No
3	Does the patient have a contraindication that would prohibit a trial of triptan 5-HT ₁ receptor agonists?	Yes	No
4	Does the patient require more than the plan allowance of 16 tablets per month? [Note: Coverage is provided up to an amount sufficient for treating at the maximum recommended dose.]	Yes	No

[RPh Note: If yes, then deny and enter a partial approval for 16 tablets/25 days or 48 tablets/75 days.]

Mapping Instructions

	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions: <ul style="list-style-type: none"> - You use this drug for acute treatment of migraine - You are an adult [Short Description: No approvable diagnosis]
2.	Go to 4	Go to 3	
3.	Go to 4	Deny	You do not meet the requirements of your plan.

			<p>Your plan covers this drug when you have tried two triptan drugs and they did not work for you, or you cannot use them.</p> <p>[Short Description: No inadequate response, intolerance or contraindication to prerequisite drug]</p>
4.	<p>Deny</p> <p>RPh Note: For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage</p>	<p>Approve, 12 months, 16 tabs/25 days* or 48 tabs/75 days* See Quantity Limit Chart</p>	<p>You have requested more than the maximum quantity allowed by your plan.</p> <p>Current plan approved criteria cover up to:</p> <ul style="list-style-type: none"> - 16 tablets/month of Nurtec ODT 75mg - 16 tablets/month of Ubrelvy 50mg - 16 tablets/month of Ubrelvy100mg <p>You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied.</p> <p>[Short Description: Over max quantity]</p>

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

QUANTITY LIMIT

Limits do not accumulate together, patient is allowed the maximum limit for each drug and strength

PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

Drug	1 Month Limit*	3 Month Limit*
Nurtec ODT (rimegepant)	16 orally disintegrating tablets / 25 days	48 orally disintegrating tablets / 75 days
Ubrelvy 50mg (ubrogepant)	16 tablets / 25 days	48 tablets / 75 days
Ubrelvy 100mg (ubrogepant)	16 tablets / 25 days	48 tablets / 75 days

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

SPECIALTY GUIDELINE MANAGEMENT

CHOLBAM (cholic acid)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Cholbam is indicated for:

1. Treatment of bile acid synthesis disorders due to single enzyme defects (SEDs)
2. Adjunctive treatment of peroxisomal disorders (PDs) including Zellweger spectrum disorders in patients who exhibit manifestations of liver disease, steatorrhea or complications from decreased fat soluble vitamin absorption

Limitation of use: The safety and effectiveness of Cholbam on extrahepatic manifestations of bile acid synthesis disorders due to SEDs or PDs including Zellweger spectrum disorders have not been established.

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: enzyme assay or genetic testing results confirming diagnosis.

III. CRITERIA FOR INITIAL APPROVAL

A. Bile acid synthesis disorders due to single enzyme defects (SEDs)

Authorization of 6 months may be granted for treatment of bile acid synthesis disorders due to single enzyme defects when the diagnosis is confirmed by mass spectrometry or other biochemical testing or genetic testing.

B. Peroxisomal disorders (PDs) including Zellweger spectrum disorders

Authorization of 6 months may be granted for adjunctive treatment of peroxisomal disorders when the diagnosis is confirmed by mass spectrometry or other biochemical testing or genetic testing, and the member exhibits manifestations of liver disease.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted to members with an indication listed in Section III who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by improvement from baseline as documented per clinical chart notes.

A. Bile acid synthesis disorders due to SEDs

Authorization of 12 months may be granted to members who have achieved and maintained improvement in liver function.

B. Peroxisomal disorders (PDs) including Zellweger spectrum disorders

Authorization of 12 months may be granted to members continuing adjunctive treatment with Cholbam who have achieved and maintained improvement in liver function (i.e. reduced transaminases, reduced bilirubin, no evidence of cholestasis on liver biopsy).

IV. REFERENCES

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SPECIALTY GUIDELINE MANAGEMENT

CIMZIA (certolizumab pegol)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Reducing signs and symptoms of Crohn's disease and maintaining clinical response in adult patients with moderately to severely active disease who have had an inadequate response to conventional therapy.
2. Treatment of adults with moderately to severely active rheumatoid arthritis.
3. Treatment of adult patients with active psoriatic arthritis.
4. Treatment of adults with active ankylosing spondylitis.
5. Treatment of adults with active non-radiographic axial spondyloarthritis with objective signs of inflammation.
6. Treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

B. Compendial Use

Axial spondyloarthritis

All other indications are considered experimental/investigational and not medically necessary

II. CRITERIA FOR INITIAL APPROVAL

A. **Moderately to severely active rheumatoid arthritis (RA)**

1. Authorization of 12 months may be granted for members who have previously received a biologic or targeted synthetic DMARD (e.g., Rinvoq, Xeljanz) indicated for moderately to severely active rheumatoid arthritis.
2. Authorization of 12 months may be granted for treatment of moderately to severely active RA when either of the following criteria is met:
 - a. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to 20 mg/week).
 - b. Member has an intolerance or contraindication to methotrexate (see Appendix A)

B. **Active psoriatic arthritis (PsA)**

Authorization of 12 months may be granted for treatment of active psoriatic arthritis (PsA).

C. **Active ankylosing spondylitis (AS) and axial spondyloarthritis**

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for active ankylosing spondylitis or axial spondyloarthritis.

2. Authorization of 12 months may be granted for treatment of active ankylosing spondylitis or axial spondyloarthritis when any of the following criteria is met:
 - a. Member has experienced an inadequate response to at least two non-steroidal anti-inflammatory drugs (NSAIDs).
 - b. Member has an intolerance or contraindication to two or more NSAIDs.

D. Moderately to severely active Crohn's disease (CD)

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for the treatment of Crohn's disease.
2. Authorization of 12 months may be granted for the treatment of moderately to severely active CD in members who had an inadequate response, intolerance or contraindication to at least one conventional therapy option (see Appendix B).
3. Authorization of 12 months may be granted for the treatment of fistulizing CD.

E. Moderate to severe plaque psoriasis (PsO)

1. Authorization of 12 months may be granted for members who have previously received Otezla or a biologic indicated for the treatment of moderate to severe plaque psoriasis.
2. Authorization of 12 months may be granted for treatment of moderate to severe plaque psoriasis when all of the following criteria are met:
 - a. At least 3% of body surface area (BSA) is affected OR crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
 - b. Member meets any of the following criteria:
 - i. Member has had an inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) or a pharmacologic treatment with methotrexate, cyclosporine or acitretin.
 - ii. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine and acitretin (see Appendix C).
 - iii. Member has severe psoriasis that warrants a biologic DMARD as first-line therapy (i.e. at least 10% of the body surface area (BSA) or crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected).

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who are using Cimzia for an indication outlined in section II and who achieve or maintain positive clinical response with Cimzia as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

For all indications: Member has had a documented negative TB test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic DMARDs or targeted synthetic DMARDs (e.g., Xeljanz), and repeated yearly for members with risk factors** for TB that are continuing therapy with biologics.

* If the screening testing for TB is positive, there must be documentation of further testing to confirm there is no active disease. Do not administer certolizumab to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of certolizumab.

** Risk factors for TB include: Persons with close contact to people with infectious TB disease; persons who have recently immigrated from areas of the world with high rates of TB (e.g., Africa, Asia, Eastern Europe, Latin America, Russia); children less than 5 years of age who have a positive TB test; groups with high rates of TB transmission (e.g., homeless persons, injection drug users, persons with HIV infection); persons who work or reside with people who are at an increased risk for active TB (e.g., hospitals, long-term care facilities, correctional facilities, homeless shelters).

For all indications: Member cannot use Cimzia concomitantly with any other biologic DMARD or targeted synthetic DMARD.

V. APPENDICES

Appendix A: Examples of Contraindications to Methotrexate

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
4. Elevated liver transaminases
5. History of intolerance or adverse event
6. Hypersensitivity
7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
8. Myelodysplasia
9. Pregnancy or planning pregnancy
10. Renal impairment
11. Significant drug interaction

Appendix B: Examples of Conventional Therapy Options for CD

1. Mild to moderate disease – induction of remission:
 - a. Oral budesonide
 - b. Alternatives: metronidazole, ciprofloxacin, rifaximin
2. Mild to moderate disease – maintenance of remission:
 - a. Azathioprine, mercaptopurine
 - b. Alternatives: oral budesonide, methotrexate intramuscularly (IM) or subcutaneously (SC), sulfasalazine
3. Moderate to severe disease – induction of remission:
 - a. Prednisone, methylprednisolone intravenously (IV)
 - b. Alternatives: methotrexate IM or SC
4. Moderate to severe disease – maintenance of remission:
 - a. Azathioprine, mercaptopurine
 - b. Alternative: methotrexate IM or SC
5. Perianal and fistulizing disease – induction of remission:
 - a. Metronidazole ± ciprofloxacin, tacrolimus
6. Perianal and fistulizing disease – maintenance of remission:
 - a. Azathioprine, mercaptopurine
 - b. Alternative: methotrexate IM or SC

Appendix C: Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine or Acitretin.

1. Alcoholism, alcoholic liver disease or other chronic liver disease

2. Breastfeeding
3. Drug interaction
4. Cannot be used due to risk of treatment-related toxicity
5. Pregnancy or planning pregnancy
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

VI. REFERENCES

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SPECIALTY GUIDELINE MANAGEMENT

CINQAIR (reslizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication¹

Cinqair is indicated for the add-on maintenance treatment of patients with severe asthma aged 18 years and older with an eosinophilic phenotype.

Limitations of Use:

- Not for treatment of other eosinophilic conditions
- Not for the relief of acute bronchospasm or status asthmaticus

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Member's chart or medical record showing baseline blood eosinophil count (initial request only)

III. CRITERIA FOR INITIAL APPROVAL¹⁻³

Authorization of 6 months may be granted for treatment of asthma when all of the following criteria are met:

- A. Member is 18 years of age or older.
- B. Member has baseline blood eosinophil count of at least 400 cells per microliter.
- C. Member has inadequate asthma control (e.g., hospitalization or emergency medical care visit within the past year) despite current treatment with both of the following medications at optimized doses:
 1. Inhaled corticosteroid
 2. Additional controller (long acting beta₂-agonist, leukotriene modifier, or sustained-release theophylline)
- D. Member will not use Cinqair as monotherapy.
- E. Member does not currently smoke.
- F. Member will not use Cinqair concomitantly with other biologics (e.g., Dupixent, Fasenra, Nucala, Xolair).

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for treatment of asthma when all of the following criteria are met:

- A. Member is 18 years of age or older.

- B. Asthma control has improved on Cinqair treatment as demonstrated by a reduction in the frequency and/or severity of symptoms and exacerbations.
- C. Member will not use Cinqair as monotherapy.
- D. Member does not currently smoke.
- E. Member will not use Cinqair concomitantly with other biologics (e.g., Dupixent, Fasenra, Nucala, Xolair).

V. REFERENCES

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ENHANCED SPECIALTY GUIDELINE MANAGEMENT

CINRYZE (C1 esterase inhibitor [human])

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Routine prophylaxis against angioedema attacks in adults, adolescents and pediatric patients (6 years of age or older) with hereditary angioedema (HAE)

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

- A. C4 levels and C1 inhibitor functional and antigenic protein levels
- B. F12, angiopoietin-1 or plasminogen gene mutation testing, if applicable
- C. Chart notes confirming family history of angioedema, if applicable

III. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for prevention of hereditary angioedema attacks when Cinryze will not be used in combination with Haegarda or Takhzyro and either of the following criteria is met:

- A. Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing.
 1. C1 inhibitor (C1-INH) antigenic level below the lower limit of normal as defined by the laboratory performing the test; or
 2. Normal C1-INH antigenic level and a low C1-INH functional level (functional C1-INH less than 50% or C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test)
- B. Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
 1. Member has an F12, angiopoietin-1, or plasminogen gene mutation as confirmed by genetic testing, or
 2. Member has a documented family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine (e.g., cetirizine) for at least one month.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy when all of the following criteria are met:

- A. Member meets the criteria for initial approval.
- B. Member has experienced reduction in frequency, severity, and/or duration of attacks since starting treatment.

Reference number(s)
1605-A

V. REFERENCES

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4. Bowen T, Cicardi M, Farkas H, et al. 2010 International consensus algorithm for the diagnosis, therapy, and management of hereditary angioedema. *Allergy Asthma Clin Immunol*. 2010;6(1):24.
5. Zuraw BL, Banerji A, Bernstein JA, et al. US Hereditary Angioedema Association Medical Advisory Board 2013 recommendations for the management of hereditary angioedema due to C1 inhibitor deficiency. *J Allergy Clin Immunol: In Practice*. 2013; 1(5): 458-467.
6. Zuraw BL, Bork K, Binkley KE, et al. Hereditary angioedema with normal C1 inhibitor function: consensus of an international expert panel. *Allergy Asthma Proc*. 2012; 33(6):S145-S156.
7. Lang DM, Aberer W, Bernstein JA, et al. International consensus on hereditary and acquired angioedema. *Ann Allergy Asthma Immunol*. 2012; 109:395-202.
8. Cicardi M, Aberer W, Banerji A, et al. Classification, diagnosis, and approach to treatment for angioedema: consensus report from the Hereditary Angioedema International Working Group. *Allergy*. 2014;69: 602-616.
9. Bowen T. Hereditary angioedema: beyond international consensus – circa December 2010 – The Canadian Society of Allergy and Clinical Immunology Dr. David McCourtie Lecture. *Allergy Asthma Clin Immunol*. 2011;7(1):1.
10. Bernstein J. Update on angioedema: Evaluation, diagnosis, and treatment. *Allergy and Asthma Proceedings*. 2011;32(6):408-412.
11. Longhurst H, Cicardi M. Hereditary angio-edema. *Lancet*. 2012;379:474-481.
12. Farkas H, Martinez-Saguer I, Bork K, et al. International consensus on the diagnosis and management of pediatric patients with hereditary angioedema with C1 inhibitor deficiency. *Allergy*. 2017;72(2):300-313.
13. Henao MP, Kraschnewski J, Kelbel T, Craig T. Diagnosis and screening of patients with hereditary angioedema in primary care. *Therapeutics and Clin Risk Management*. 2016; 12: 701-711.

Reference number(s)
1942-A

SPECIALTY GUIDELINE MANAGEMENT

COAGADEX (coagulation Factor X [human])

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Coagadex is indicated in adults and children with hereditary Factor X deficiency for:

- A. Routine prophylaxis to reduce the frequency of bleeding episodes
- B. On-demand treatment and control of bleeding episodes
- C. Perioperative management of bleeding in patients with mild and moderate hereditary Factor X deficiency.

Limitation of Use:

Perioperative management of bleeding in major surgery in patients with severe hereditary Factor X deficiency has not been studied.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Hereditary Factor X Deficiency

- A. Indefinite authorization may be granted for prophylaxis to reduce the frequency of bleeding episodes
- B. Indefinite authorization may be granted for on-demand treatment and control of bleeding episodes.
- C. Authorization of 1 month may be granted for perioperative management of bleeding in members with mild or moderate hereditary Factor X deficiency (i.e., baseline Factor X assay level $\geq 1\%$).

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Coagadex [package insert]. Durham, NC: Bio Products Laboratory USA, Inc.; September 2018.
2. National Hemophilia Foundation. MASAC recommendations concerning products licensed for the treatment of hemophilia and other bleeding disorders. Revised April 2018. MASAC Document # 253. Accessed December 6, 2018.

Reference number(s)
1942-A

3. Mumford AD, Ackroyd S, Alikhan R, et al. Guideline for the diagnosis and management of the rare coagulation disorders: a United Kingdom Haemophilia Centre Doctors' Organization guideline on behalf of the British Committee for Standards in Haematology. *Br J Haematol*. 2014;167(3):304-26.
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SPECIALTY GUIDELINE MANAGEMENT

COMETRIQ (cabozantinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Treatment of progressive, metastatic medullary thyroid cancer (MTC).

B. Compendial Uses

1. Follicular, Hurthle cell, and papillary thyroid carcinoma
2. Non-small cell lung cancer with RET gene arrangements

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of RET gene rearrangement documentation is necessary to initiate the prior authorization review for the indication of non-small cell lung cancer.

III. CRITERIA FOR INITIAL APPROVAL

A. **Thyroid carcinoma (follicular, Hürthle cell, papillary)**

Authorization of 12 months may be granted for the treatment of radioiodine refractory follicular, Hürthle cell, or papillary thyroid carcinoma.

B. **Medullary thyroid carcinoma**

Authorization of 12 months may be granted for the treatment of medullary thyroid carcinoma.

C. **Non-small cell lung cancer (NSCLC)**

Authorization of 12 months may be granted for the treatment of NSCLC with RET gene rearrangements.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy for an indication outlined in Section III when there is no evidence of unacceptable toxicity or disease progression on the current regimen.

V. REFERENCES

1. Cometriq [package insert]. South San Francisco, CA: Exelixis; January 2018.

Reference number
1854-A

2. The NCCN Drugs & Biologics Compendium® © 2018 National Comprehensive Cancer Network, Inc. Available at: <https://www.nccn.org>. Accessed October 23, 2018.
3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology® Thyroid Carcinoma (Version 1.2018). <https://www.nccn.org>. Accessed November 9, 2018.
4. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology® Non-Small Cell Lung Cancer (Version 1.2019). <https://www.nccn.org>. Accessed November 9, 2018.

SPECIALTY GUIDELINE MANAGEMENT

COPAXONE (glatiramer acetate) GLATOPA (glatiramer acetate) glatiramer acetate

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Copaxone is indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.
2. Glatopa and glatiramer acetate are indicated for the treatment of patients with relapsing forms of multiple sclerosis.

B. Compendial Use

Relapsing-remitting multiple sclerosis, including patients who have experienced a first clinical episode and have MRI features consistent with multiple sclerosis

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Relapsing forms of multiple sclerosis**

Authorization of 12 months may be granted to members who have been diagnosed with a relapsing form of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse)

B. **Clinically isolated syndrome**

Authorization of 12 months may be granted to members for the treatment of clinically isolated syndrome of multiple sclerosis.

III. CONTINUATION OF THERAPY

For all indications: Authorization of 12 months may be granted for members who are experiencing disease stability or improvement while receiving Copaxone, Glatopa, or glatiramer acetate.

IV. OTHER CRITERIA

Members will not use Copaxone, Glatopa, or glatiramer acetate concomitantly with other medications used for the treatment of multiple sclerosis, excluding Ampyra.

Reference number(s)
1841-A

V. REFERENCES

1. Copaxone [package insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; July 2019.
2. Glatopa [package insert]. Princeton, NJ: Sandoz Inc.; October 2018.
3. Glatiramer acetate [package insert]. Morgantown, WV: Mylan Pharmaceuticals Inc.; November 2018.
4. IBM Micromedex [database online]. Ann Arbor, MI: IBM Watson Health. Updated periodically. www.micromedexsolutions.com [available with subscription]. May 01, 2019.
5. AHFS DI (Adult and Pediatric) [database online]. Hudson, OH: Lexi-Comp, Inc.; http://online.lexi.com/lco/action/index/dataset/complete_ashp [available with subscription]. Accessed May 01, 2019.
6. The Multiple Sclerosis Coalition. *The use of disease-modifying therapies in multiple sclerosis: principles and current evidence*. http://www.nationalmssociety.org/getmedia/5ca284d3-fc7c-4ba5-b005-ab537d495c3c/DMT_Consensus_MS_Coalition_color. Accessed May 01, 2019.

SPECIALTY GUIDELINE MANAGEMENT

COPIKTRA (duvelisib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL)
Copiktra is indicated for the treatment of adult patients with relapsed or refractory CLL or SLL after at least two prior therapies.
2. Follicular lymphoma
Copiktra is indicated for the treatment of adult patients with relapsed or refractory FL after at least two prior systemic therapies.

This indication is approved under accelerated approval based on overall response rate (ORR); continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

B. Compendial Use

1. Chronic lymphocytic leukemia/small lymphocytic lymphoma, preferred therapy as a single agent for relapsed or refractory disease with or without del(17p)/TP53
2. Follicular lymphoma, second-line or subsequent therapy for relapsed, refractory or progressive disease after 2 prior therapies
3. Gastric MALT lymphoma, subsequent therapy for relapsed or refractory disease after 2 prior therapies
4. Non-gastric MALT lymphoma, subsequent therapy for relapsed or refractory disease after 2 prior therapies
5. Nodal marginal zone lymphoma, subsequent therapy for relapsed or refractory disease after 2 prior therapies
6. Splenic marginal zone lymphoma, subsequent therapy for relapsed or refractory disease after 2 prior therapies

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL)**

Authorization of 12 months may be granted for treatment of relapsed or refractory CLL/SLL when the requested medication is used as single agent.

B. **Follicular lymphoma (FL)**

Authorization of 12 months may be granted for treatment of FL when the requested medication will be used as second-line or subsequent therapy.

C. Gastric MALT Lymphoma and Non-gastric MALT Lymphoma

Authorization of 12 months may be granted for treatment of gastric or non-gastric MALT lymphoma when the requested medication will be used as subsequent therapy after at least two prior therapies.

D. Nodal Marginal Zone Lymphoma

Authorization of 12 months may be granted for treatment of nodal marginal zone lymphoma when the requested medication will be used as subsequent therapy after at least two prior therapies.

E. Splenic Marginal Zone Lymphoma

Authorization of 12 months may be granted for treatment of splenic marginal zone lymphoma when the requested medication will be used as subsequent therapy after at least two prior therapies.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced disease progression or an unacceptable toxicity.

IV. REFERENCES

1. Copiktra [package insert]. Needham, MA: Verastem, Inc.; September 2018.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network. The NCCN Drugs & Biologics Compendium. <http://www.nccn.org>. Accessed July 09, 2019.
3. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for B-cell Lymphomas V.4.2019. © National Comprehensive Cancer Network, Inc 2019. All rights reserved. Accessed July 09, 2019.
4. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma V.5.2019. © National Comprehensive Cancer Network, Inc 2019. All rights reserved. Accessed July 09, 2019.

SPECIALTY GUIDELINE MANAGEMENT

CORIFACT (coagulation Factor XIII concentrate [human])

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Corifact is indicated in adults and pediatric patients with congenital factor XIII deficiency for routine prophylactic treatment and peri-operative management of surgical bleeding.

B. Compendial Uses

Acquired factor XIII deficiency

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Factor XIII Deficiency

Indefinite authorization may be granted for treatment of factor XIII deficiency.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Corifact [package insert]. Kankakee, IL: CSL Behring LLC; September 2017.
2. National Hemophilia Foundation. MASAC recommendations concerning products licensed for the treatment of hemophilia and other bleeding disorders. Revised April 2018. MASAC Document #253. Accessed December 3, 2019.
3. Mumford AD, Ackroyd S, Alikhan R, et al. Guideline for the diagnosis and management of the rare coagulation disorders: a United Kingdom Haemophilia Centre Doctors' Organization guideline on behalf of the British Committee for Standards in Haematology. *Br J Haematol*. 2014;167(3):304-26.
4. AHFS DI (Adult and Pediatric) [database online]. Hudson, OH: Lexi-Comp, Inc.; http://online.lexi.com/lco/action/index/dataset/complete_ashp [available with subscription]. Accessed December 4, 2019.

SPECIALTY GUIDELINE MANAGEMENT

COSENTYX (secukinumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

1. Moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy
2. Adults with active psoriatic arthritis (PsA)
3. Adults with active ankylosing spondylitis

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Moderate to severe plaque psoriasis (PsO)

1. Authorization of 12 months may be granted for members who have previously received Otezla or a biologic indicated for the treatment of moderate to severe plaque psoriasis.
2. Authorization of 12 months may be granted for treatment of moderate to severe plaque psoriasis in members when all of the following criteria are met:
 - a. At least 3% of body surface area (BSA) is affected OR crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
 - b. Member meets any of the following criteria:
 - i. Member has had an inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) or pharmacologic treatment with methotrexate, cyclosporine or acitretin.
 - ii. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine and acitretin (see Appendix A).
 - iii. Member has severe psoriasis that warrants a biologic DMARD as first-line therapy (i.e. at least 10% of the body surface area (BSA) or crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected).

B. Active psoriatic arthritis (PsA)

Authorization of 12 months may be granted for treatment of active psoriatic arthritis.

C. Active ankylosing spondylitis (AS)

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for active ankylosing spondylitis.
2. Authorization of 12 months may be granted for treatment of active ankylosing spondylitis when any of the following criteria is met:

- a. Member has experienced an inadequate response to at least two non-steroidal anti-inflammatory drugs (NSAIDs).
- b. Member has an intolerance or contraindication to two or more NSAIDs.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who are using Cosentyx for an indication outlined in section II and who achieve or maintain positive clinical response with Cosentyx as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

For all indications: Member has had a documented negative TB test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic DMARDs or targeted synthetic DMARDs (e.g., Xeljanz), and repeated yearly for members with risk factors** for TB that are continuing therapy with biologics.

* If the screening testing for TB is positive, there must be documentation of further testing to confirm there is no active disease. Do not administer secukinumab to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of secukinumab.

** Risk factors for TB include: Persons with close contact to people with infectious TB disease; persons who have recently immigrated from areas of the world with high rates of TB (e.g., Africa, Asia, Eastern Europe, Latin America, Russia); children less than 5 years of age who have a positive TB test; groups with high rates of TB transmission (e.g., homeless persons, injection drug users, persons with HIV infection); persons who work or reside with people who are at an increased risk for active TB (e.g., hospitals, long-term care facilities, correctional facilities, homeless shelters).

For all indications: Member cannot use Cosentyx concomitantly with any other biologic DMARD or targeted synthetic DMARD.

V. APPENDIX

Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine or Acitretin.

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Drug interaction
4. Cannot be used due to risk of treatment-related toxicity
5. Pregnancy or planning pregnancy
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

VI. REFERENCES

1. Cosentyx [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; June 2018.
2. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 6: Guidelines of care for the treatment of psoriasis and psoriatic arthritis: case-based presentations and evidence-based conclusions. *J Am Acad Dermatol.* 2011;65(1):137-174.

Reference number
2017-A

3. Gossec L, Smolen JS, Ramiro S, et al. European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies: 2015 update. *Ann Rheum Dis*. 2016;75(3):499-510.
4. McInnes IB, Mease PJ, Kirkham B, et al. Secukinumab, a human anti-interleukin-17A monoclonal antibody, in patients with psoriatic arthritis (FUTURE 2): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet*. 2015;386(9999):1137-46.
5. Braun J, van den Berg R, Baraliakos X et al. 2010 update of the ASAS/EULAR recommendations for the management of ankylosing spondylitis. *Ann Rheum Dis*. 2011;70:896–904.
6. Ward MM, Deodhar A, Akl EA, et al. American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network 2015 recommendations for the treatment of ankylosing spondylitis and nonradiographic axial spondyloarthritis. *Arthritis Rheumatol*. 2015: 10.1002/art.39298. [Epub ahead of print].
7. Baeten D, Sieper J, Braun J, et al. Secukinumab, an Interleukin-17A Inhibitor, in Ankylosing Spondylitis. *N Engl J Med*. 2015;373(26):2534-48.
8. Menter A, Strober BE, Kaplan DH, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. *J Am Acad Dermatol*. 2019;80(4):1029-1072.
9. Tuberculosis (TB). TB risk factors. Centers for Disease Control and Prevention. Retrieved on 21 June 2019 from: <https://www.cdc.gov/tb/topic/basics/risk.htm>.

SPECIALTY GUIDELINE MANAGEMENT

COTELLIC (cobimetinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Cotellic is indicated for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation, in combination with vemurafenib.

B. Compendial Uses

1. Glioma, BRAF V600 activating mutation-positive
2. Meningioma, BRAF V600 activating mutation-positive
3. Astrocytoma, BRAF V600 activating mutation-positive
4. Brain metastases with melanoma

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of BRAF mutation documentation is necessary to initiate the prior authorization review for applicable indications as outlined in section III.

III. CRITERIA FOR INITIAL APPROVAL

A. **Melanoma**

Authorization for 12 months may be granted for treatment of unresectable or metastatic melanoma (including brain metastases with melanoma) when all of the following criteria are met:

1. Cotellic is used in combination with vemurafenib (Zelboraf)
2. Tumor is positive for BRAF V600E or V600K mutation

B. **Central Nervous System Cancer**

Authorization of 12 months may be granted for treatment of BRAF V600 mutation-positive gliomas, meningiomas, or astrocytomas.

IV. CONTINUATION OF THERAPY

Reference number
1784-A

Authorization of 12 months may be granted for continuation of therapy for an indication outlined in Section III when there is no evidence of unacceptable toxicity or disease progression on the current regimen.

V. REFERENCES

1. Cotellic [package insert]. South San Francisco, CA: Genentech USA, Inc.; January 2018.
2. The NCCN Drugs & Biologics Compendium 2018 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed May 15, 2019.
3. Usualieva A, Pierson CR, Kavran CA, et al. Primary Meningeal Pleomorphic Xanthoastrocytoma With Anaplastic Features: A Report of 2 Cases, One With *BRAFV600E* Mutation and Clinical Response to the *BRAF* Inhibitor Dabrafenib. *Journal of neuropathology and experimental neurology*. 2015;74(10):960-969. doi:10.1097/NEN.0000000000000240.
4. Mordechai O, Postovsky S, Vlodavsky E, et al. Metastatic Rhabdoid Meningioma with *BRAF V600E* Mutation and Good Response to Personalized Therapy: Case Report and Review of the Literature. *Pediatric Hematology and Oncology*. 2015; 32:3, 207-211, DOI: 10.3109/08880018.2014.936058
5. Lassaletta, A, Guerreiro Stucklin, A, Ramaswamy, V, et al. Profound clinical and radiological response to BRAF inhibition in a 2-month-old diencephalic child with hypothalamic/chiasmatic glioma. *Pediatric Blood and Cancer*. 2016; 63: 2038-2041. doi:10.1002/pbc.26086.
6. Meletah SK, Pavlick D, Brennan T, et al. Personalized Treatment for a Patient with a BRAF V600E Mutation using Dabrafenib and a Tumor Treatment Fields Device in a High-Grade Glioma Arising from Ganglioglioma. *Journal of the National Comprehensive Cancer Network*. 2016; 14(11): 1345-1350.

SPECIALTY GUIDELINE MANAGEMENT

CRYSVITA (burosumab-twza)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Crysvita is indicated for the treatment of X-linked hypophosphatemia (XLH) in adult and pediatric patients 1 year of age and older.

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

At least one of the following information is necessary to initiate the prior authorization review:

- A. Genetic testing results confirming the member has a PHEX (phosphate regulating gene with homology to endopeptidases located on the X chromosome) mutation
- B. Genetic testing results confirming a PHEX mutation in a directly related family member with appropriate X-linked inheritance
- C. Lab test results confirming the member's serum fibroblast growth factor 23 (FGF23) level is greater than 30 pg/ml

III. CRITERIA FOR INITIAL APPROVAL

X-linked hypophosphatemia

Authorization of 12 months may be granted for treatment of X-linked hypophosphatemia when one of the following criteria is met:

- A. Genetic testing was conducted to confirm a PHEX mutation in the member and genetic testing results were submitted confirming diagnosis.
- B. Genetic testing was conducted to confirm a PHEX mutation in a directly related family member with appropriate X-linked inheritance and genetic testing results were submitted confirming diagnosis.
- C. Member's FGF23 level is greater than 30 pg/ml and lab test results were submitted confirming diagnosis.

IV. CONTINUATION OF THERAPY

Authorization of 12 months will be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who are currently receiving the requested medication through a paid pharmacy or medical benefit and who are experiencing benefit from therapy as evidenced by disease improvement or disease stability.

Reference number(s)
2562-A

V. REFERENCES

1. Crysvita [package insert]. Bedminster, NJ: Kyowa Kirin, Inc.; September 2018.
2. NIH. U.S. National Library of Medicine. ClinicalTrials.gov website.
<http://clinicaltrials.gov/ct2/show/NCT02163577>. Accessed October 24, 2018.
3. NIH. U.S. National Library of Medicine. ClinicalTrials.gov website.
<http://clinicaltrials.gov/ct2/show/NCT02526160>. Accessed October 24, 2018.

SPECIALTY GUIDELINE MANAGEMENT

CYRAMZA (ramucirumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Gastric Cancer: Cyramza as a single agent, or in combination with paclitaxel, is indicated for the treatment of patients with advanced or metastatic, gastric or gastro-esophageal junction (GEJ) adenocarcinoma with disease progression on or after prior fluoropyrimidine-or platinum-containing chemotherapy.
2. Non-Small Cell Lung Cancer (NSCLC): Cyramza, in combination with docetaxel, is indicated for the treatment of patients with metastatic NSCLC with disease progression on or after platinum-based chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Cyramza.
3. Colorectal Cancer: Cyramza, in combination with FOLFIRI (irinotecan, folinic acid, and 5-fluorouracil), is indicated for the treatment of patients with metastatic colorectal cancer with disease progression on or after prior therapy with bevacizumab, oxaliplatin, and a fluoropyrimidine.
4. Hepatocellular Cancer: Cyramza as a single agent, is indicated for the treatment of of hepatocellular carcinoma in patients who have an alpha fetoprotein of ≥ 400 ng/mL and have been treated with sorafenib.

B. Compendial Uses

1. Esophageal adenocarcinoma
2. Colorectal cancer, advanced
3. Hepatobiliary cancer

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Gastric, Gastro-esophageal Junction (GEJ), and Esophageal Adenocarcinoma**

Authorization of 12 months may be granted for treatment of gastric, gastro-esophageal junction (GEJ), and esophageal adenocarcinoma for members who are not surgical candidates or have unresectable locally advanced, recurrent or metastatic disease, when used as subsequent therapy as a single agent or in combination with paclitaxel.

B. **Non-Small Cell Lung Cancer (NSCLC)**

Authorization of 12 months may be granted for the subsequent therapy of recurrent, advanced or metastatic NSCLC in combination with docetaxel.

C. **Colorectal Cancer**

Reference number(s)
1679-A

Authorization of 12 months may be granted for treatment of advanced or metastatic colorectal cancer in combination with FOLFIRI (irinotecan, folinic acid, and 5-fluorouracil) or irinotecan.

D. Hepatocellular cancer

Authorization of 12 months may be granted for treatment of hepatocellular carcinoma as subsequent therapy as a single agent in patients who have an alpha fetoprotein (AFP) of greater than or equal to 400 ng/mL.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced disease progression or an unacceptable toxicity.

IV. REFERENCES

1. Cyramza [package insert]. Indianapolis, IN: Eli Lilly and Company; July 2019.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. Available at: <https://www.nccn.org>. Accessed September 18, 2019.
3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology™ Gastric Cancer (Version 2.2018) <https://www.nccn.org>. Accessed September 18, 2019.
4. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology™ Esophageal and Esophagogastric Junction Cancers (Version 2.2018). <https://www.nccn.org>. Accessed September 18, 2019.
5. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology™ Non-Small Cell Lung Cancer (Version 3.2019). <https://www.nccn.org>. Accessed September 18, 2019.
6. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology™ Colon Cancer (Version 4.2018). <https://www.nccn.org>. Accessed September 18, 2019.
7. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology™ Rectal Cancer (Version 3.2018). <https://www.nccn.org>. Accessed September 18, 2019.
8. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology™ Hepatobiliary Cancers (Version 1.2019). <https://www.nccn.org>. Accessed September 18, 2019.

SPECIALTY GUIDELINE MANAGEMENT

CYSTADANE (betaine anhydrous)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Cystadane is indicated for the treatment of homocystinuria to decrease the elevated homocysteine blood concentrations in pediatric and adult patients. Included within the category of homocystinuria are:

- A. Cystathionine beta-synthase (CBS) deficiency
- B. 5,10-methylenetetrahydrofolate reductase (MTHFR) deficiency
- C. Cobalamin cofactor metabolism (cbl) defect

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

- A. For cystathionine beta-synthase (CBS) deficiency, enzyme analysis of CBS activity or genetic testing results
- B. For 5,10-methylenetetrahydrofolate reductase (MTHFR) deficiency, enzyme analysis of MTHFR activity or genetic testing results
- C. For cobalamin cofactor metabolism (cbl) defect, genetic testing results

III. CRITERIA FOR INITIAL APPROVAL

Homocystinuria

Authorization of 12 months may be granted for treatment of homocystinuria to decrease elevated homocysteine blood levels when all of the following criteria are met:

- A. The member has one of the following types of homocystinuria and the diagnosis was confirmed by enzyme assay or genetic testing:
 - 1. Cystathionine beta-synthase (CBS) deficiency
 - 2. 5,10-methylenetetrahydrofolate reductase (MTHFR) deficiency
 - 3. Cobalamin cofactor metabolism (cbl) defect
- B. If the member has CBS deficiency, plasma methionine concentrations will be monitored and kept below 1,000 micromol/L through dietary modification, and if necessary, a reduction in Cystadane dose.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for homocystinuria when all of the following criteria are met:

Reference number(s)
2988-A

1. The total homocysteine level is undetectable or present only in small amounts
2. If the member has CBS deficiency, plasma methionine concentrations will be monitored and kept below 1,000 micromol/L through dietary modification, and if necessary, a reduction in Cystadane dose.

V. REFERENCES

1. Cystadane [package insert]. Lebanon, NJ: Recordati Rare Diseases, Inc.; October 2019.

Reference number
2089-A

SPECIALTY GUIDELINE MANAGEMENT

CYSTAGON (cysteamine bitartrate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Cystagon is indicated for the management of nephropathic cystinosis in children and adults.

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: assay detecting increased cystine concentration in leukocytes or genetic testing results supporting diagnosis.

III. CRITERIA FOR INITIAL APPROVAL

Nephropathic cystinosis

Authorization of 12 months may be granted for treatment of nephropathic cystinosis when all of the following criteria are met:

1. Diagnosis of cystinosis was confirmed by the presence of increased cystine concentration in leukocytes or by genetic testing; and
2. Member will not use Cystagon in combination with Procysbi.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for nephropathic cystinosis who are responding to therapy (e.g., improvement, stabilization, or slowing of disease progression for serum creatinine, calculated creatinine clearance, or leukocyte cystine concentration).

V. REFERENCES

1. Cystagon [package insert]. Morgantown, WV: Mylan Pharmaceuticals Inc.; June 2018.

SPECIALTY GUIDELINE MANAGEMENT

CYSTARAN (cysteamine ophthalmic solution)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Cystaran is indicated for the treatment of corneal cystine crystal accumulation in patients with cystinosis.

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: detecting an increased cystine concentration in leukocytes or genetic testing results supporting diagnosis.

III. CRITERIA FOR INITIAL APPROVAL

Cystinosis

Authorization of 12 months may be granted for treatment of corneal cystine crystal accumulation when all of the following criteria are met:

1. Diagnosis of cystinosis was confirmed by the presence of increased cystine concentration in leukocytes or by genetic testing; and
2. Member has corneal cystine crystal accumulation.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for corneal cystine crystal accumulation with cystinosis who are responding to therapy met by either of the following criteria:

1. Member has experienced a decrease in corneal cystine crystal accumulation; or
2. Member did not experience an increase in corneal cystine crystal accumulation.

V. REFERENCES

1. Cystaran [package insert]. Gaithersburg, MD: Leditant Biosciences, Inc.; May 2018.
2. Ivanova E, De Leo MG, De Matteis MA, Levchenko E. Cystinosis: clinical presentation, pathogenesis, and treatment. *Pediatr Endocrinol Rev.* 2014;12(1):176-184.

SPECIALTY GUIDELINE MANAGEMENT

DAKLINZA (daclatasvir)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Daklinza is indicated for use with sofosbuvir, with or without ribavirin, for the treatment of patients with chronic hepatitis C virus (HCV) genotype 1 or genotype 3 infection.

Limitations of Use:

Sustained virologic response (SVR12) rates are reduced in HCV genotype 3-infected patients with cirrhosis receiving Daklinza in combination with sofosbuvir for 12 weeks.

B. Compendial Uses

Chronic hepatitis C genotype 2, 4, 5 or 6 infection

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR APPROVAL

A. Chronic hepatitis C virus infection, in combination with Sovaldi

1. Genotype 1 infection

- Authorization of up to 12 weeks total may be granted for treatment-naïve members without cirrhosis or with compensated cirrhosis.
- Authorization of up to 12 weeks total may be granted for members without cirrhosis who failed prior treatment with peginterferon alfa (PEG-IFN) and ribavirin (RBV).

2. Genotype 2 infection

- Authorization of up to 12 weeks total may be granted for treatment-naïve members without cirrhosis.
- Authorization of up to 24 weeks total may be granted for treatment-naïve members with compensated cirrhosis.
- Authorization of up to 12 weeks total may be granted for members without cirrhosis who failed prior treatment with PEG-IFN and RBV.
- Authorization of up to 24 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV.

3. Genotype 3 infection

- Authorization of up to 12 weeks total may be granted for treatment-naïve members without cirrhosis.
- Authorization of up to 12 weeks total may be granted for members without cirrhosis who failed prior treatment with PEG-IFN and RBV.
- Authorization of up to 24 weeks total may be granted for treatment-naïve members with compensated cirrhosis.

4. Decompensated cirrhosis (Child Turcotte Pugh [CTP] class B or C)

Authorization of up to 24 weeks total may be granted for members with HCV genotype 1, 2, 3 or 4 infection and documented anemia (baseline hemoglobin [Hgb] below 10 g/dL) or RBV ineligibility (see Section III).

B. Chronic hepatitis C virus, in combination with Sovaldi and Ribavirin**1. Genotype 3 infection**

- a. Authorization of up to 24 weeks total may be granted for treatment-naïve members with compensated cirrhosis.
- b. Authorization of up to 12 weeks total may be granted for members without cirrhosis who failed prior treatment with PEG-IFN and RBV and have the Y93H substitution associated with daclatasvir resistance.

2. Decompensated cirrhosis (CTP class B or C)

Authorization of up to 12 weeks total may be granted for members with HCV genotype 1, 2, 3 or 4 infection.

3. Recurrent HCV infection post liver transplantation

- a. Authorization of up to 12 weeks total may be granted for members with recurrent HCV genotype 1, 2, or 3 infection post liver transplantation.
- b. Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who have recurrent HCV genotype 4, 5 or 6 infection post liver transplantation.

4. Kidney transplant recipients

Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who have HCV genotype 2, 3, 5, or 6 infection.

C. HCV and HIV coinfection

Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in Section A or B above are met.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. APPENDIX: RIBAVIRIN INELIGIBILITY

RBV ineligibility is defined as one or more of the below:

- Intolerance to RBV
- Pregnant female or male whose female partner is pregnant
- Hemoglobinopathy
- Coadministration with didanosine
- History of significant or unstable cardiac disease

V. REFERENCES

Reference number(s)
2136-A, 2675-A

1. Daklinza [package insert]. Princeton, NJ: Bristol Myers Squibb Company; November 2017.
2. AASLD/IDSA/IAS–USA. Recommendations for testing, managing, and treating hepatitis C. <http://www.hcvguidelines.org>. Last changes made May 24, 2018. Accessed July 16, 2018.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

DALIRESP
(roflumilast)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

Ref # 646-A

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Daliresp is indicated as a treatment to reduce the risk of COPD exacerbations in patients with severe COPD associated with chronic bronchitis and a history of exacerbations.

Limitations of Use

Daliresp is not a bronchodilator and is not indicated for the relief of acute bronchospasm.

Daliresp 250 mcg is a starting dose, for the first 4 weeks of treatment only and is not the effective (therapeutic) dose.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed to reduce the risk of chronic obstructive pulmonary disease (COPD) exacerbations in a patient with severe COPD associated with chronic bronchitis and a history of exacerbations

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Daliresp is indicated as a treatment to reduce the risk of COPD exacerbations in patients with severe COPD associated with chronic bronchitis and a history of exacerbations. Daliresp is not a bronchodilator and is not indicated for the relief of acute bronchospasm.

REFERENCES

1. Daliresp [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; January 2018.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed November 2018.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed November 2018.

Written by: UM Development (RP)

Date Written: 04/2011

Revised: (RP) 06/2011 (revised question #2, added question #3), 02/2012; 10/2012 (extended duration); (RP) 02/2013, (TM) 11/2013; (RP) 11/2014, 11/2015 (no clinical changes), 11/2016, 11/2017 (no clinical changes); (KC) 11/2018 (no clinical changes), 04/2019 (changed DOA to 12 months)

Reviewed: Medical Affairs (KP) 04/2011, 06/2011, 02/2012, 10/2012; (LS) 02/2013, (DC) 11/2013; (LMS) 11/2014; (ME) 11/2016; (GAD) 04/2019

External Review: 06/2011, 06/2012, 06/2013, 04/2014, 02/2015, 02/2016, 02/2017, 02/2018, 02/2019, 06/2019

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed to reduce the risk of chronic obstructive pulmonary disease (COPD) exacerbations in a patient with severe COPD associated with chronic bronchitis and a history of exacerbations?	Yes	No
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Mapping Instructions

	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions: - You have severe chronic obstructive pulmonary disease (COPD) - Your condition is associated with chronic bronchitis and a history of exacerbations Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

FARXIGA
(dapagliflozin)

QTERN
(dapagliflozin / saxagliptin)

QTERNMET XR
(dapagliflozin / saxagliptin / metformin extended-release)

XIGDUO XR
(dapagliflozin / metformin extended-release)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

Ref # 1091-A

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Farxiga

Farxiga (dapagliflozin) is indicated:

- as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus
- to reduce the risk of hospitalization for heart failure in adults with type 2 diabetes mellitus and established cardiovascular disease (CVD) or multiple cardiovascular (CV) risk factors

Limitation of Use

Farxiga is not recommended for patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis.

Qtern

Qtern (dapagliflozin and saxagliptin) is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use

Qtern is not indicated for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis.

Qternmet XR

Qternmet XR (dapagliflozin, saxagliptin, and metformin hydrochloride) extended-release tablets is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use

Qternmet XR is not indicated for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis.

Qternmet XR initiation is intended only for patients currently taking metformin.

Xigduo XR

Xigduo XR (dapagliflozin and metformin HCl extended-release) is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both dapagliflozin and metformin is appropriate.

Limitation of Use

Xigduo XR is not recommended for patients with type 1 diabetes mellitus or diabetic ketoacidosis.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has been receiving the requested drug for at least 3 months **AND**
 - The patient has demonstrated a reduction in A1c (hemoglobin A1c) since starting this therapy**OR**
 - The request is for Farxiga (dapagliflozin) **AND**
 - The patient has established cardiovascular disease or multiple cardiovascular risk factors

OR

- Patient has the diagnosis of type 2 diabetes mellitus **AND**
 - The patient has experienced an inadequate treatment response, intolerance, or contraindication to metformin**OR**
 - The patient requires combination therapy **AND** has an A1c (hemoglobin A1c) of 7.5 percent or greater**OR**
 - The request is for Farxiga (dapagliflozin) **AND**
 - The patient has established cardiovascular disease or multiple cardiovascular risk factors

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Farxiga (dapagliflozin), Qtern (dapagliflozin/saxagliptin), Qternmet XR (dapagliflozin/saxagliptin/metformin), and Xigduo XR (dapagliflozin/metformin) are indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Farxiga (dapagliflozin) is also indicated to reduce the risk for hospitalization for heart failure in adults with type 2 diabetes mellitus and established cardiovascular disease (CVD) or multiple cardiovascular (CV) risk factors.

Clinical guidelines from the American Diabetes Association and the American Association of Clinical Endocrinologists and American College of Endocrinology for the management of hyperglycemia in type 2 diabetes indicate that metformin monotherapy should be started at diagnosis of type 2 diabetes unless there are contraindications. Metformin is effective and safe, is inexpensive, and may reduce risk of cardiovascular events and death. In patients with contraindications or intolerance of metformin, initial therapy should be based on patient factors: consider a drug from another class.^{7,8}

The clinical guidelines also state that the A1c test is the major tool for assessing glycemic control and has strong predictive value for diabetes complications. Thus, A1c testing should be performed routinely in all patients with diabetes at initial assessment and as part of continuing care. The guidelines set goals for therapeutic effectiveness which must be evaluated frequently (e.g., every 3 months) until stable, using multiple criteria, including A1c. Less frequent monitoring is acceptable once targets are achieved.⁷ Therefore, continued use of Farxiga, Qtern, Qternmet XR, or Xigduo XR will be approved for patients who have demonstrated a reduction in A1c since starting Farxiga, Qtern, Qternmet XR, or Xigduo XR therapy for at least three months.

If the A1c target is not achieved after approximately 3 months and patient does not have atherosclerotic cardiovascular disease (ASCVD) or chronic kidney disease (CKD), consider a combination of metformin and one of the preferred six treatment options: sulfonylurea, thiazolidinedione, dipeptidyl peptidase 4 (DPP-4) inhibitors, sodium-glucose cotransporter 2 (SGLT2) inhibitors, glucagon-like peptide 1 (GLP-1) receptor agonists, or basal insulin; the choice of which agent to add is based on drug-specific effects and patient factors. For patients in whom ASCVD, Heart Failure or CKD predominates, the best choice for a second agent is a GLP-1 receptor agonist or SGLT2 inhibitor with demonstrated cardiovascular risk reduction, after consideration of drug-specific and patient factors.⁷

In patients with an initial A1c of 7.5% or greater, or in patients who are unable to achieve their glycemic goals with monotherapy, combination therapy is recommended.⁸ Add-on therapy with dapagliflozin plus saxagliptin in patients on metformin (i.e., Qternmet XR) were conducted – in one study (24-week randomized, double-blind, active-controlled, parallel group study in patients with an HbA1c $\geq 7.5\%$ and $\leq 10.0\%$) patients were on a stable dose of metformin HCl (≥ 1500 mg per day) for at least 8 weeks prior to being randomized to one of three double-blind treatment groups to receive 5 mg dapagliflozin and 5 mg saxagliptin added to metformin, 5 mg saxagliptin and placebo added to metformin, or 5 mg dapagliflozin and placebo added to metformin. At Week 24, concomitant addition of 5 mg dapagliflozin and 5 mg

saxagliptin plus metformin resulted in statistically significant decreases in HbA1c, and a larger proportion of patients achieving the therapeutic glycemic goal of HbA1c <7%, compared to dapagliflozin plus metformin or saxagliptin plus metformin.²⁻³

The DECLARE trial compared the effect of dapagliflozin 10 mg relative to placebo on cardiovascular outcomes when added to current background therapy. Concomitant antidiabetic and atherosclerotic therapies could be adjusted, at the discretion of investigators, to ensure participants were treated according to the standard of care for these diseases.¹ Therefore, Farxiga will be approved for initial therapy and continuation of therapy for patients who have established cardiovascular disease or multiple cardiovascular risk factors.

REFERENCES

1. Farxiga [package insert]. Wilmington, Delaware: AstraZeneca Pharmaceuticals LP; October 2019.
2. Qtern [package insert]. Wilmington, Delaware: AstraZeneca Pharmaceuticals LP; May 2019.
3. Qternmet XR [package insert]. Wilmington, Delaware: AstraZeneca Pharmaceuticals LP; May 2019.
4. Xigduo XR [package insert]. Wilmington, Delaware: AstraZeneca Pharmaceuticals LP; February 2019.
5. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed June 2019.
6. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed June 2019.
7. American Diabetes Association. Standards of Medical Care in Diabetes-2019: *Diabetes Care* January 2019;42(Supplement1).
8. Garber AJ, Abrahamson MJ, Barzilay JI, et al. Consensus Statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the Comprehensive Type 2 Diabetes Management Algorithm 2019, *Endocr Pract.* January 2019; 25 (No 1);69-100.

Written by: UM Development (PL)
 Date Written: 01/2014
 Revised: (MS) 07/2014, 11/2014 (added Xigduo XR), (SE) 12/2014, (DN/SE) 07/2015, (KM) 07/2016 (changed Xigduo XR contraindication), 03/2017 (added Qtern); (KM) 07/2017, 07/2018 (no clinical changes); (RP) 05/2019 (Added Qternmet XR; renamed criteria to Dapagliflozin, Combinations); (DFW) 07/2019 (no clinical changes); 10/2019 (updated Farxiga indication/questions)
 Reviewed: Medical Affairs: (KP) 01/2014, (SS) 07/2014, 11/2014, (DNC) 12/2014, 07/2015; (ME) 07/2016; (DNC) 03/2017; (SD) 07/2017; () 07/2018; (MCM) 05/2019, (CHART) 08/01/2019, (CHART) 11/21/2019
 External Review: 02/2014, 10/2014, 12/2014, 10/2015, 10/2016, 10/2017, 10/2018, 06/2019, 10/2019, 12/2019 (FYI)

CRITERIA FOR APPROVAL

1	Has the patient been receiving the requested drug for at least 3 months? [If no, then skip to question 4.]	Yes	No
2	Has the patient demonstrated a reduction in A1c (hemoglobin A1c) since starting this therapy? [If yes, then no further questions.]	Yes	No
3	Is this a request for Farxiga (dapagliflozin)? [If yes, then skip to question 8.] [If no, then no further questions.]	Yes	No
4	Does the patient have a diagnosis of type 2 diabetes mellitus?	Yes	No
5	Has the patient experienced an inadequate treatment response, intolerance, or contraindication to metformin? [If yes, then no further questions.]	Yes	No

6	Does the patient require combination therapy AND have an A1c (hemoglobin A1c) of 7.5 percent or greater? [If yes, then no further questions.]	Yes	No
7	Is this a request for Farxiga (dapagliflozin)?	Yes	No
8	Does the patient have established cardiovascular disease or multiple cardiovascular risk factors?	Yes	No

Mapping Instructions			
	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Go to 4	
2.	Approve, 36 months	Go to 3	
3.	Go to 8	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you meet these conditions:</p> <ul style="list-style-type: none"> - You have been receiving the requested drug for at least 3 months - You had a reduction in A1c (hemoglobin A1c) since starting this therapy <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No response to treatment]</p>
4.	Go to 5	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you have type 2 diabetes mellitus. Your request has been denied based on the information we have.</p> <p>[Short Description: No approvable diagnosis]</p>
5.	Approve, 36 months	Go to 6	
6.	Approve, 36 months	Go to 7	
7.	Go to 8	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you meet any of these conditions:</p> <ul style="list-style-type: none"> - You have tried metformin and it did not work for you, or you cannot use it - You require combination therapy and you have an A1c (hemoglobin A1c) of 7.5 percent or greater <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No inadequate response, intolerance or contraindication to metformin, no confirmation of combination therapy requirement]</p>
8.	Approve, 36 months	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you meet any of these conditions:</p> <ul style="list-style-type: none"> - You have been taking the requested drug for at least 3 months and you had a reduction in A1c (hemoglobin A1c) since starting this therapy - You have tried metformin and it did not work for you, or you cannot use it - You require combination therapy and you have an A1c (hemoglobin A1c) of 7.5 percent or greater - You have cardiovascular (heart) disease or multiple cardiovascular risk factors <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No response to treatment, No inadequate response, intolerance or contraindication to metformin, No confirmation of combination therapy requirement, No established CV disease or multiple CV risk factors for Farxiga]</p>

Specialty Guideline Management

DARZALEX (daratumumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Darzalex is indicated for the treatment of adult patients with multiple myeloma:

- A. in combination with lenalidomide and dexamethasone in newly diagnosed patients who are ineligible for autologous stem cell transplant and in patients with relapsed or refractory multiple myeloma who have received at least one prior therapy.
- B. in combination with bortezomib, melphalan and prednisone in newly diagnosed patients who are ineligible for autologous stem cell transplant.
- C. in combination with bortezomib, thalidomide, and dexamethasone in newly diagnosed patients who are eligible for autologous stem cell transplant.
- D. in combination with bortezomib and dexamethasone in patients who have received at least one prior therapy.
- E. in combination with pomalidomide and dexamethasone in patients who have received at least two prior therapies including lenalidomide and a proteasome inhibitor.
- F. as monotherapy, in patients who have received at least three prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory agent or who are double-refractory to a PI and an immunomodulatory agent.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Multiple Myeloma

Authorization of 12 months may be granted for the treatment of multiple myeloma when the requested medication will be used in any of the following regimens:

- A. In combination with bortezomib, melphalan, and prednisone
- B. In combination with bortezomib, thalidomide, and dexamethasone as primary therapy in members who are eligible for autologous stem cell transplant and the requested medication will be used for a maximum of 16 doses.
- C. In combination with bortezomib and dexamethasone
- D. In combination with lenalidomide and dexamethasone
- E. In combination with pomalidomide and dexamethasone in members who have received at least two prior therapies including a proteasome inhibitor (PI) and an immunomodulatory agent
- F. As a single agent in members who have received at least three prior therapies, including a PI and an immunomodulatory agent, or who are double refractory to a PI and an immunomodulatory agent

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when either of the following regimen specific criteria is met:

- A. All members (including new members) requesting the requested medication in combination with bortezomib, thalidomide, and dexamethasone must meet all initial criteria.
- B. For all other regimens listed in Section II, the member has not experienced an unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Darzalex [package insert]. Horsham, PA: Janssen Biotech Inc; September 2019.
2. The NCCN Drugs & Biologics Compendium 2018 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 29, 2019.
3. The NCCN Clinical Practice Guidelines in Oncology Multiple Myeloma (Version 1.2019) 2018 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed March 29, 2019.

SPECIALTY GUIDELINE MANAGEMENT

DAURISMO (glasdegib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Daurismo is indicated, in combination with low-dose cytarabine, for the treatment of newly-diagnosed acute myeloid leukemia (AML) in adult patients who are ≥ 75 years old or who have comorbidities that preclude use of intensive induction chemotherapy.

Limitation of Use: Daurismo has not been studied in patients with the comorbidities of severe renal impairment or moderate-to-severe hepatic impairment.

Compendial Uses

1. Post remission therapy following response to previous therapy with the same regimen
2. Relapsed/refractory disease as a component of repeating the initial successful induction regimen

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Acute Myeloid Leukemia (AML)

Authorization of 12 months may be granted for treatment of AML when all of the following criteria is met (A, B, and C):

- A. The requested medication is used in combination with cytarabine
- B. One of the following criteria is met:
 1. Member is 75 years of age or older.
 2. Member has comorbidities that preclude treatment with intensive induction chemotherapy.
- C. The requested medication will be used as treatment for induction therapy, post-remission therapy, or relapsed/refractory disease.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced disease progression or an unacceptable toxicity.

IV. REFERENCES

1. Daurismo [package insert]. New York, NY: Pfizer, Inc.; November 2018.

Reference number(s)
2793-A

2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc.
Available at: <https://www.nccn.org> Accessed June 18, 2019.

SPECIALTY GUIDELINE MANAGEMENT

DACOGEN (decitabine) decitabine (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Myelodysplastic syndromes (MDS): Dacogen (decitabine) is indicated for treatment of patients with myelodysplastic syndromes (MDS) including previously treated and untreated, *de novo* and secondary MDS of all French-American-British subtypes (refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, refractory anemia with excess blasts in transformation, and chronic myelomonocytic leukemia) and intermediate-1, intermediate-2, and high-risk International Prognostic Scoring System groups.

B. Compendial Uses

1. Chronic myeloid leukemia (CML)
2. Acute myeloid leukemia (AML)
3. Accelerated phase or blast phase myelofibrosis
4. Lower risk myelodysplastic syndromes (MDS) associated with thrombocytopenia, neutropenia, symptomatic anemia, or increased marrow blasts

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Myelodysplastic Syndromes (MDS)**

Authorization of 12 months may be granted for the treatment of MDS.

B. **Chronic myeloid leukemia (CML)**

Authorization of 12 months may be granted for the treatment of CML.

C. **Acute Myeloid Leukemia (AML)**

Authorization of 12 months may be granted for the treatment of AML.

D. **Accelerated Phase or Blast Phase Myelofibrosis**

Authorization of 12 months may be granted for the treatment of accelerated phase or blast phase myelofibrosis.

Reference number
2288-A

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced disease progression or an unacceptable toxicity.

IV. REFERENCES

1. Dacogen [package insert]. Rockville, MD: Otsuka America Pharmaceutical, Inc.; December 2018.
2. National Comprehensive Cancer Network. The NCCN Drugs & Biologics Compendium. <http://www.nccn.org>. Accessed July 10, 2019.

SPECIALTY GUIDELINE MANAGEMENT

EXJADE (deferasirox; tablets for suspension) JADENU (deferasirox; tablets, sprinkle granules)

deferasirox tablet for suspension

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Chronic iron overload due to blood transfusions (transfusional iron overload)
2. Chronic iron overload in patients with non-transfusion-dependent thalassemia (NTDT) syndromes and with a liver iron concentration (LIC) of at least 5 milligrams of iron per gram of liver dry weight (mg Fe/g dw) and a serum ferritin greater than 300 mcg/L

B. Compendial Use

Hereditary hemochromatosis

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

- A. Chronic Iron Overload due to Blood Transfusions (transfusional iron overload):
 1. Initial requests: pretreatment serum ferritin level
 2. Continuation requests: current serum ferritin level
- B. Chronic Iron Overload in Patients with Non-transfusion Dependent Thalassemia Syndromes:
 1. Initial requests: pretreatment serum ferritin level and liver iron concentration
 2. Continuation requests: current serum ferritin level

III. CRITERIA FOR INITIAL APPROVAL

A. **Chronic Iron Overload due to Blood Transfusions (transfusional iron overload)**

Authorization of 6 months may be granted for treatment of chronic iron overload due to blood transfusions when all of the following criteria are met:

1. Pretreatment serum ferritin level is consistently greater than 1000 mcg/L.
2. Dose of deferiasirox/Exjade will not exceed 40 mg/kg, dose of Jadenu will not exceed 28 mg/kg.
3. Member's renal function has been evaluated.

B. **Chronic Iron Overload in Patients with Non-transfusion Dependent Thalassemia Syndromes**

Authorization of 6 months may be granted for treatment of chronic iron overload in members with non-transfusion dependent thalassemia syndromes when all of the following criteria are met:

1. Pretreatment serum ferritin level is greater than 300 mcg/L.
2. Pretreatment liver iron concentration (LIC) is at least 5 milligrams of iron per gram of liver dry weight (mg Fe/g dw).
3. Dose of deferasirox/Exjade will not exceed 20 mg/kg, dose of Jadenu will not exceed 14 mg/kg.
4. Member's renal function has been evaluated.

C. Hereditary Hemochromatosis

Authorization of 6 months may be granted for treatment of hereditary hemochromatosis when both of the following criteria are met:

1. Phlebotomy is not an option (e.g., poor venous access, poor candidate due to underlying medical disorders) or the member had an unsatisfactory response to phlebotomy.
2. Member's renal function has been evaluated.

IV. CONTINUATION OF THERAPY

Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when the following criteria are met:

A. Chronic Iron Overload due to Blood Transfusions (transfusional iron overload)

1. Member is experiencing benefit from therapy as evidenced by a decrease in serum ferritin levels as compared to pretreatment baseline.
2. Serum ferritin level is not consistently below 500 mcg/L.
3. Member's renal function has been evaluated.

B. Chronic Iron Overload in Patients with Non-transfusion Dependent Thalassemia Syndromes

1. Member is experiencing benefit from therapy as evidenced by a decrease in serum ferritin levels as compared to pretreatment baseline.
2. Serum ferritin level is not consistently below 300 mcg/L.
3. Member's renal function has been evaluated.

C. Hereditary Hemochromatosis

1. Member is experiencing benefit from therapy as evidenced by a decrease in serum ferritin levels as compared to pretreatment baseline.
2. Member's renal function has been evaluated.

V. REFERENCES

1. Exjade [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; May 2018.
2. Jadenu [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; May 2018.
3. Micromedex Solutions [database online]. Truven Health Analytics, Inc. Ann Arbor, MI. Available at: www.micromedexsolutions.com. Accessed October 24, 2018.
4. AHFS DI (Adult and Pediatric) [database online]. Lexi-Comp, Inc. Hudson, OH. Available at: http://online.lexi.com/lco/action/index/dataset/complete_ashp [available with subscription]. Accessed December 1, 2017.
5. Clinical Pharmacology [Internet]. Elsevier. Tampa (FL). Available from: <http://www.clinicalpharmacology.com>. Accessed October 24, 2018.
6. Cappellini MD, Cohen A, Porter J, et al. Guidelines for the management of transfusion dependent thalassaemia (TDT) 3rd Edition [Internet]. *Thalassaemia International Federation* 2014;20:1-253.

Reference number(s)
1622-A

7. Hoffbrand AV, Taher A, Cappellini MD. How I treat transfusional iron overload. *Blood* 2012;120(18):3657-69.
8. Taher A, Musallam K, Cappellini M, et al. Guidelines for the management of non-transfusion dependent thalassaemia (NTDT) 2nd Edition. *Thalassaemia International Federation* 2018;1-117.
9. Phatak P, Brissot P, Bonkovsky H et al. A phase I/II, open-label, dose-escalation trial of once daily oral chelator deferasirox to treat iron overload in HFE-related hereditary hemochromatosis: Final Results of the Core Study. *Blood* 2009;114: 1514.
10. Adams P, Barton J, et al. How I Treat Hemochromatosis. *Blood* 2010;(116): 317-325.

Reference number(s)
1620-A

SPECIALTY GUIDELINE MANAGEMENT

DESFERAL (deferoxamine) deferoxamine mesylate (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Chronic iron overload due to transfusion-dependent anemias

B. Compendial Uses

1. Aluminum toxicity in patients undergoing dialysis
2. Hereditary hemochromatosis

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
Chronic iron overload due to transfusion-dependent anemias:

- A. Initial requests: pretreatment serum ferritin level
- B. Continuation requests: current serum ferritin level

III. CRITERIA FOR INITIAL APPROVAL

A. **Chronic Iron Overload due to Transfusion-Dependent Anemias**

Authorization of 6 months may be granted for treatment of chronic iron overload due to transfusion-dependent anemias when the pretreatment serum ferritin level is consistently greater than 1000 mcg/L.

B. **Aluminum toxicity in Patients Undergoing Dialysis**

Authorization of 6 months may be granted for treatment of aluminum toxicity in members undergoing dialysis.

C. **Hereditary Hemochromatosis**

Authorization of 6 months may be granted for treatment of hereditary hemochromatosis when phlebotomy is not an option (e.g., poor candidate due to underlying medical disorders) or the member had an unsatisfactory response to phlebotomy.

IV. CONTINUATION OF THERAPY

Reference number(s)
1620-A

Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when the following criteria are met:

A. Chronic Iron Overload due to Transfusion-Dependent Anemias

Member is experiencing benefit from therapy as evidenced by a decrease in serum ferritin levels as compared to pretreatment baseline.

B. Aluminum toxicity in Patients Undergoing Dialysis

Member is experiencing benefit from therapy as evidenced by any of the following:

1. Decreased serum aluminum concentrations
2. Symptomatic improvement (e.g., neurological symptom improvement, decreased bone pain)

C. Hereditary Hemochromatosis

Member is experiencing benefit from therapy as evidenced by a decrease in serum ferritin levels as compared to pretreatment baseline.

V. REFERENCES

1. Desferal [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; December 2011.
2. Deferoxamine mesylate [package insert]. Lake Forest, IL: Hospira, Inc.; February 2018.
3. Micromedex Solutions [database online]. Truven Health Analytics, Inc. Ann Arbor, MI. Available at: www.micromedexsolutions.com. Accessed October 15, 2018.
4. AHFS DI (Adult and Pediatric) [database online]. Lexi-Comp, Inc. Hudson, OH. Available at: http://online.lexi.com/lco/action/index/dataset/complete_ashp [available with subscription]. Accessed October 15, 2018.
5. Clinical Pharmacology [Internet]. Elsevier. Tampa (FL). Available from: <http://www.clinicalpharmacology.com>. October 15, 2018.
6. Cappellini MD, Cohen A, Porter J, et al. Guidelines for the management of transfusion dependent thalassaemia (TDT) 3rd Edition [Internet]. *Thalassaemia International Federation* 2014;20:1-253.
7. Hoffbrand AV, Taher A, Cappellini MD. How I treat transfusional iron overload. *Blood* 2012;120(18):3657-69.
8. NKF-K/DOQI. Clinical practice guidelines for bone metabolism and disease in chronic kidney disease. *Am J Kidney Dis* 2003; 42:S108–S122.
9. Adams P, Barton J, et al. How I Treat Hemochromatosis. *Blood* 2010; (116): 317-325.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

DIFICID
(fidaxomicin)

Status: CVS Caremark Criteria

Type: Initial Prior Authorization

Ref# 662-A

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA APPROVED INDICATIONS

Dificid is indicated in adult and pediatric patients aged 6 months and older for the treatment of *C. difficile*-associated diarrhea (CDAD).

Usage

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Dificid and other antibacterial drugs, Dificid should be used only to treat infections that are proven or strongly suspected to be caused by *C. difficile*. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has the diagnosis of *C. difficile*-associated diarrhea (CDAD) confirmed by a positive stool assay
- AND**
- The patient requires additional medication to complete a 10 day course of the requested drug for therapy that was initiated in the hospital
- OR**
- The patient has experienced an inadequate treatment response to oral vancomycin
- OR**
- The patient has experienced an intolerance to vancomycin
- OR**
- The patient has a contraindication that would prohibit a trial of vancomycin
- OR**
- The requested drug is being prescribed for a pediatric patient **AND**
 - The patient has experienced an inadequate treatment response to oral metronidazole
- OR**
- The patient has experienced an intolerance to metronidazole
- OR**
- The patient has a contraindication that would prohibit a trial of metronidazole

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Dificid is indicated in adult and pediatric patients aged 6 months and older for the treatment of *C. difficile*-associated diarrhea (CDAD).

The recommended dose for adults is 200 mg orally twice daily for 10 days. The recommended dosing for pediatric patients, who weigh at least 12.5 kg and are able to swallow tablets, is 200 mg orally twice daily for 10 days. If unable to swallow tablets or weigh less than 12.5 kg, Difcid oral suspension is available for use. The recommended dosing for pediatric patients is based on body weight and administered via oral syringe twice daily for 10 days.

Clostridium difficile infection (CDI) is defined by the presence of symptoms (usually diarrhea) and either a stool test positive for *C. difficile* toxins or detection of toxigenic *C. difficile*, or colonoscopic or histopathologic findings revealing pseudomembranous colitis.⁴

In two randomized, double blinded trials in adult patients, Difcid had a clinical response rate at the end of the 10-day treatment period that was non-inferior to oral vancomycin. Difcid demonstrated superior sustained clinical response to oral vancomycin, defined as clinical response at the end of treatment and survival without proven or suspected CDAD recurrence through 25 days beyond the end of treatment. This difference was due to lower rates of proven or suspected CDAD during the follow-up period in Difcid-treated patients. Similar rates of clinical response at the end of treatment and proven or suspected CDAD during the follow-up period were seen in Difcid-treated and vancomycin-treated patients infected with a BI isolate.

The safety and efficacy of Difcid in pediatric patients 6 months to less than 18 years was investigated in a Phase 3, multicenter, investigator-blinded, randomized, comparative trial.

For adult patients, the 2017 Update to the Infectious Disease Society of America (IDSA) Clinical Practice Guidelines for *Clostridium difficile* Infection recommends using either vancomycin or fidaxomicin over metronidazole for an initial episode of CDI. The dosage is vancomycin 125 mg orally 4 times per day or fidaxomicin 200 mg twice daily for 10 days. For fulminant CDI, oral vancomycin dosed at 500 mg 4 times per day is the regimen of choice. The options to treat a first recurrence of CDI include oral vancomycin as a tapered and pulsed regimen rather than a second standard 10-day course, a 10-day course of fidaxomicin, or a standard 10-day course of oral vancomycin rather than a second course of metronidazole if metronidazole was used for the primary episode. The recommended treatment options for patients with more than one recurrence are oral vancomycin using a tapered and pulsed regimen, a standard course of oral vancomycin followed by rifaximin, or fidaxomicin.⁴

For pediatric patients, the 2017 Update to the Infectious Disease Society of America (IDSA) Clinical Practice Guidelines for *Clostridium difficile* Infection recommends metronidazole or vancomycin for initial episodes or first recurrence of nonsevere CDI. For children with an initial episode of severe CDI, oral vancomycin is recommended over metronidazole. For children with a second or greater episode of recurrent CDI, oral vancomycin is recommended over metronidazole.

Since the recommended duration of treatment with Difcid for *C. difficile*-associated diarrhea is 10 days, the duration of approval will be 10 days if coverage criteria is met.

REFERENCES

1. Difcid [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; January 2020.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed December 2019.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed December 2019.
4. McDonald LC, et al. Clinical Practice Guidelines for *Clostridium difficile* Infection in Adults and Children: 2017 Update by the Infectious Diseases Society of America (IDSA) and the Society for Healthcare Epidemiology of America (SHEA). Available online at: http://www.idsociety.org/Guidelines/Patient_Care/IDSA_Practice_Guidelines/Infections_By_Organ_System-81567/Gastrointestinal/Clostridium_difficile/#recommendations. Accessed January 2020.

Written by: UM Development (RP)
Date Written: 02/2012
Revised: 06/2012, 07/2012; (PL) 03/2013; (RP) 02/2014, 12/2014, 04/2015, 05/2015 (added denial reasons), 12/2015 (no clinical changes), 12/2016 (no clinical changes; MDC-1 designation); (DS) 12/2017, (SF) 12/2018 (no clinical changes), (MAC) 12/2019 (removed MDC-1 designation from title/document), 01/2020 (new indication for pediatrics)

CRITERIA FOR APPROVAL

1	Does the patient have the diagnosis of <i>C. difficile</i> -associated diarrhea (CDAD) confirmed by a positive stool assay?	Yes	No
2	Does the patient require additional medication to complete a 10 day course of the requested drug for therapy that was initiated in the hospital? [If yes, then no further questions.]	Yes	No
3	Has the patient experienced an inadequate treatment response to oral vancomycin? [If yes, then no further questions.]	Yes	No
4	Has the patient experienced an intolerance to vancomycin? [If yes, then no further questions.]	Yes	No
5	Does the patient have a contraindication that would prohibit a trial of vancomycin? [If yes, then no further questions.]	Yes	No
6	Is the requested drug being prescribed for a pediatric patient? [If no, then no further questions.]	Yes	No
7	Has the patient experienced an inadequate treatment response to oral metronidazole? [If yes, no further questions.]	Yes	No
8	Has the patient experienced an intolerance to metronidazole? [If yes, no further questions.]	Yes	No
9	Does the patient have a contraindication that would prohibit a trial of metronidazole?	Yes	No

Mapping Instructions			
	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have these conditions: - You have bacteria certain type of bacterial infection that is causing diarrhea - The type of bacteria has been confirmed by a stool test Your request has been denied based on the information we have. [Short Description: No approvable diagnosis, no confirmation of diagnosis]
2.	Approve, 10 days	Go to 3	
3.	Approve, 10 days	Go to 4	
4.	Approve, 10 days	Go to 5	
5.	Approve, 10 days	Go to 6	
6.	Go to 7	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you are an adult and you have tried oral vancomycin or you cannot take vancomycin. Your request has been denied based on the information we have. [Short Description: No inadequate response, intolerance, or contraindication to vancomycin for adult patient]

7.	Approve, 10 days	Go to 8	
8.	Approve, 10 days	Go to 9	
9.	Approve, 10 days	Deny	<p>You do not meet the requirements of your plan.</p> <p>Your plan covers this drug when you meet any of these conditions:</p> <ul style="list-style-type: none"> -You have tried oral vancomycin and it did not work for you, or you cannot take vancomycin -You are a pediatric patient and oral metronidazole did not work for you or you cannot take metronidazole <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No inadequate response, intolerance, or contraindication to vancomycin or metronidazole for pediatric patient]</p>

SPECIALTY GUIDELINE MANAGEMENT

TAXOTERE (docetaxel) DOCEFREZ (docetaxel) docetaxel (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Breast Cancer (BC)
 - a. Docetaxel is indicated for the treatment of patients with locally advanced or metastatic breast cancer after failure of prior chemotherapy.
 - b. Docetaxel in combination with doxorubicin and cyclophosphamide is indicated for the adjuvant treatment of patients with operable node-positive breast cancer.
2. Non-Small Cell Lung Cancer (NSCLC)
 - a. Docetaxel as a single agent is indicated for the treatment of patients with locally advanced or metastatic NSCLC after failure of prior platinum-based chemotherapy.
 - b. Docetaxel in combination with cisplatin is indicated for the treatment of patients with unresectable, locally advanced or metastatic NSCLC who have not previously received chemotherapy for this condition.
3. Prostate Cancer
 - a. Docetaxel in combination with prednisone is indicated for the treatment of patients with metastatic castration-resistant prostate cancer.
 - b. Docetaxel in combination with prednisone is indicated for the treatment of patients with androgen independent (hormone refractory) metastatic prostate cancer.
4. Gastric Adenocarcinoma (GC)
Docetaxel in combination with cisplatin and fluorouracil is indicated for the treatment of patients with advanced gastric adenocarcinoma, including adenocarcinoma of the gastroesophageal junction, who have not received prior chemotherapy for advanced disease.
5. Head and Neck Cancer
Docetaxel in combination with cisplatin and fluorouracil is indicated for the induction treatment of patients with locally advanced squamous cell carcinoma of the head and neck (SCCHN).

B. Compendial Uses

1. Bladder cancer, primary carcinoma of the urethra, upper genitourinary (GU) tract tumors, and urothelial carcinoma of the prostate
2. Bone cancer: Ewing's sarcoma and osteosarcoma
3. Breast cancer
4. Esophageal and esophagogastric junction cancers

Reference number(s)
1901-A

5. Gastric cancer
6. Head and neck cancer (including very advanced head and neck cancer and cancers of the oropharynx, hypopharynx, nasopharynx, glottic larynx, supraglottic larynx, and occult primary cancer)
7. Non-small cell lung cancer
8. Occult primary tumors (cancer of unknown primary)
9. Ovarian cancer/fallopian tube cancer/primary peritoneal cancer: epithelial ovarian cancer, fallopian tube cancer, primary peritoneal cancer, malignant germ cell tumors, malignant sex cord-stromal tumors, carcinosarcoma (malignant mixed Müllerian tumors), clear cell carcinoma, mucinous carcinoma, low-grade serious carcinoma/ovarian borderline epithelial tumors (low malignant potential) with invasive implants, and grade 1 endometrioid epithelial carcinoma.
10. Prostate cancer
11. Small cell lung cancer
12. Soft tissue sarcoma (including extremity/superficial trunk, head/neck, retroperitoneal/intra-abdominal, angiosarcoma, and pleomorphic rhabdomyosarcoma)
13. Thyroid carcinoma: anaplastic carcinoma
14. Uterine neoplasms: endometrial carcinoma and uterine sarcoma

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Bladder Cancer, Primary Carcinoma of the Urethra, Upper Genitourinary Tract Tumors, and Urothelial Carcinoma of the Prostate

1. Bladder Cancer

Authorization of 6 months may be granted for treatment of bladder cancer.

2. Primary Carcinoma of the Urethra

Authorization of 6 months may be granted for treatment of recurrent or metastatic primary carcinoma of the urethra.

3. Upper Genitourinary Tract Tumors and Urothelial Carcinoma of the Prostate

Authorization of 6 months may be granted for treatment of metastatic upper genitourinary tract tumors or urothelial carcinoma of the prostate.

B. Bone Cancer

1. Ewing's Sarcoma

Authorization of 6 months may be granted for treatment of relapsed, progressive, or metastatic Ewing's sarcoma.

2. Osteosarcoma

Authorization of 6 months may be granted for treatment of relapsed, refractory, or metastatic osteosarcoma.

C. Breast Cancer

Authorization of 6 months may be granted for treatment of breast cancer in members when any of the following criteria are met:

1. Member has human epidermal growth factor receptor 2 (HER2)-negative recurrent or metastatic disease, as a single agent or in combination with capecitabine; OR

2. Member has human epidermal growth factor receptor 2 (HER2)-positive disease; and docetaxel will be used in one of the following regimens:
 - a. In combination with pertuzumab and trastuzumab; or
 - b. In combination with trastuzumab; OR
3. Docetaxel will be used as adjuvant therapy.

D. Esophageal and Esophagogastric Junction Cancers

Authorization of 6 months may be granted for treatment of esophageal or esophagogastric junction cancer.

E. Gastric Cancer

Authorization of 6 months may be granted for treatment of gastric cancer.

F. Head and Neck Cancer

Authorization of 6 months may granted for treatment of head and neck cancer (including very advanced head and neck cancer, cancers of the oropharynx, hypopharynx, nasopharynx, glottic larynx, supraglottic larynx, and occult primary cancer).

G. Non-Small Cell Lung Cancer (NSCLC)

Authorization of 6 months may be granted for treatment of non-small cell lung cancer.

H. Occult Primary Tumors (cancer of unknown primary)

Authorization of 6 months may be granted for treatment of occult primary cancer.

I. Ovarian Cancer, Fallopian Tube Cancer, and Primary Peritoneal Cancer

1. Epithelial Ovarian Cancer, Fallopian Tube Cancer, and Primary Peritoneal Cancer

Authorization of 6 months may be granted for treatment of epithelial ovarian cancer, fallopian tube cancer, and primary peritoneal cancer.

2. Malignant Germ Cell Tumors

Authorization of 6 months may be granted for treatment of malignant germ cell tumors.

3. Malignant Sex-Cord Stromal Tumors

Authorization of 6 months may be granted for treatment of malignant sex-cord stromal tumors.

4. Carcinosarcoma (Malignant Mixed Müllerian Tumors)

Authorization of 6 months may be granted for treatment of carcinosarcoma (malignant mixed Müllerian tumors).

5. Clear Cell Carcinoma

Authorization of 6 months may be granted for treatment of clear cell carcinoma.

6. Mucinous Carcinoma

Authorization of 6 months may be granted for treatment of mucinous carcinoma.

7. Low-Grade Serous Carcinoma and Ovarian Borderline Epithelial Tumors (Low Malignant Potential) with Invasive Implants

Authorization of 6 months may be granted for treatment of low-grade serous carcinoma and ovarian borderline epithelial tumors (low malignant potential) with invasive implants.

8. Grade 1 Endometrioid Epithelial Carcinoma

Authorization of 6 months may be granted for treatment of grade 1 endometrioid epithelial carcinoma.

Reference number(s)
1901-A

J. Prostate Cancer

Authorization of 6 months may be granted for treatment of prostate cancer.

K. Small Cell Lung Cancer (SCLC)

Authorization of 6 months may be granted for treatment of small cell lung cancer.

L. Soft Tissue Sarcoma

Authorization of 6 months may be granted for treatment of soft tissue sarcoma (including extremity/superficial trunk, head/neck, retroperitoneal/intra-abdominal, angiosarcoma, and pleomorphic rhabdomyosarcoma).

M. Thyroid Carcinoma – Anaplastic Carcinoma

Authorization of 6 months may be granted for treatment of thyroid carcinoma-anaplastic carcinoma.

N. Uterine Neoplasms

Authorization of 6 months may be granted for treatment of uterine neoplasms (including endometrial carcinoma and uterine sarcoma).

III. CONTINUATION OF THERAPY

Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for an indication in Section II who are experiencing clinical benefit to therapy or who have not experienced an unacceptable toxicity.

IV. REFERENCES

1. Taxotere [package insert]. Bridgewater, NJ: sanofi-aventis U.S. LLC; June 2019.
2. Docefrez [package insert]. Gujarat, India: Sun Pharmaceutical Ind. Ltd; October 2014.
3. Docetaxel [package insert]. Gujarat, India: Sun Pharmaceutical Ind. Ltd; January 2019.
4. The NCCN Drugs & Biologics Compendium 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed July 05, 2019.
5. AHFS DI (Adult and Pediatric) [database online]. Hudson, OH: Lexi-Comp, Inc.; http://online.lexi.com/lco/action/index/dataset/complete_ashp [available with subscription]. Accessed (July 2019).

SPECIALTY GUIDELINE MANAGEMENT

TIKOSYN (dofetilide) dofetilide (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Maintenance of normal sinus rhythm (delay in time to recurrence of atrial flutter/atrial fibrillation [AF/AFI]) in patients with AF/AFI of greater than one week duration who have been converted to normal sinus rhythm
2. Conversion of AF/AFI to normal sinus rhythm

B. Compendial Uses

1. Supraventricular tachycardia
2. Ventricular tachyarrhythmia

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR APPROVAL

1. **Atrial Flutter/Atrial fibrillation**

Authorization of 12 months may be granted for the maintenance of, or conversion to, normal sinus rhythm after atrial flutter or atrial fibrillation.

2. **Supraventricular tachycardia**

Authorization of 12 months may be granted for the treatment and prevention of supraventricular tachycardia.

3. **Ventricular tachyarrhythmia**

Authorization of 12 months may be granted for the treatment and prevention of ventricular tachyarrhythmia.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet ALL initial authorization criteria.

IV. REFERENCES

1. Tikosyn [package insert]. New York, NY: Pfizer Inc.; July 2016.
2. Dofetilide [package insert]. Greenville, NC: Mayne Pharma; March 2016.

3. Micromedex Solutions [database online]. Cambridge, MA: IBM Watson Health. Updated periodically. www.micromedexsolutions.com [available with subscription]. Accessed April 9, 2019.
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SPECIALTY GUIDELINE MANAGEMENT

DOPTelet (avatrombopag)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. **Treatment of Thrombocytopenia in Patients with Chronic Liver Disease (CLD)**
Doptelet is indicated for the treatment of thrombocytopenia in adult patients with chronic liver disease who are scheduled to undergo a procedure.
2. **Treatment of Thrombocytopenia in Patients with Chronic Immune Thrombocytopenia (ITP)**
Doptelet is indicated for the treatment of thrombocytopenia in adult patients with chronic immune thrombocytopenia who have had an insufficient response to a previous treatment.

B. Compendial Uses

Severe thrombocytopenia post cancer chemotherapy

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

- A. Thrombocytopenia in chronic liver disease: pretreatment platelet count
- B. Immune thrombocytopenia: pretreatment and current platelet counts
- C. Severe thrombocytopenia post cancer chemotherapy: pretreatment and current platelet counts

III. EXCLUSIONS

Coverage will not be provided for members with the following exclusion: concomitant use of Doptelet with other thrombopoietin receptor agonists (e.g., Muplesta, Promacta, Nplate) or with spleen tyrosine kinase inhibitors (e.g., Tavalisse)

IV. CRITERIA FOR INITIAL APPROVAL

A. **Thrombocytopenia in chronic liver disease**

Authorization of 30 days may be granted for treatment of thrombocytopenia in members with chronic liver disease when both of the following criteria are met:

1. Member has a baseline platelet count of less than $50 \times 10^9/L$ taken within 14 days of the request.
2. Member is scheduled to undergo a procedure.

B. Chronic or persistent primary immune thrombocytopenia (ITP)

Authorization of 6 months may be granted for treatment of chronic or persistent ITP when both of the following criteria are met:

1. Inadequate response or intolerance to prior therapy (for example, corticosteroids or immunoglobulins).
2. Untransfused platelet count at time of diagnosis is less than $30 \times 10^9/L$ OR $30 \times 10^9/L$ to $50 \times 10^9/L$ with symptomatic bleeding (e.g., significant mucous membrane bleeding, gastrointestinal bleeding or trauma) or risk factors for bleeding (see Section VI).

C. Severe thrombocytopenia post cancer chemotherapy

Authorization of 6 months may be granted for treatment of severe thrombocytopenia post cancer chemotherapy when the platelet count is less than $50 \times 10^9/L$.

V. CONTINUATION OF THERAPY**A. Thrombocytopenia in chronic liver disease**

Continuation of therapy, defined as use beyond the initial approval for same procedure, is not approvable. All members (including new members) requesting authorization due to newly scheduled procedure must meet all initial authorization criteria.

B. Chronic or persistent ITP

1. Authorization of 3 months may be granted to members with current platelet count less than $50 \times 10^9/L$ for whom the platelet count is not sufficient to prevent clinically important bleeding and who have not received a maximal Doptelet dose for at least 4 weeks.
2. Authorization of 12 months may be granted to members with current platelet count less than $50 \times 10^9/L$ for whom the current platelet count is sufficient to prevent clinically important bleeding.
3. Authorization of 12 months may be granted to members with current platelet count of $50 \times 10^9/L$ to $200 \times 10^9/L$.
4. Authorization of 12 months may be granted to members with current platelet count greater than $200 \times 10^9/L$ to less than or equal to $400 \times 10^9/L$ for whom Doptelet dosing will be adjusted to achieve a platelet count sufficient to avoid clinically important bleeding.

C. Severe thrombocytopenia post cancer chemotherapy

Authorization of 6 months may be granted for continued treatment of severe thrombocytopenia post cancer chemotherapy in members who experience benefit from therapy (e.g., increased platelet counts, decreased bleeding events, reduced need for platelet transfusions) and the platelet count remains less than $100 \times 10^9/L$.

VI. APPENDIX**Examples of risk factors for bleeding (not all inclusive)**

- Undergoing a medical or dental procedure where blood loss is anticipated
- Comorbidity (e.g., peptic ulcer disease, hypertension)
- Mandated anticoagulation therapy
- Profession (e.g., construction worker) or lifestyle (e.g., plays contact sports) that predisposes patient to trauma

VII. REFERENCES

1. Doptelet [package insert]. Durham, NC: AkaRx, Inc.; June 2019.

Reference number(s)
3081-A

2. Jurczak W, Chojnowski K, et al. Phase 3 randomised study of avatrombopag, a novel thrombopoietin receptor agonist for the treatment of chronic immune thrombocytopenia. *Br J Haematol*. 2018;183(3):479-490.
3. Neunert C, Lim W, Crowther M, et al. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. *Blood*. 2011;117(16):4190-4207.
4. Provan D, Stasi R, Newland AC, et al. International consensus report on the investigation and management of primary immune thrombocytopenia. *Blood*. 2010;115(2):168-186.
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6. NCCN hematopoietic growth factors. Short-term recommendations specific to issues with COVID-19 (SARS-CoV-2). National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org/covid-19/pdf/HGF_COVID-19.pdf. Accessed April 16, 2020.

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	DIPEPTIDYL PEPTIDASE-4 (DPP-4) INHIBITORS
BRAND NAME* (generic)	<p>JANUMET (sitagliptin/metformin)</p> <p>JANUMET XR (sitagliptin/metformin extended-release)</p> <p>JANUVIA (sitagliptin)</p> <p>JENTADUETO (linagliptin/metformin)</p> <p>JENTADUETO XR (linagliptin/metformin extended-release)</p> <p>KAZANO (alogliptin/metformin)</p> <p>KOMBIGLYZE XR (saxagliptin/metformin extended-release)</p> <p>NESINA (alogliptin)</p> <p>ONGLYZA (saxagliptin)</p> <p>OSENI (alogliptin/pioglitazone)</p> <p>TRADJENTA (linagliptin)</p>
<p>Status: CVS Caremark Criteria Type: Initial Prior Authorization Ref # 673-A</p>	

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Janumet/Janumet XR

Janumet/Janumet XR are indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both sitagliptin and metformin is appropriate.

Important Limitations of Use:

- Janumet/Janumet XR should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis.
- Janumet/Janumet XR have not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at increased risk for the development of pancreatitis while using Janumet/Janumet XR.

Januvia

Monotherapy and Combination Therapy

Januvia is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Important Limitations of Use:

- Januvia should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis, as it would not be effective in these settings.
- Januvia has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at increased risk for the development of pancreatitis while using Januvia.

Jentadueto/Jentadueto XR

Jentadueto/Jentadueto XR are indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Important Limitations of Use:

- Jentadueto/Jentadueto XR should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis, as it would not be effective in these settings.
- Jentadueto/Jentadueto XR have not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at increased risk for the development of pancreatitis while using Jentadueto/Jentadueto XR.

Kazano

Monotherapy and Combination Therapy

Kazano is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both alogliptin and metformin is appropriate.

Important Limitations of Use:

- Kazano is not indicated for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis, as it would not be effective in these settings.

Kombiglyze XR

Kombiglyze XR is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both saxagliptin and metformin is appropriate.

Important Limitations of Use:

- Kombiglyze XR is not indicated for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis.

Nesina

Monotherapy and Combination Therapy

Nesina is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Important Limitations of Use:

- Nesina is not indicated for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis, as it would not be effective in these settings.

Onglyza

Monotherapy and Combination Therapy

Onglyza is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Important Limitations of Use:

- Onglyza is not indicated for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis, as it would not be effective in these settings.

Oseni

Monotherapy and Combination Therapy

Oseni is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both alogliptin and pioglitazone is appropriate.

Important Limitations of Use:

- Oseni is not indicated for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis, as it would not be effective in these settings.

Tradjenta

Tradjenta tablets are indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Important Limitations of Use:

- Tradjenta should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis, as it would not be effective in these settings.
- Tradjenta has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at an increased risk for the development of pancreatitis while using Tradjenta.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- Patient has been receiving the requested drug for at least 3 months AND demonstrated a reduction in A1c (hemoglobin A1c) since starting this therapy

OR

- Patient has the diagnosis of type 2 diabetes mellitus AND
 - Patient has experienced an inadequate treatment response, intolerance, or contraindication to metformin

OR

- Patient requires combination therapy AND has an A1c (hemoglobin A1c) of 7.5 percent or greater

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Janumet, Janumet XR, Januvia, Jentadueto, Jentadueto XR, Kazano, Kombiglyze XR, Nesina, Onglyza, Oseni and Tradjenta are indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. These agents should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis.

Clinical guidelines from the American Diabetes Association and the American Association of Clinical Endocrinologists and American College of Endocrinology for the management of hyperglycemia in type 2 diabetes indicate that metformin monotherapy should be started at diagnosis of type 2 diabetes unless there are contraindications. Metformin is effective and safe, is inexpensive, and may reduce risk of cardiovascular events and death. In patients with contraindications or intolerance of metformin, initial therapy should be based on patient factors; consider a drug from another class.^{14, 15}

The clinical guidelines also state that the A1c (hemoglobin A1c) test is the major tool for assessing glycemic control and has strong predictive value for diabetes complications. Thus, A1c testing should be performed routinely in all patients with diabetes at initial assessment and as part of continuing care.¹⁴ The guidelines set goals for therapeutic effectiveness which must be evaluated frequently (e.g., every 3 months) until stable, using multiple criteria, including A1c. Less frequent monitoring is acceptable once targets are achieved.^{14, 15}

If the A1c target is not achieved after approximately 3 months and patient does not have atherosclerotic cardiovascular disease (ASCVD) or chronic kidney disease (CKD), consider a combination of metformin and one of the preferred six treatment options: sulfonylurea, thiazolidinedione, dipeptidyl peptidase 4 (DPP-4) inhibitors, sodium glucose co-transporter 2 (SGLT2) inhibitors, glucagon-like peptide 1 (GLP-1) receptor agonists, or basal insulin; the choice of which agent to add is based on drug-specific effects and patient factors.^{14, 15}

In patients with an initial A1c of 7.5% or greater, or in patients who are unable to achieve their glycemic goals with monotherapy, combination therapy is recommended.¹⁵

REFERENCES

1. Janumet [package insert]. Whitehouse Station, NJ: Merck Sharp & Dohme Corp; June 2019.
2. Janumet XR [package insert]. Whitehouse Station, NJ: Merck Sharp & Dohme Corp; June 2019.
3. Januvia [package insert]. Whitehouse Station, NJ: Merck Sharp & Dohme Corp; June 2019.

4. Jentadueto [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; July 2019.
5. Jentadueto XR [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; July 2019.
6. Kazano [package insert]. Deerfield, IL: Takeda Pharmaceuticals America, Inc.; June 2019.
7. Kombiglyze XR [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals; June 2019.
8. Nesina [package insert]. Deerfield, IL: Takeda Pharmaceuticals America, Inc.; June 2019.
9. Onglyza [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals; June 2019.
10. Oseni [package insert]. Deerfield, IL: Takeda Pharmaceuticals America, Inc.; June 2019.
11. Tradjenta [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; July 2019.
12. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed July 2019.
13. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed July 2019.
14. American Diabetes Association. Standards of Medical Care in Diabetes-2019: *Diabetes Care* January 2019;42(Supplement1).
15. Garber AJ, Abrahamson MJ, Barzilay JI, et al. Consensus Statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the Comprehensive Type 2 Diabetes Management Algorithm 2019, *Endocr Pract.* 2019; 25 (No 1); 69-100.

Written by: UM Development (SE)
 Date Written: 06/2011
 Revised: (PL) 11/2011 (Added Juvisync 06/2011(2)) (PL) 02/2012 (Added Janumet XR + Jentadueto 06/2011(3)), (PL) 08/2012; (NB) 10/2012 (extended duration); (MS) 02/2013 (added Kazano, Nesina, Oseni), 07/2013, 10/2013; (RP) 07/2014, 07/2015, 07/2016 (Added Jentadueto XR; no other clinical changes), 03/2017 (Non-clinical operational change to Note for CIs), 07/2017, (RP) 07/2018 (no clinical changes), 07/2019 (no clinical changes; removed MDC designation)
 Reviewed: Medical Affairs: (KP) 06/2011, 11/2011, 02/2012; (LS) 08/2012; (KP) 02/2013; (LS) 04/2013; (DC) 07/2013; (KP) 10/2013; (AD) 07/2014; (DNC) 07/2015; (ME) 07/2016, 07/2017; (CHART) 08/01/2019
 External Review: 08/2011, 12/2011, 02/2012, 3/2012, 10/2012, 04/2013, 10/2013, 10/2014, 10/2015, 10/2016, 10/2017, 10/2018, 10/2019

CRITERIA FOR APPROVAL

1	Has the patient been receiving the requested drug for at least 3 months? [If no, then skip to question 3.]	Yes	No
2	Has the patient demonstrated a reduction in A1c (hemoglobin A1c) since starting this therapy? [No further questions.]	Yes	No
3	Does the patient have a diagnosis of type 2 diabetes mellitus?	Yes	No
4	Has the patient experienced an inadequate treatment response, intolerance, or contraindication to metformin? [If yes, then no further questions.]	Yes	No
5	Does the patient require combination therapy AND have an A1c (hemoglobin A1c) of 7.5 percent or greater?	Yes	No

Guidelines for Approval					
Duration of Approval 36 Months					
Set 1		Set 2		Set 3	
Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)
1	None	3	1	3	1
2		4		5	4

Mapping Instructions			
	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Go to 3	
2.	Approve, 36 months	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you meet these conditions:</p> <ul style="list-style-type: none"> - You have been taking the requested drug for at least 3 months - You had a reduction in A1c (hemoglobin A1c) since starting this therapy <p>Your request has been denied based on the information we have. [Short Description: No response to treatment]</p>
3.	Go to 4	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you have type 2 diabetes mellitus. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]</p>
4.	Approve, 36 months	Go to 5	
5.	Approve, 36 months	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you meet any of these conditions:</p> <ul style="list-style-type: none"> - You have tried metformin and it did not work for you, or you cannot use it - You require combination therapy and you have an A1c (hemoglobin A1c) of 7.5 percent or greater <p>Your request has been denied based on the information we have. [Short Description: No inadequate response, intolerance or contraindication to metformin; No combination therapy requirement]</p>

STEP THERAPY CRITERIA

DRUG CLASS **DIPEPTIDYL PEPTIDASE-4 (DPP-4) INHIBITORS**

BRAND NAME*
(generic)

JANUMET
(sitagliptin/metformin)

JANUMET XR
(sitagliptin/metformin extended-release)

JANUVIA
(sitagliptin)

JENTADUETO
(linagliptin/metformin)

JENTADUETO XR
(linagliptin/metformin extended-release)

KAZANO
(alogliptin/metformin)

KOMBIGLYZE XR
(saxagliptin/metformin extended-release)

NESINA
(alogliptin)

ONGLYZA
(saxagliptin)

OSENI
(alogliptin/pioglitazone)

TRADJENTA
(linagliptin)

Status: CVS Caremark Criteria

Type: Initial Step Therapy; Post Step Therapy Prior Authorization

Ref # 1009-D

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Janumet/Janumet XR

Janumet/Janumet XR are indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both sitagliptin and metformin is appropriate.

Important Limitations of Use:

- Janumet/Janumet XR should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis.
- Janumet/Janumet XR have not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at increased risk for the development of pancreatitis while using Janumet/Janumet XR.

Januvia

Monotherapy and Combination Therapy

Januvia is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Important Limitations of Use:

- Januvia should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis, as it would not be effective in these settings.
- Januvia has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at increased risk for the development of pancreatitis while using Januvia.

Jentadueto/Jentadueto XR

Jentadueto/Jentadueto XR are indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Important Limitations of Use:

- Jentadueto/Jentadueto XR should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis, as it would not be effective in these settings.
- Jentadueto/Jentadueto XR have not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at increased risk for the development of pancreatitis while using Jentadueto/Jentadueto XR.

Kazano

Monotherapy and Combination Therapy

Kazano is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both alogliptin and metformin is appropriate.

Important Limitations of Use:

- Kazano is not indicated for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis, as it would not be effective in these settings.

Kombiglyze XR

Kombiglyze XR is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both saxagliptin and metformin is appropriate.

Important Limitations of Use:

- Kombiglyze XR is not indicated for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis.

Nesina

Monotherapy and Combination Therapy

Nesina is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Important Limitations of Use:

- Nesina is not indicated for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis, as it would not be effective in these settings.

Onglyza

Monotherapy and Combination Therapy

Onglyza is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Important Limitations of Use:

- Onglyza is not indicated for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis, as it would not be effective in these settings.

Oseni

Monotherapy and Combination Therapy

Oseni is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both alogliptin and pioglitazone is appropriate.

Important Limitations of Use:

- Oseni is not indicated for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis, as it would not be effective in these settings.

Tradjenta

Tradjenta tablets are indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Important Limitations of Use:

- Tradjenta should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis, as it would not be effective in these settings.
- Tradjenta has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at an increased risk for the development of pancreatitis while using Tradjenta.

INITIAL STEP THERAPY

**Include Rx and OTC products unless otherwise stated.*

If the patient has filled a prescription for at least a 30 day supply of metformin within the past 180 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit. If the patient does not meet the initial step therapy criteria, then the system will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- Patient has been receiving the requested drug for at least 3 months AND demonstrated a reduction in A1c (hemoglobin A1c) since starting this therapy

OR

- Patient has the diagnosis of type 2 diabetes mellitus AND
 - Patient has experienced an inadequate treatment response, intolerance, or contraindication to metformin
- OR**
- Patient requires combination therapy AND has an A1c (hemoglobin A1c) of 7.5 percent or greater

RATIONALE

If the patient has filled a prescription for at least a 30 day supply of metformin within the past 180 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.

If the patient does not meet the initial step therapy criteria, then prior authorization is required.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Janumet, Janumet XR, Januvia, Jentadueto, Jentadueto XR, Kazano, Kombiglyze XR, Nesina, Onglyza, Oseni and Tradjenta are indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. These agents should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis.

Clinical guidelines from the American Diabetes Association and the American Association of Clinical Endocrinologists and American College of Endocrinology for the management of hyperglycemia in type 2 diabetes indicate that metformin monotherapy should be started at diagnosis of type 2 diabetes unless there are contraindications. Metformin is effective and safe, is inexpensive, and may reduce risk of cardiovascular events and death. In patients with contraindications or intolerance of metformin, initial therapy should be based on patient factors; consider a drug from another class.^{14,15}

The clinical guidelines also state that the A1c (hemoglobin A1c) test is the major tool for assessing glycemic control and has strong predictive value for diabetes complications. Thus, A1c testing should be performed routinely in all patients with diabetes at initial assessment and as part of continuing care.¹⁴ The guidelines set goals for therapeutic effectiveness which must be evaluated frequently (e.g., every 3 months) until stable, using multiple criteria, including A1c. Less frequent monitoring is acceptable once targets are achieved.^{14,15}

If the A1c target is not achieved after approximately 3 months and patient does not have atherosclerotic cardiovascular disease (ASCVD) or chronic kidney disease (CKD), consider a combination of metformin and one of the preferred six treatment options: sulfonylurea, thiazolidinedione, dipeptidyl peptidase 4 (DPP-4) inhibitors, sodium glucose co-transporter 2 (SGLT2) inhibitors, glucagon-like peptide 1 (GLP-1) receptor agonists, or basal insulin; the choice of which agent to add is based on drug-specific effects and patient factors.^{14,15}

In patients with an initial A1c of 7.5% or greater, or in patients who are unable to achieve their glycemic goals with monotherapy, combination therapy is recommended.¹⁵

REFERENCES

1. Janumet [package insert]. Whitehouse Station, NJ: Merck Sharp & Dohme Corp; June 2019.
2. Janumet XR [package insert]. Whitehouse Station, NJ: Merck Sharp & Dohme Corp; June 2019.
3. Januvia [package insert]. Whitehouse Station, NJ: Merck Sharp & Dohme Corp; June 2019.
4. Jentadueto [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; July 2019.
5. Jentadueto XR [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; July 2019.
6. Kazano [package insert]. Deerfield, IL: Takeda Pharmaceuticals America, Inc.; June 2019.
7. Kombiglyze XR [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals; June 2019.
8. Nesina [package insert]. Deerfield, IL: Takeda Pharmaceuticals America, Inc.; June 2019.
9. Onglyza [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals; June 2019.
10. Oseni [package insert]. Deerfield, IL: Takeda Pharmaceuticals America, Inc.; June 2019.
11. Tradjenta [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; July 2019.
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13. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed July 2019.
14. American Diabetes Association. Standards of Medical Care in Diabetes-2019: *Diabetes Care* January 2019;42(Supplement1).
15. Garber AJ, Abrahamson MJ, Barzilay JI, et al. Consensus Statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the Comprehensive Type 2 Diabetes Management Algorithm 2019, *Endocr Pract.* 2019; 25 (No 1); 69-100.

Written by: UM Development (MS)
 Date Written: 07/2013
 Revised: (RP) 07/2014, 07/2015, 07/2016 (Added Jentadueto XR; no other clinical changes), 03/2017 (Non-clinical operational change to Note for CIs), 07/2017, (RP) 07/2018 (no clinical changes), 07/2019 (no clinical changes)
 Reviewed: Medical Affairs (DC) 07/2013; (AD) 07/2014; (DNC) 07/2015; (ME) 07/2016, 07/2017; (CHART) 08/01/2019
 External Review: 10/2013, 10/2014, 10/2015, 10/2016, 10/2017, 10/2018, 10/2019

CRITERIA FOR APPROVAL

1	Has the patient been receiving the requested drug for at least 3 months? [If no, then skip to question 3.]	Yes	No
2	Has the patient demonstrated a reduction in A1c (hemoglobin A1c) since starting this therapy? [No further questions.]	Yes	No
3	Does the patient have the diagnosis of type 2 diabetes mellitus?	Yes	No
4	Has the patient experienced an inadequate treatment response, intolerance, or contraindication to metformin? [If yes, then no further questions.]	Yes	No

5	Does the patient require combination therapy AND have an A1c (hemoglobin A1c) of 7.5 percent or greater?	Yes	No
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Mapping Instructions			
	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Go to 3	
2.	Approve, 36 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet these conditions: - You have been taking the requested drug for at least 3 months - You had a reduction in A1c (hemoglobin A1c) since starting this therapy Your request has been denied based on the information we have. [Short Description: No response to treatment]
3.	Go to 4	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have type 2 diabetes mellitus. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
4.	Approve, 36 months	Go to 5	
5.	Approve, 36 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet any of these conditions: - You have tried metformin and it did not work for you, or you cannot use it - You require combination therapy and you have an A1c (hemoglobin A1c) of 7.5 percent or greater Your request has been denied based on the information we have. [Short Description: No inadequate response, intolerance or contraindication to metformin, No combination therapy requirement]

SPECIALTY GUIDELINE MANAGEMENT

DUOPA (carbidopa and levodopa enteral suspension)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Duopa is indicated for the treatment of motor fluctuations in patients with advanced Parkinson's disease.

All other indications are considered experimental/investigational and are not a covered benefit.

II. EXCLUSIONS

Coverage will not be provided for members who are receiving concomitant treatment with nonselective monoamine oxidase (MAO) inhibitors (e.g. phenelzine, tranylcypromine)

III. CRITERIA FOR INITIAL APPROVAL

Parkinson's disease

Authorization of 12 months may be granted for treatment of motor fluctuations in members with advanced Parkinson's disease when all of the following criteria are met:

- A. Member is levodopa responsive with clearly defined "on" periods; *and*
- B. The member has off periods greater than 3 hours per day despite optimization efforts; *and*
- C. The member must have had an inadequate response or intolerable adverse event with oral carbidopa-levodopa (IR or CR) and one of the following anti-Parkinson agents:
 1. Catechol-O-methyl transferase (COMT) inhibitor (e.g. entacapone)
 2. Monoamine oxidase B (MAO)-B inhibitor (e.g. oral selegiline, Azilect)
 3. Dopamine agonists (e.g. pramipexole, ropinirole, Neupro)

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for Parkinson's disease who have demonstrated a positive clinical response to Duopa therapy.

V. REFERENCES

1. Duopa [package insert]. North Chicago, IL: AbbVie, Inc; September 2016.
2. C. Warren Olanow, Karl Keiburtz, Per Odin, et al. Double blind, double dummy, randomized study of continuous intrajejunal infusion of levodopa-carbidopa intestinal gel in advanced Parkinson's disease, *Lancet Neurol.* 2014 February; 13 (2): 141-149.

ENHANCED SPECIALTY GUIDELINE MANAGEMENT

DUPIXENT (dupilumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

- A. Dupixent is indicated for the treatment of patients aged 12 years and older with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. Dupixent can be used with or without topical corticosteroids.
- B. Dupixent is indicated as an add-on maintenance treatment in patients with moderate-to-severe asthma aged 12 years and older with an eosinophilic phenotype or with oral corticosteroid dependent asthma.
- C. Dupixent is indicated as an add-on maintenance treatment in adult patients with inadequately controlled chronic rhinosinusitis with nasal polyposis (CRSwNP).

Limitation of Use: Dupixent is not indicated for the relief of acute bronchospasm or status asthmaticus

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

- A. Atopic dermatitis (initial requests): Member's chart or medical record showing prerequisite therapies and affected area(s) and body surface area (see section IV.A.1).
- B. Asthma (initial requests): Member's chart or medical record showing pretreatment blood eosinophil count and prerequisite therapies. For oral glucocorticoid use history, the documentation must also include drug, dose, frequency and duration.
- C. Chronic rhinosinusitis with nasal polyposis (for initial requests): Member's chart or medical record showing nasal endoscopy or anterior rhinoscopy details (e.g., location, size).

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with one of the following:

- A. Atopic dermatitis: dermatologist or allergist/immunologist
- B. Asthma: allergist/immunologist or pulmonologist
- C. Chronic rhinosinusitis with nasal polyposis: allergist/immunologist or otolaryngologist

IV. CRITERIA FOR INITIAL APPROVAL

A. Moderate-to-severe atopic dermatitis

Authorization of 4 months may be granted for treatment of moderate-to-severe atopic dermatitis in members 12 years of age or older when all of the following criteria are met:

1. Affected body surface area is greater than or equal to 10% OR crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
2. Member has had an inadequate treatment response to topical tacrolimus (Protopic) and at least two medium or higher potency topical corticosteroids in the past 180 days, OR topical corticosteroids or topical tacrolimus are not advisable for the member.

B. Moderate-to-severe asthma

Authorization of 6 months may be granted for treatment of moderate-to-severe asthma in members 12 years of age or older when all of the following criteria are met:

1. Member meets one of the following criteria:
 - a. Member has inadequate asthma control (e.g. hospitalization or emergency medical care visit within the past year) despite current treatment with all of the following medications at optimized doses*:
 - i. High-dose inhaled corticosteroid
 - ii. Additional controller (long acting beta2-agonist, leukotriene modifier, or sustained-release theophylline)
 - iii. Oral glucocorticoids (at least 5 mg per day of prednisone/prednisolone or equivalent)

*Members should be receiving treatment with inhaled corticosteroid and additional controller for at least the previous 3 months, and oral glucocorticoids for most days during the previous 6 months (e.g. 50% of days, 3 steroid bursts in the previous 6 months).
 - b. Member has a baseline blood eosinophil count of at least 150 cells per microliter and asthma is inadequately controlled despite treatment for at least 3 months with both of the following at optimized doses:
 - i. Medium-to-high-dose inhaled corticosteroid
 - ii. Additional controller (long acting beta2-agonist, leukotriene modifier, or sustained-release theophylline)
2. Member will not use Dupixent as monotherapy
3. Member will not use Dupixent concomitantly with other biologics (e.g., Cinqair, Fasenna, Nucala or Xolair).

C. Chronic rhinosinusitis with nasal polyposis (CRSwNP)

Authorization of 6 months may be granted for treatment of CRSwNP in members 18 years of age or older when all of the following criteria are met:

1. Member has bilateral nasal polyposis and chronic symptoms of sinusitis despite intranasal corticosteroid treatment for at least 2 months unless contraindicated or not tolerated; and
2. The member has CRSwNP despite one of the following:
 - a. Prior sino-nasal surgery; or
 - b. Prior treatment with systemic corticosteroids within the last two years was ineffective, unless contraindicated or not tolerated; and
3. Member has a bilateral nasal endoscopy or anterior rhinoscopy showing polyps reaching below the lower border of the middle turbinate or beyond in each nostril; and
4. Member has nasal obstruction plus one additional symptom:
 - a. Rhinorrhea (anterior/posterior); or
 - b. Reduction or loss of smell; and

5. Member will be using a daily intranasal corticosteroid while being treated with Dupixent, unless contraindicated or not tolerated.

V. CONTINUATION OF THERAPY

A. Moderate-to-severe atopic dermatitis

Authorization of 6 months may be granted for members 12 years of age or older who achieve or maintain positive clinical response with Dupixent therapy for moderate-to-severe atopic dermatitis as evidenced by low disease activity (i.e., clear or almost clear skin) or improvement in signs and symptoms of atopic dermatitis (e.g., redness, itching, oozing/crusting).

B. Moderate-to-severe asthma

Authorization of 12 months may be granted for members 12 years of age or older when all of the following criteria are met:

1. Member has achieved and maintained positive clinical response with Dupixent therapy for asthma as evidenced by at least one of the following:
 - a. A reduction in the frequency and/or severity of symptoms and exacerbations
 - b. A reduction in the daily maintenance oral corticosteroid dose
2. Member will not use Dupixent as monotherapy
3. Member will not use Dupixent concomitantly with other biologics (e.g., Cinqair, Fasenra, Nucala or Xolair)

C. Chronic rhinosinusitis with nasal polyposis (CRSwNP)

Authorization of 12 months may be granted for members 18 years of age or older who achieve or maintain positive clinical response to Dupixent therapy as evidenced by improvement in signs and symptoms of CRSwNP (e.g., improvement in nasal congestion, nasal polyp size, loss of smell, anterior or posterior rhinorrhea, sinonasal inflammation, hyposmia and/or facial pressure or pain or reduction in corticosteroid use).

VI. OTHER

Note: If the member is a current smoker, they should be counseled on the harmful effects of smoking on pulmonary conditions and available smoking cessation options.

VII. APPENDIX: Relative potency of select topical corticosteroid products⁵

Potency	Drug	Dosage form	Strength
I. Very high potency	Augmented betamethasone dipropionate	Ointment, Gel	0.05%
	Clobetasol propionate	Cream, Ointment	0.05%
	Diflorasone diacetate	Ointment	0.05%
	Halobetasol propionate	Cream, Ointment	0.05%

Potency	Drug	Dosage form	Strength
II. High potency	Amcinonide	Cream, Lotion, Ointment	0.1%
	Augmented betamethasone dipropionate	Cream, Lotion	0.05%
	Betamethasone dipropionate	Cream, Ointment	0.05%
	Betamethasone valerate	Ointment	0.1%
	Desoximetasone	Cream, Ointment	0.25%
		Gel	0.05%
	Diflorasone diacetate	Cream, Ointment (emollient base)	0.05%
	Fluocinonide	Cream, Ointment, Gel	0.05%
	Halcinonide	Cream, Ointment	0.1%
III. Medium potency	Triamcinolone acetonide	Cream, Ointment	0.5%
	Betamethasone dipropionate	Lotion	0.05%
	Betamethasone valerate	Cream	0.1%
	Clocortolone pivalate	Cream	0.1%
	Desoximetasone	Cream	0.05%
	Fluocinolone acetonide	Cream, Ointment	0.025%
	Flurandrenolide	Cream, Ointment, Lotion	0.05%
		Tape	4 mcg/cm ²
	Fluticasone propionate	Cream	0.05%
		Ointment	0.005%
	Hydrocortisone butyrate	Ointment, Solution	0.1%
	Hydrocortisone valerate	Cream, Ointment	0.2%
	Mometasone furoate	Cream, Ointment, Lotion	0.1%
	Prednicarbate	Cream, Ointment	0.1%
	Triamcinolone acetonide	Cream, Ointment, Lotion	0.025%, 0.1%
IV. Low potency	Alclometasone dipropionate	Cream, Ointment	0.05%
	Desonide	Cream	0.05%
	Fluocinolone acetonide	Cream, Solution	0.01%
	Hydrocortisone	Lotion	0.25%
		Cream, Ointment, Lotion, Aerosol	0.5%
		Cream, Ointment, Lotion, Solution	1%
		Cream, Ointment, Lotion	2.5%
	Hydrocortisone acetate	Cream, Ointment	0.5%, 1%

VIII. REFERENCES

1. Dupixent [package insert]. Tarrytown, NY: Regeneron Pharmaceuticals, Inc.; June 2019.
2. Eichenfield LF, Tom WL, et. al. Guidelines of care for the management of atopic dermatitis: Section 2. Management and treatment of atopic dermatitis with topical therapies. *J Am Acad Dermatol*. 2014;71:116-32.
3. Simpson E.L., et al. Two phase 3 trials of dupilumab versus placebo in atopic dermatitis. *N Engl J Med*. 2016 [Epub ahead of print].
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9. ClinicalTrials.gov. National Library of Medicine (US). Identifier NCT02898454, A Controlled Clinical Study of Dupilumab in Patients with Nasal Polyps (SINUS-52) 2016 Sep 13. Available from: <https://clinicaltrials.gov/ct2/show/NCT02898454>.

SPECIALTY GUIDELINE MANAGEMENT

DYSPORT (abobotulinumtoxin A)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Treatment of cervical dystonia in adults
2. Treatment of spasticity (upper and/or lower limb) in adults
3. Treatment of upper limb spasticity in pediatric patients 2 years of age and older, excluding spasticity caused by cerebral palsy
4. Treatment of lower limb spasticity in pediatric patients 2 years of age and older

B. Compendial Uses

1. Blepharospasm
2. Hemifacial spasm
3. Chronic anal fissures
4. Excessive salivation
5. Primary axillary hyperhidrosis

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

Coverage will not be provided for cosmetic use.

III. CRITERIA FOR INITIAL APPROVAL

A. **Cervical dystonia**

Authorization of 12 months may be granted for treatment of cervical dystonia (e.g., torticollis) when there is sustained head torsion and/or tilt with limited range of motion.

B. **Upper limb spasticity**

Authorization of 12 months may be granted for treatment of upper limb spasticity.

C. **Lower limb spasticity**

Authorization of 12 months may be granted for treatment of lower limb spasticity.

D. **Blepharospasm**

Authorization of 12 months may be granted for treatment of blepharospasm.

E. Hemifacial spasm

Authorization of 12 months may be granted for treatment of hemifacial spasm.

F. Chronic anal fissures

Authorization of 12 months may be granted for treatment of chronic anal fissures when the member has not responded to first-line therapy such as topical calcium channel blockers or topical nitrates.

G. Excessive salivation

Authorization of 12 months may be granted for treatment of excessive salivation (chronic sialorrhea) when the member has been refractory to pharmacotherapy (e.g., anticholinergics).

H. Primary axillary hyperhidrosis

Authorization of 12 months may be granted for treatment of primary axillary hyperhidrosis when all of the following criteria are met:

1. Member is unresponsive or unable to tolerate pharmacotherapy prescribed for excessive sweating (e.g., anticholinergics, beta-blockers, or benzodiazepines); and
2. Significant disruption of professional and/or social life has occurred because of excessive sweating; and
3. Topical aluminum chloride or other extra-strength antiperspirants are ineffective or result in a severe rash.

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. REFERENCES

1. Dysport [package insert]. Wrexham, UK: Ipsen Biopharm, Ltd.; September 2019.
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7. Lakraj AA, Moghimi N, Jabbari B. Sialorrhea: Anatomy, Pathophysiology and Treatment with Emphasis on the Role of Botulinum Toxins. *Toxins* 2013, 5, 1010-1031
8. Glader L, Delsing C, Hughes A et al. Sialorrhea in cerebral palsy. American Academy for Cerebral Palsy and Developmental Medicine Care Pathways. <https://www.aacpdm.org/publications/care-pathways/sialorrhea>. Accessed August 23, 2019.
9. Garuti G, Rao F, Ribuffo V et al. Sialorrhea in patients with ALS: current treatment options. *Degener Neurol Neuromuscul Dis*. 2019; 9: 19–26.

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	ALPROSTADILS
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BRAND NAME* (generic)	
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	CAVERJECT (alprostadil)
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	EDEX (alprostadil)
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	MUSE (alprostadil)
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Status: CVS Caremark Criteria

Type: Initial Prior Authorization with Quantity Limit

Ref # 1044-C

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Caverject

Caverject is indicated for the treatment of erectile dysfunction.

Caverject is also indicated as an adjunct to other diagnostic tests in the diagnosis of erectile dysfunction.

Edex

Edex is indicated for the treatment of erectile dysfunction due to neurogenic, vasculogenic, psychogenic, or mixed etiology.

MUSE

MUSE is indicated for the treatment of erectile dysfunction. Studies that established benefit demonstrated improvements in success rates for sexual intercourse compared with similarly administered placebo.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for erectile dysfunction in a patient that is 18 years of age or older

Quantity Limits apply.

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Caverject, Edex, and MUSE are indicated for the treatment of erectile dysfunction. These drugs are not indicated for use in newborns or children.¹⁻⁶

According to the American Urological Association (AUA) Guideline on the Management of Erectile Dysfunction, patients presenting with symptoms of erectile dysfunction (ED) should undergo a thorough medical, sexual, and psychosocial history; a physical examination; and selective laboratory testing. Shared decision-making is the cornerstone of patient-centered care for ED. Determining an appropriate treatment requires that the patient, his clinician, and ideally the partner navigate all of these issues in order to arrive at a treatment choice that is aligned with the patient and the partner's priorities and values. Patients should be informed of all treatment options that are not medically contraindicated and

supported in the shared decision-making process to determine the appropriate treatment.⁷ The dose of alprostadil should be individualized for each patient by careful titration under supervision by the physician.¹⁻⁶

Since Caverject, Edex, and MUSE are used as needed, the quantity limit for these drugs are based upon coital frequency from studies of data analysis. According to the Predictors of Adult Sexual Activity in The United States survey, men and women between the ages of 25 and 45 have sex a mean 5.7 and 6.4 times per month, respectively.⁸ A Study of Sexuality and Health among Older Adults in the United States found that the prevalence of sexual activity declined with age and that 54% of sexually active persons age 75-85 reported having sex at least two to three times per month.⁹ Therefore, the quantity for approval for alprostadil will be 6 units per month.

PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases, the filling limit and day supply may be less than what is indicated.

REFERENCES

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4. MUSE [package insert]. Somerset, New Jersey: Meda Pharmaceuticals; April 2018.
5. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. April 2019.
6. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed April 2019.
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8. Eisenberg M, Shindel A, Smith J, et al. Socioeconomic, Anthropomorphic, and Demographic Predictors of Adult Sexual Activity in The United States: Data from the National Survey of Family Growth. *J Sex Med.* 2010;7:50-58.
9. Lindau S, Schumm L, Laumann E, et al. A Study of Sexuality and Health among Older Adults in the United States *N Engl J Med.* 2007 August 23;357(8):762-774.

Written by: UM Development (GP)
Date Written: 5/1998
Last Revised: 6/1998; (LS) 05/2000; (JG) 04/2002, 12/2003, 01/2005; (CT) 01/2006, 09/2006, 01/2007; (NB) 07/2007, 07/2008, 08/2009; (TM) 08/2010, 07/2011, 10/2011, 11/2011, 04/2012, 07/2012; (NB/PL) 10/2012 (extended duration); (TM) 04/2013; (JK) 10/2013 (separate form for alprostadil); (CF) 04/2014, 04/2015; (JH) 04/2016 (no clinical changes), 09/2016 (updated for TGC); (KM) 04/2017 (removed contraindication question, added partial approval question); (KC) 04/2018 (no clinical changes); (CF/KC) 04/2019 (no clinical changes)
Reviewed: Medical Affairs: 05/1998, 5/2000, 04/2002, 12/2003; (MM) 01/2005, 01/2006; (WF) 01/2007, 07/2007, 07/2008, 08/2009; (KP) 08/2010, 07/2011, 10/2011, 11/2011; (LB) 05/2012, 07/2012; (KP) 10/2012; (DC) 04/2013; (SES) 04/2014; (ADA) 04/2015; (ME) 09/2016; (JG) 04/2017
External Review: 05/2002, 02/2004, 04/2006, 12/2006, 06/2007, 02/2009, 12/2009, 12/2010, 12/2011, 06/2012, 10/2012, 08/2013, 08/2014, 08/2015, 08/2016, 08/2017, 08/2018, 08/2019

CRITERIA FOR APPROVAL

- | | | | |
|---|--|-----|----|
| 1 | Is the requested drug being prescribed for erectile dysfunction in a patient that is 18 years of age or older? | Yes | No |
| 2 | Does the patient require MORE than the plan allowance of 6 units per month of the requested drug? | Yes | No |
| [RPh Note: If yes, then deny and enter a partial approval for 6 units per month of the requested drug.] | | | |

Guidelines for Approval	
Duration of Approval	36 Months
Quantity for Approval	6 units per 25 days* 18 units per 75 days*
Set 1	
Yes to question(s)	No to question(s)
1	2

* The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.

Mapping Instructions			
	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions:</p> <ul style="list-style-type: none"> - You are 18 years of age or older - You have erectile dysfunction <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No approvable diagnosis.]</p>
2.	Deny	Approve for 36 months (6 units/25 days* or 18 units/75 days*)	<p>You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 6 units per month of the requested drug and strength. You have been approved for the maximum quantity that your plan covers for a duration of 36 months. Your request for additional quantities of the requested drug and strength has been denied.</p> <p>[Short Description: Over max quantity.]</p>

* The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.

QUANTITY LIMIT CRITERIA

DRUG CLASS	ERECTILE DYSFUNCTION - BPH DRUGS
------------	----------------------------------

BRAND NAME*

(generic)

ALPROSTADILS:

CAVERJECT
(alprostadil)

EDEX
(alprostadil)

MUSE
(alprostadil)

**PHOSPHODIESTERASE
TYPE 5 (PDE-5) INHIBITORS:**

CIALIS
(tadalafil)

LEVITRA
(vardenafil hydrochloride)

STAXYN
(vardenafil hydrochloride orally disintegrating)

STENDRA
(avanafil)

VIAGRA
(sildenafil)

Status: CVS Caremark Criteria

Type: Quantity Limit

Ref # 84-H

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATION

Alprostadils

Caverject

Caverject is indicated for the treatment of erectile dysfunction.

Caverject is also indicated as an adjunct to other diagnostic tests in the diagnosis of erectile dysfunction.

Edex

Edex is indicated for the treatment of erectile dysfunction due to neurogenic, vasculogenic, psychogenic, or mixed etiology.

MUSE

MUSE is indicated for the treatment of erectile dysfunction. Studies that established benefit demonstrated improvements in success rates for sexual intercourse compared with similarly administered placebo.

Phosphodiesterase type 5 (PDE-5) Inhibitors

Cialis

Erectile Dysfunction

Cialis is indicated for the treatment of erectile dysfunction (ED).

Benign Prostatic Hyperplasia

Cialis is indicated for the treatment of the signs and symptoms of benign prostatic hyperplasia (BPH).

Erectile Dysfunction and Benign Prostatic Hyperplasia

Cialis is indicated for the treatment of ED and the signs and symptoms of BPH (ED/BPH).

Limitation of Use

If Cialis is used with finasteride to initiate BPH treatment, such use is recommended for up to 26 weeks because the incremental benefit of Cialis decreases from 4 weeks until 26 weeks, and the incremental benefit of Cialis beyond 26 weeks is unknown.

Levitra

Levitra is indicated for the treatment of erectile dysfunction.

Staxyn

Staxyn is indicated for the treatment of erectile dysfunction.

Stendra

Stendra is a phosphodiesterase 5 (PDE5) inhibitor indicated for the treatment of erectile dysfunction.

Viagra

Viagra is indicated for the treatment of erectile dysfunction.

RATIONALE

Alprostadil and Phosphodiesterase type 5 (PDE-5) Inhibitors [Caverject (alprostadil), Edex (alprostadil), MUSE (alprostadil), Cialis (tadalafil), Levitra (vardenafil hydrochloride), Staxyn (vardenafil hydrochloride orally disintegrating), Stendra (avanafil), Viagra (sildenafil)] are indicated for the treatment of erectile dysfunction (ED). Cialis is also indicated for the treatment of the signs and symptoms of benign prostatic hyperplasia (BPH), and for the treatment of ED and the signs and symptoms of BPH (ED/BPH).¹⁻¹¹

Since erectile dysfunction drugs are used as needed (excluding Cialis 2.5 mg and 5 mg), the quantity limits are based upon coital frequency from studies of data analysis. According to the Predictors of Adult Sexual Activity in The United States survey, men and women between the ages of 25 and 45 have sex a mean 5.7 and 6.4 times per month, respectively.¹³ A Study of Sexuality and Health among Older Adults in the United States found that the prevalence of sexual activity declined with age and that 54% of sexually active persons age 75-85 reported having sex at least two to

three times per month.¹⁴ Therefore, the quantity limit for erectile dysfunction drugs (excluding Cialis 2.5 mg and 5 mg) will be set at 6 units per month.

The recommended starting dose of Cialis for daily use for ED is 2.5 mg taken at approximately the same time every day, without regard to timing of sexual activity. The Cialis dose for once daily use may be increased to 5 mg based on individual efficacy and tolerability.^{3,10,11} Therefore, the initial quantity limit for Cialis 2.5 mg and 5 mg will be 30 tablets per month for ED for once daily use.

If the patient is requesting more than the initial quantity limit, then the claim will reject with a message indicating that quantity limits are exceeded.

Please note manufacturer package sizes may vary. It is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases, the filling limit and day supply may be less than what is indicated in the Limit Criteria chart.

REFERENCES

1. Caverject [package insert]. New York, NY: Pharmacia and Upjohn Company; March 2019.
2. Caverject Impulse [package insert]. New York, NY: Pharmacia and Upjohn Company; February 2017.
3. Cialis [package insert]. Indianapolis, IN: Eli Lilly and Company; February 2018.
4. Edex [package insert]. Malvern, PA: Endo Pharmaceuticals Inc; August 2018.
5. Levitra [package insert]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc; November 2018.
6. MUSE [package insert]. Somerset, New Jersey: Meda Pharmaceuticals; April 2018.
7. Staxyn [package insert]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc; August 2017.
8. Stendra [package insert]. Cranford, NJ: Mist Pharmaceuticals, LLC; August 2018.
9. Viagra [package insert]. New York, NY: Pfizer Labs; December 2017.
10. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. April 2019.
11. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed April 2019.
12. American Urological Association Guideline on the Management of Erectile Dysfunction. 2018. [http://www.auanet.org/guidelines/male-sexual-dysfunction-erectile-dysfunction-\(2018\)](http://www.auanet.org/guidelines/male-sexual-dysfunction-erectile-dysfunction-(2018)). Accessed April 2019.
13. Eisenberg M, Shindel A, Smith J, et al. Socioeconomic, Anthropomorphic, and Demographic Predictors of Adult Sexual Activity in The United States: Data from the National Survey of Family Growth. *J Sex Med.* 2010;7:50-58.
14. Lindau S, Schumm L, Laumann E, et al. A Study of Sexuality and Health among Older Adults in the United States *N Engl J Med.* 2007 August 23;357(8):762–774.

Written by: UM Development (DP)
Date Written: 03/1998
Last Revised: (LS) 12/1998, 04/2000, 02/2001; (JG) 12/2002, 08/2003, 11/2003, 08/2004; (PJ) 10/2005; (CT) 01/2006, 09/2006, 01/2007; (NB) 07/2007; (MS) 07/2008; (NB) 08/2009; (TM) 08/2010, 07/2011, 10/2011, 04/2012, 04/2013; (CF) 04/2014, 04/2015; (JH) 04/2016 (no clinical changes); (KM) 04/2017 (no clinical changes); (KC) 04/2018 (no clinical changes); (CF/KC) 04/2019 (no clinical changes), 07/2019 (increased Cialis 5 mg QL to 30)
Reviewed: Medical Affairs: 12/1998, 04/2000, 01/2001, 12/2002, 08/2003, 11/2003, 08/2004, 10/2005; (MM) 01/2006, 09/2006; (WF) 01/2007, 07/2007, 07/200, 08/2009; (KP) 08/2010, 07/2011, 10/2011; (LB) 05/2012; (DC) 04/2013; (SES) 04/2014; (ADA) 04/2015; (CHART) 8/22/19
External Review: 02/2003, 10/2003, 12/2003, 10/2004, 04/2006, 12/2006, 02/2008, 02/2009, 12/2009, 12/2010, 12/2011, 06/2012, 08/2013, 08/2014, 08/2015, 08/2016, 08/2017, 08/2018, 08/2019

LIMIT CRITERIA

Limits should accumulate across all drugs and strengths up to highest quantity listed depending on the order the claims are processed.

PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

Medication	1 Month Limit*	3 Month Limit*
Cialis (tadalafil) 2.5 mg, 5 mg	30 tablets / 25 days	90 tablets / 75 days
Cialis (tadalafil) 10 mg, 20 mg	6 tablets / 25 days	18 tablets / 75 days
Levitra (vardenafil HCl)	6 tablets / 25 days	18 tablets / 75 days
Staxyn (vardenafil HCl orally disintegrating)	6 tablets / 25 days	18 tablets / 75 days
Stendra (avanafil)	6 tablets / 25 days	18 tablets / 75 days
Viagra (sildenafil)	6 tablets / 25 days	18 tablets / 75 days
Caverject (alprostadil)	6 units / 25 days	18 units / 75 days
Edex (alprostadil)	6 units / 25 days	18 units / 75 days
MUSE (alprostadil)	6 units / 25 days	18 units / 75 days

** The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	PHOSPHODIESTERASE TYPE 5 (PDE-5) INHIBITORS
BRAND NAME* (generic)	<p>CIALIS (tadalafil)</p> <p>LEVITRA (vardenafil hydrochloride)</p> <p>STAXYN (vardenafil hydrochloride orally disintegrating)</p> <p>STENDRA (avanafil)</p> <p>VIAGRA (sildenafil)</p>
<p>Status: CVS Caremark Criteria Type: Initial Prior Authorization with Quantity Limit</p>	
Ref # 83-C	

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Cialis

Erectile Dysfunction

Cialis is indicated for the treatment of erectile dysfunction (ED).

Benign Prostatic Hyperplasia

Cialis is indicated for the treatment of the signs and symptoms of benign prostatic hyperplasia (BPH).

Erectile Dysfunction and Benign Prostatic Hyperplasia

Cialis is indicated for the treatment of ED and the signs and symptoms of BPH (ED/BPH).

Limitation of Use

If Cialis is used with finasteride to initiate BPH treatment, such use is recommended for up to 26 weeks because the incremental benefit of Cialis decreases from 4 weeks until 26 weeks, and the incremental benefit of Cialis beyond 26 weeks is unknown.

Levitra

Levitra is indicated for the treatment of erectile dysfunction.

Staxyn

Staxyn is indicated for the treatment of erectile dysfunction.

Stendra

Stendra is a phosphodiesterase 5 (PDE5) inhibitor indicated for the treatment of erectile dysfunction.

Viagra

Viagra is indicated for the treatment of erectile dysfunction.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- Cialis (tadalafil) 2.5 mg or 5 mg is being prescribed for daily use for symptomatic benign prostatic hyperplasia (BPH) with or without erectile dysfunction (ED) in a patient that is 18 years of age or older
[Note: Examples of signs and symptoms of BPH are incomplete emptying, weak stream, straining, urinary frequency, intermittency, urgency, or acute urinary retention.]

OR

- The requested drug is being prescribed for erectile dysfunction in a patient that is 18 years of age or older

Quantity Limits apply.

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Phosphodiesterase type 5 (PDE-5) Inhibitors [Cialis (tadalafil), Levitra (vardenafil hydrochloride), Staxyn (vardenafil hydrochloride orally disintegrating), Stendra (avanafil), and Viagra (sildenafil)] are indicated for the treatment of erectile dysfunction (ED). Cialis is also indicated for the treatment of the signs and symptoms of benign prostatic hyperplasia (BPH), and for the treatment of ED and the signs and symptoms of BPH (ED/BPH). These drugs are not indicated for use in children.¹⁻⁷ Since BPH is typically a condition that occurs in older patients, the Criteria for Approval does not specify this information related to the BPH diagnosis. The age must still be specified for a diagnosis of ED.

ED only

According to the American Urological Association (AUA) Guideline on the Management of Erectile Dysfunction, patients presenting with symptoms of erectile dysfunction (ED) should undergo a thorough medical, sexual, and psychosocial history; a physical examination; and selective laboratory testing. Shared decision-making is the cornerstone of patient-centered care for ED. Determining an appropriate treatment requires that the patient, his clinician, and ideally the partner navigate all of these issues in order to arrive at a treatment choice that is aligned with the patient and the partner's priorities and values. Patients should be informed of all treatment options that are not medically contraindicated and supported in the shared decision-making process to determine the appropriate treatment.⁸

Since erectile dysfunction drugs are used as needed (excluding Cialis 2.5 mg and 5 mg), the quantity limits for these drugs are based upon coital frequency from studies of data analysis. According to the Predictors of Adult Sexual Activity in The United States survey, men and women between the ages of 25 and 45 have sex a mean 5.7 and 6.4 times per month, respectively.⁹ A Study of Sexuality and Health among Older Adults in the United States found that the prevalence of sexual activity declined with age and that 54% of sexually active persons aged 75-85 reported having sex at least two to three times per month.¹⁰ Therefore, the quantity for approval for erectile dysfunction drugs (excluding Cialis 2.5 mg and 5 mg) will be 6 units per month.

The recommended starting dose of Cialis for daily use for ED is 2.5 mg taken at approximately the same time every day, without regard to timing of sexual activity. The Cialis dose for once daily use may be increased to 5 mg based on individual efficacy and tolerability.^{1,6,7} Therefore, the quantity for approval for Cialis 2.5 mg and 5 mg will be 30 tablets per month for ED for once daily use.

BPH and ED/BPH

According to the American Urological Association (AUA) BPH guidelines, lower urinary tract symptoms (LUTS) secondary to BPH may include incomplete emptying, weak stream, straining, urinary frequency, intermittency, or urgency. The presence of moderate-to-severe LUTS is also associated with the development of acute urinary retention (AUR) as a symptom of BPH progression. If drug therapy is considered, decisions will be influenced by coexisting overactive bladder symptoms and prostate size or serum PSA levels. Also, the overall benefit and risks of therapy must be considered. Per AUA BPH guidelines, the primary goal of treatment is to alleviate bothersome LUTS that result from prostatic enlargement and on the alteration of disease progression and prevention of complications that can be associated with BPH/LUTS. If treatment is successful, a yearly follow-up should include a repeat of the initial evaluation to detect any changes that have occurred, if symptoms have progressed, or if a complication has developed.¹¹

The recommended dose of Cialis for once daily use for BPH and ED/BPH is 5 mg, taken at approximately the same time every day, without regard to timing of sexual activity. For BPH and ED/BPH a starting dose of 2.5 mg is recommended for creatinine clearance 30 to 50 mL/min.¹ The quantity for approval for Cialis (tadalafil) 2.5 mg and 5 mg will be 30 tablets per month for once daily use for BPH and ED/BPH.

PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

REFERENCES

1. Cialis [package insert]. Indianapolis, IN: Eli Lilly and Company; February 2018.
2. Levitra [package insert]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc; November 2018.
3. Staxyn [package insert]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc; August 2017.
4. Stendra [package insert]. Cranford, NJ: Mist Pharmaceuticals, LLC; August 2018.
5. Viagra [package insert]. New York, NY: Pfizer Labs; December 2017.
6. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. April 2019.
7. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed April 2019.
8. American Urological Association Guideline on the Management of Erectile Dysfunction. 2018. [http://www.auanet.org/guidelines/male-sexual-dysfunction-erectile-dysfunction-\(2018\)](http://www.auanet.org/guidelines/male-sexual-dysfunction-erectile-dysfunction-(2018)). Accessed April 2019.
9. Eisenberg M, Shindel A, Smith J, et al. Socioeconomic, Anthropomorphic, and Demographic Predictors of Adult Sexual Activity in The United States: Data from the National Survey of Family Growth. *J Sex Med.* 2010;7:50-58.
10. Lindau S, Schumm L, Laumann E, et al. A Study of Sexuality and Health among Older Adults in the United States *N Engl J Med.* 2007 August 23;357(8):762-774.
11. American Urological Association Guideline Management of Benign Prostatic Hyperplasia (BPH). 2010. <https://www.auanet.org/Documents/education/clinical-guidance/Benign-Prostatic-Hyperplasia.pdf>. Accessed April 2019.

Written by: UM Development (GP)
 Date Written: 5/1998
 Last Revised: 6/1998; (LS) 05/2000; (JG) 04/2002, 12/2003, 01/2005; (CT) 01/2006, 09/2006, 01/2007; (NB) 07/2007, 07/2008, 08/2009; (TM) 08/2010, 07/2011, 10/2011, 11/2011, 04/2012, 07/2012; (NB/PL) 10/2012 (extended duration); (TM) 04/2013; (JK) 10/2013 (separate form for PDE-5 inhibitors); (CF) 04/2014, 09/2014 (changed Cialis 5 mg qty), 04/2015; (JH) 04/2016, 09/2016 (updated for TGC); (KM) 04/2017 (removed contraindication question, added limit questions); (KC) 04/2018 (no clinical changes); (CF/KC) 04/2019 (no clinical changes), 07/2019 (increased Cialis 5 mg QL to 30 for ED), 10/2019 (split out Cialis 2.5 mg and 5 mg question per Ops request)
 Reviewed: Medical Affairs: 05/1998, 5/2000, 04/2002, 12/2003; (MM) 01/2005, 01/2006; (WF) 01/2007, 07/2007, 07/2008, 08/2009; (KP) 08/2010, 07/2011, 10/2011, 11/2011; (LB) 05/2012, 07/2012; (KP) 10/2012; (DC) 04/2013; (SES) 04/2014, 09/2014; (ADA) 04/2015; (TP) 04/2016; (ME) 09/2016; (JG) 04/2017; (CHART) 8/22/19
 External Review: 05/2002, 02/2004, 04/2006, 12/2006, 06/2007, 02/2009, 12/2009, 12/2010, 12/2011, 06/2012, 10/2012, 08/2013, 08/2014, 09/2014, 10/2014, 08/2015, 08/2016, 08/2017, 08/2018, 08/2019

CRITERIA FOR APPROVAL

1	Is this request for Cialis (tadalafil) 2.5 mg or 5 mg? [If no, then skip to question 4.]	Yes	No
2	Is Cialis (tadalafil) 2.5 mg or 5 mg being prescribed for daily use for symptomatic benign prostatic hyperplasia (BPH) with or without erectile dysfunction (ED) in a patient that is 18 years of age or older? [Note: Examples of signs and symptoms of BPH are incomplete emptying, weak stream, straining, urinary frequency, intermittency, urgency, or acute urinary retention.] [If no, then skip to question 4.]	Yes	No

3	Does the patient require MORE than the plan allowance of 1 tablet per day? [No further questions.]	Yes	No
[RPh Note: If yes, then deny and enter a partial approval for 30 tablets per month of Cialis 2.5 mg or Cialis 5 mg.]			
4	Is the requested drug being prescribed for erectile dysfunction in a patient that is 18 years of age or older?	Yes	No
5	Does the patient require MORE than the plan allowance of 30 tablets per month of Cialis 2.5 mg, 5 mg OR MORE than the plan allowance of 6 tablets per month of Cialis 10 mg, 20 mg, Levitra, Staxyn, Stendra, or Viagra?	Yes	No
[RPh Note: If yes, then deny and enter a partial approval per Limit Criteria for Erectile Dysfunction Chart.]			

Guidelines for Approval			
Duration of Approval		36 months	
Quantity for Approval	Cialis 2.5 mg OR Cialis 5 mg 30 tablets per 25 days* 90 tablets per 75 days*	Quantity for Approval	*See Limit Criteria for Erectile Dysfunction chart below
Set 1		Set 2	
Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)
1	3	4	1
2			5

*The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.

Mapping Instructions			
	Yes	No	
1.	Go to 2	Go to 4	
2.	Go to 3	Go to 4	
3.	Deny	Approve for 36 months Cialis 2.5 mg OR Cialis 5 mg 30 tablets per 25 days* 90 tablets per 75 days*	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 30 tablets per month of the requested drug and strength. You have been approved for the maximum quantity that your plan covers for a duration of 36 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity.]
4.	Go to 5	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet any of these conditions: - You are 18 years of age or older and you have erectile dysfunction - You are using Cialis 2.5 mg or Cialis 5 mg, you are 18 years of age or older, and you have benign prostatic hyperplasia (BPH) that is causing symptoms Your request has been denied based on the information we have. [Short Description: No approvable diagnosis.]

5.	Deny RPh Note: For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage	Approve for 36 months *See Limit Criteria for Erectile Dysfunction chart below	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 30 tablets per month of Cialis 2.5 mg, 5 mg - 6 tablets per month of Cialis 10 mg, or 20 mg, Levitra, Staxyn, Stendra, or Viagra You have been approved for the maximum quantity that your plan covers for a duration of 36 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity.]
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*The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.

***LIMIT CRITERIA FOR ERECTILE DYSFUNCTION**

PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

Medication	1 Month Limit*	3 Month Limit*
Cialis (tadalafil) 2.5 mg, 5 mg	30 tablets / 25 days	90 tablets / 75 days
Cialis (tadalafil) 10 mg, 20 mg	6 tablets / 25 days	18 tablets / 75 days
Levitra (vardenafil HCl)	6 tablets / 25 days	18 tablets / 75 days
Staxyn (vardenafil HCl orally disintegrating)	6 tablets / 25 days	18 tablets / 75 days
Stendra (avanafil)	6 tablets / 25 days	18 tablets / 75 days
Viagra (sildenafil)	6 tablets / 25 days	18 tablets / 75 days

* The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.

Reference number
1872-A

SPECIALTY GUIDELINE MANAGEMENT

EGRIFTA (tesamorelin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Egrifta is indicated for the reduction of excess abdominal fat in human immunodeficiency virus (HIV)-infected patients with lipodystrophy.

Limitations of Use:

- A. Long-term cardiovascular benefit and safety of Egrifta have not been studied.
- B. Egrifta is not indicated for weight loss management (weight neutral effect).
- C. There are no data to support improved compliance with anti-retroviral therapies in HIV-positive patients taking Egrifta.

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

Coverage will not be provided for weight loss.

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with an infectious disease specialist.

IV. CRITERIA FOR INITIAL APPROVAL

Reduction of excess abdominal fat in human immunodeficiency virus (HIV)-infected patients with lipodystrophy

Authorization of 6 months may be granted to members who meet all of the following criteria:

- A. The member has HIV infection and lipodystrophy
- B. The member is currently receiving anti-retroviral therapy
- C. Egrifta is used to reduce excess abdominal fat

Reference number
1872-A

V. CONTINUATION OF THERAPY

Reduction of excess abdominal fat in human immunodeficiency virus (HIV)-infected patients with lipodystrophy

Authorization of 6 months may be granted to members who meet ALL the following criteria:

- A. The member has HIV infection and lipodystrophy
- B. The member is currently receiving anti-retroviral therapy
- C. The member has demonstrated a clear clinical improvement from baseline that is supported by waist circumference measurement or CT scan

VI. REFERENCES

1. Egrifta [package insert]. Montreal, Québec: Theratechnologies, Inc.; July 2018.
2. Brown TT. Approach to the human immunodeficiency virus-infected patient with lipodystrophy. *J Clin Endocrinol Metab.* 2008;93(8):2937-2945.

Reference number
2052-A

SPECIALTY GUIDELINE MANAGEMENT

ELAPRASE (idursulfase)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Elaprase is indicated for patients with Hunter syndrome (Mucopolysaccharidosis II, MPS II). Elaprase has been shown to improve walking capacity in patients 5 years and older. In patients 16 months to 5 years of age, no data are available to demonstrate improvement in disease-related symptoms or long term clinical outcome; however, treatment with Elaprase has reduced spleen volume similarly to that of adults and children 5 years of age and older. The safety and efficacy of Elaprase have not been established in pediatric patients less than 16 months of age.

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: iduronate 2-sulfatase enzyme assay or genetic testing results supporting diagnosis.

III. CRITERIA FOR INITIAL APPROVAL

Mucopolysaccharidosis II (MPS II)

Authorization of 12 months may be granted for treatment of MPS II when the diagnosis of MPS II was confirmed by enzyme assay demonstrating a deficiency of iduronate 2-sulfatase enzyme activity or by genetic testing.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for Mucopolysaccharidosis II (MPS II) who are responding to therapy (e.g., improvement, stabilization, or slowing of disease progression for 6-minute walk test [6-MWT], percent predicted forced vital capacity [%-predicted FVC], spleen volume, or liver volume).

V. REFERENCES

1. Elaprase [package insert]. Lexington, MA: Shire Human Genetic Therapies, Inc.; November 2018.

SPECIALTY GUIDELINE MANAGEMENT

ELELYSO (taliglucerase alfa)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Elelyso is indicated for the treatment of patients with a confirmed diagnosis of type 1 Gaucher disease.

B. Compendial Uses

Gaucher disease type 3

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: beta-glucocerebrosidase enzyme assay or genetic testing results supporting diagnosis

III. CRITERIA FOR INITIAL APPROVAL

Gaucher disease type 1

Authorization of 12 months may be granted for treatment of Gaucher disease type 1 when the diagnosis of Gaucher disease was confirmed by enzyme assay demonstrating a deficiency of beta-glucocerebrosidase (glucosidase) enzyme activity or by genetic testing.

Gaucher disease type 3

Authorization of 12 months may be granted for treatment of Gaucher disease type 3 when the diagnosis of Gaucher disease was confirmed by enzyme assay demonstrating a deficiency of beta-glucocerebrosidase (glucosidase) enzyme activity or by genetic testing.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for Gaucher disease type 1 or type 3 who are not experiencing an inadequate response or any intolerable adverse events from therapy.

V. REFERENCES

1. Elelyso [package insert]. New York, NY: Pfizer, Inc; December 2016.

Reference number
2053-A

2. Zimran A, Brill-Almon E, Chertkoff R, et al. Pivotal trial with plant cell-expressed recombinant glucocerebrosidase, taliglucerase alfa, a novel enzyme replacement therapy for Gaucher disease. *Blood*. 2011;118:5767-5773.
3. Pastores GM, Hughes DA. Gaucher Disease. [Updated June 21, 2018]. In: Pagon RA, Adam MP, Ardinger HH, et al, editors. GeneReviews® [Internet]. Seattle, WA: University of Washington, Seattle; 1993-2018.
4. Kaplan P, Baris H, De Meirleir L, et al. Revised recommendations for the management of Gaucher disease in children. *Eur J Pediatr*. 2013;172:447-458.
5. Vellodi A, Tylki-Szymanska A, Davies EH, et al. Management of neuronopathic Gaucher disease: revised recommendations. European Working Group on Gaucher Disease. *J Inherit Metab Dis*. 2009;32(5):660.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

ELIDEL
(pimecrolimus)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

Ref # 759-A
Ref # MDC-2 491-A

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Elidel is indicated as second-line therapy for the short-term and non-continuous chronic treatment of mild to moderate atopic dermatitis in non-immunocompromised adults and children 2 years of age and older, who have failed to respond adequately to other topical prescription treatments, or when those treatments are not advisable. Elidel is not indicated for use in children less than 2 years of age.

Compendial/Off label Uses

Psoriasis³ - on the face, genitals, or skin folds⁶
Atopic Dermatitis for patients under 2 years of age^{4, 5}
Vitiligo on the head or neck^{7, 8}

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for psoriasis on the face, genitals, or skin folds OR vitiligo on the head or neck
- OR**
- The requested drug is being prescribed for mild to moderate atopic dermatitis (eczema)
- AND**
- The requested drug will be used around the eyes, on the face, genitals, or skin folds
- OR**
- The patient has experienced an inadequate treatment response, intolerance, or contraindication to at least one first line therapy agent (e.g., medium or higher potency topical corticosteroid)
- OR**
- The patient is less than 2 years of age AND unable to use a first line therapy agent (e.g., medium or higher potency topical corticosteroid)

RATIONALE

These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Elidel (pimecrolimus) is indicated as second-line therapy for the short-term and non-continuous chronic treatment of mild to moderate atopic dermatitis in non-immunocompromised adults and children 2 years of age and older, who have failed to respond adequately to other topical prescription treatments, or when those treatments are not advisable.

According to the American Academy of Dermatology Association (AAD) atopic dermatitis (AD) guidelines, Topical Corticosteroids (TCS) are used in the management of AD and are the mainstay of anti-inflammatory therapy (see examples in Table 1). TCS are recommended for AD affected individuals who have failed to respond to good skin care

and regular use of emollients alone. Topical calcineurin inhibitors (TCI), such as Elidel, are considered second-line therapy. Situations in which TCI may be preferable to topical steroids include recalcitrance to steroids, use on sensitive areas (e.g., face, anogenital, skin folds), steroid-induced atrophy, and long-term uninterrupted topical steroid use. TCI have the benefit of not carrying risk for cutaneous atrophy, with little negative effect on collagen synthesis and skin thickness; therefore, can be used as steroid-sparing agents and long term studies (to 12 months) have shown that they reduce the need for TCS use.⁴

TABLE 1: EXAMPLES OF TOPICAL CORTICOSTEROIDS FOR TREATMENT OF ATOPIC DERMATITIS ^{2,3,4}

Medium Potency	betamethasone dipropionate lotion, spray 0.05%
	betamethasone valerate cream/lotion 0.1%/foam 0.12%
	clocortolone pivalate cream 0.1%
	desonide lotion, ointment 0.05%
	desoximetasone cream 0.05%
	fluocinolone acetonide cream/ointment/kit 0.025%
	flurandrenolide cream/ointment/lotion 0.05%
	fluticasone propionate cream/lotion 0.05%/ointment 0.005%
	hydrocortisone butyrate cream/lipocream/lotion/ointment/soln 0.1%
	hydrocortisone probutate cream 0.1%
	hydrocortisone valerate cream/ointment 0.2%
	mometasone furoate cream/lotion/solution 0.1%
	prednicarbate cream/ointment 0.1%
	triamcinolone acetonide cream/ointment/lotion/kit 0.1%
	triamcinolone acetonide cream/ointment/lotion 0.025%
	triamcinolone acetonide ointment 0.05%
High Potency	amcinonide cream/ointment/lotion 0.1%
	betamethasone dipropionate cream/ointment 0.05%
	betamethasone dipropionate augmented cream/lotion 0.05%
	betamethasone valerate ointment 0.1%
	desoximetasone cream/ointment/spray 0.25%/gel/ointment 0.05%
	diflorasone diacetate cream (emollient base) 0.05% diflorasone cream 0.05%
	halcinonide cream/ointment 0.1%
	fluocinonide cream/emulsified cream/ointment/gel/soln 0.05%
	mometasone furoate ointment 0.1%
	triamcinolone acetonide cream/ointment 0.5%
	triamcinolone acetonide aerosol soln 0.147 mg/g
Very High Potency	betamethasone dipropionate augmented ointment/gel 0.05%
	clobetasol propionate cream/ointment/foam/shampoo/gel/lotion/soln/spray 0.05%/cream 0.025%
	diflorasone diacetate ointment 0.05%
	flurandrenolide tape 4mcg/cm ²
	halobetasol propionate cream/ointment/lotion/kit 0.05%
	fluocinonide cream 0.1%

The AAD guidelines indicate that children have a proportionately greater body surface area to weight ratio, and as a result, have a higher degree of absorption for the same amount applied. But during significant acute flares, the use of mid- or higher-potency TCS for short courses may be appropriate to gain rapid control of symptoms, even in children. For patients less than 2 years of age with AD, off label use of 0.03% tacrolimus or 1% pimecrolimus can be recommended. Evidence from clinical trials supports the safe and effective use of topical tacrolimus 0.03% and pimecrolimus in children younger than 2 years, including in infants.⁴ In a 5-year open label study ('Petite'), 2418 infants with AD were randomized to pimecrolimus 1% with short term topical corticosteroids for flares or topical corticosteroids (low potency, e.g., hydrocortisone 1%; or medium potency, e.g., hydrocortisone butyrate 0.1%). Both pimecrolimus and topical corticosteroids had a rapid onset of action with greater than 50% of patients achieving treatment success by week 3. After 5 years, greater than 85% and 95% of patients in each group achieved overall and facial treatment success, respectively. The pimecrolimus group required substantially fewer steroid days than the topical corticosteroid group (7 v 178). The profile and frequency of adverse events was similar in the 2 groups; in both groups, there was no evidence for impairment of humoral or cell immunity. The study concluded that long-term management of mild to moderate AD in infants with pimecrolimus or TCS was safe without any effect on the immune system. Pimecrolimus was steroid-sparing. The data suggest pimecrolimus had similar efficacy to TCS and support the use of pimecrolimus as a first-line treatment

of mild to moderate AD in infants and children.⁵ However, Elidel is not indicated for the use in children less than 2 years of age and long term safety and effects on the developing immune system are unknown. Two phase 3 trials involving 436 infants age 3-23 months were conducted and overall a higher proportion of detectable blood levels was seen in the pediatric patient population as compared to the adult patient population following twice daily application of Elidel for 3 weeks.¹ Therefore, taking safety for the infant population into consideration, Elidel will be covered for mild to moderate AD for short-term use, up to 3 months.

According to the AAD psoriasis guidelines, TCS are the cornerstone of treatment for the majority of patients with psoriasis, particularly those with limited disease. Lower potency corticosteroids should generally be used for limited periods of time on the face, intertriginous areas, areas with thin skin, and in infants. In other areas and in adults, mid- or high-potency agents are generally recommended as initial therapy. Patients with thick, chronic plaques often require treatment with the highest potency corticosteroids. The compendia indicate use of TCI in psoriasis, however per AAD guidelines, even though TCI are generally not effective for plaque psoriasis, they may be used on thinner skin areas to treat facial and intertriginous psoriasis with no evidence of resultant skin atrophy as compared with the use of topical corticosteroids in these regions.^{3, 6}

Based on the Cochrane review on interventions for vitiligo, TCI seem to be reasonable alternative to TCS, particularly on anatomical sites where there may be a higher risk of adverse effects with TCS. Standardized methodologies for describing and classifying vitiligo and for assessing the effect of interventions need to be developed and used by trial investigators. The establishment of a Vitiligo European Task Force (VETF) is an important step in this direction and the work of this group should hopefully lead to studies measuring repigmentation in a more standardized way. However, many studies still use their own measures, so the work of the VETF group needs to be disseminated as widely as possible.^{7, 8} The guidelines developed by this taskforce recommend that TCI be considered in adults and children with vitiligo as an alternative to topical steroids due to better safety profile, and restricted to selected areas, in particular the head and neck region.⁸

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Written by: UM Development (KD)
Date Written: 04/2010
Revised: (MS) 02/2011, 03/2012 (new non-Medicare version), 03/2013, (CF) 03/2014, 03/2015, 01/2016 (updated question #4); (KM) 03/2016 (no clinical changes), 03/2017, 03/2018 (combined 759-A, 491-A); (RP) 03/2019 (no clinical changes)
Reviewed: Medical Affairs (KP) 04/2010, 02/2011, 03/2012, 03/20213; (LMS) 03/2014; (KRU) 03/2015; (DNC) 06/2015; (GAD) 03/2017; (AN) 06/2018
External Review: 07/2010; 08/2011; 06/2012, 06/2013, 04/2014, 06/2014, 06/2015, 06/2016, 06/2017, 06/2018, 06/2019

CRITERIA FOR APPROVAL

- | | | | |
|---|--|-----|----|
| 1 | Is the requested drug being prescribed for mild to moderate atopic dermatitis (eczema)?
[If no, then skip to question 5.] | Yes | No |
| 2 | Will the requested drug be used around the eyes, on the face, genitals, or skin folds?
[If yes, then no further questions.] | Yes | No |
| 3 | Has the patient experienced an inadequate treatment response, intolerance, or contraindication to at least one first line therapy agent (e.g., medium or higher potency topical corticosteroid)?
[If yes, then no further questions.] | Yes | No |
| 4 | Is the patient less than 2 years of age AND unable to use a first line therapy agent (e.g., medium or higher potency topical corticosteroid)?
[No further questions.] | Yes | No |
| 5 | Is the requested drug being prescribed for psoriasis on the face, genitals, or skin folds OR vitiligo on the head or neck? | Yes | No |

Mapping Instructions (759-A)

	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Go to 5	
2.	Approve for 36 months	Go to 3	
3.	Approve for 36 months	Go to 4	
4.	Approve for 3 months	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you meet any of these conditions:</p> <ul style="list-style-type: none"> - You have atopic dermatitis (eczema) around the eyes, on the face, genitals, or skin folds - You tried a first line drug for atopic dermatitis (eczema) and it did not work for you or you cannot use it (examples of first line drugs are medium or stronger steroid creams or ointments) - You are less than 2 years of age and cannot use a first line drug (examples of first line drugs are medium or stronger steroid creams or ointments) <p>Your request has been denied based on the information we have. [Short Description: No inadequate response, intolerance or contraindication to first line agents (e.g., medium or higher potency topical corticosteroids)]</p>
5.	Approve for 36 months	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you have any of these conditions:</p> <ul style="list-style-type: none"> - Mild to moderate atopic dermatitis (eczema) - Psoriasis on the face, genitals, or skin folds - Vitiligo on the head or neck <p>Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]</p>

Guidelines for Approval (MDC-2 491-A)					
Duration of Approval			12 Months		
Set 1		Set 2		Set 3	
Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)
1	2	1	None	5	1
3		2			
Duration of Approval			3 Months		
Set 1					
Yes to question(s)			No to question(s)		
1			2		
4			3		

Mapping Instructions (MDC-2 491-A)			
	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Go to 5	
2.	Approve for 12 months	Go to 3	
3.	Approve for 12 months	Go to 4	
4.	Approve for 3 months	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you meet any of these conditions:</p> <ul style="list-style-type: none"> - You have atopic dermatitis (eczema) around the eyes, on the face, genitals, or skin folds - You tried a first line drug for atopic dermatitis (eczema) and it did not work for you or you cannot use it (examples of first line drugs are medium or stronger steroid creams or ointments) - You are less than 2 years of age and cannot use a first line drug (examples of first line drugs are medium or stronger steroid creams or ointments) <p>Your request has been denied based on the information we have. [Short Description: No inadequate response, intolerance or contraindication to first line agents (e.g., medium or higher potency topical corticosteroids)]</p>
5.	Approve for 12 months	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you have any of these conditions:</p> <ul style="list-style-type: none"> - Mild to moderate atopic dermatitis (eczema) - Psoriasis on the face, genitals, or skin folds - Vitiligo on the head or neck <p>Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]</p>

SPECIALTY GUIDELINE MANAGEMENT

ELIGARD (leuprolide acetate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Palliative treatment of advanced prostate cancer

B. Compendial Uses

1. Prostate cancer
2. Metastatic androgen receptor positive salivary gland tumors
3. Gender Dysphoria (also known as gender non-conforming or transgender persons)

NOTE: Some plans may opt-out of coverage for gender dysphoria.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Prostate cancer**

Authorization of 12 months may be granted for treatment of prostate cancer.

B. **Gender dysphoria**

1. Authorization of 12 months may be granted for pubertal suppression in preparation for gender reassignment in an adolescent member when all of the following criteria are met:
 - a. The member has a diagnosis of gender dysphoria.
 - b. The member has reached Tanner stage 2 of puberty.
2. Authorization of 12 months may be granted for gender reassignment in an adult member when all of the following criteria are met:
 - a. The member has a diagnosis of gender dysphoria.
 - b. The member will receive Eligard concomitantly with cross sex hormones.

C. **Salivary gland tumors**

Authorization of 12 months may be granted for treatment of metastatic salivary gland tumors when the tumor is androgen receptor positive.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

Reference number(s)
1966-A, 2084-A

IV. REFERENCES

1. Eligard [package insert]. For Collins, CO: Tolmar Pharmaceuticals; February 2019.
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SPECIALTY GUIDELINE MANAGEMENT

ELZONRIS (tagraxofusp-erzs)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Elzonris is a CD123-directed cytotoxin for the treatment of blastic plasmacytoid dendritic cell neoplasm (BPDCN) in adults and in pediatric patients 2 years and older.

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

Medical record documentation confirming the member is positive for CD123 expression

III. CRITERIA FOR INITIAL APPROVAL

Blastic plasmacytoid dendritic cell neoplasm (BPDCN)

Authorization of 12 months may be granted for treatment of blastic plasmacytoid dendritic cell neoplasm (BPDCN) when the member's disease is positive for CD123 expression.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES

1. Elzonris [package insert]. New York, NY: Stemline Therapeutics, Inc.; December 2018.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

CINVANTI (ALL PRODUCTS)
(aprepitant)

EMEND (ALL PRODUCTS)
(aprepitant)

EMEND (ALL PRODUCTS)
(fosaprepitant dimeglumine)

Status: CVS Caremark Criteria

Type: Post Limit Prior Authorization

Ref # 79-J

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated*

FDA-APPROVED INDICATIONS

Cinvanti (aprepitant) injectable emulsion

Cinvanti, in combination with other antiemetic agents, is indicated in adults for the prevention of:

- acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC) including high-dose cisplatin.
- nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC).

Limitations of Use

- Cinvanti has not been studied for the treatment of established nausea and vomiting.

Emend (aprepitant) capsules and oral suspension

Prevention of Chemotherapy Induced Nausea and Vomiting (CINV)

Emend for oral suspension, in combination with other antiemetic agents, is indicated in patients 6 months of age and older for the prevention of:

- acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC) including high-dose cisplatin.
- nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC).

Emend capsules, in combination with other antiemetic agents, is indicated in patients 12 years of age and older for the prevention of:

- acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC) including high-dose cisplatin.
- nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC).

Prevention of Postoperative Nausea and Vomiting (PONV)

Emend capsules are indicated in adults for the prevention of postoperative nausea and vomiting.

Limitations of Use

- Emend has not been studied for the treatment of established nausea and vomiting.
- Chronic continuous administration of Emend is not recommended because it has not been studied and because the drug interaction profile may change during chronic continuous use.

Emend (fosaprepitant dimeglumine) for injection

Emend for injection, in combination with other antiemetic agents, is indicated in adults for the prevention of:

- acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC) including high-dose cisplatin.
- delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC).

Limitations of Use

- Emend has not been studied for the treatment of established nausea and vomiting.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the prevention of nausea and vomiting associated with highly or moderately emetogenic chemotherapy AND will be used in combination with other antiemetic agents
OR
- Emend capsules are being prescribed for the prevention of postoperative nausea and vomiting

Quantity Limits apply.

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Cinvanti and Emend for Injection are indicated in adults for use in combination with other antiemetic agents for the prevention of acute and delayed nausea and vomiting associated with highly emetogenic cancer chemotherapy (HEC) including high dose cisplatin and for the prevention of nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC). Emend for oral suspension, in combination with other antiemetic agents, is indicated in patients 6 months of age and older for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC) including high dose cisplatin, and for the prevention of nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC). Emend capsules, in combination with other antiemetic agents, are indicated in patients 12 years of age and older for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC) including high dose cisplatin, and for the prevention of nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC). Emend capsules are also indicated for the prevention of postoperative nausea and vomiting. Emend has not been studied for the treatment of established nausea and vomiting.¹⁻³

For adults and pediatric patients 12 years of age and older who can swallow oral capsules, for the prevention of nausea and vomiting associated with the administration of HEC or MEC, the recommended oral dosage of Emend capsules is Emend 125 mg 1 hour prior to chemotherapy treatment on Day 1 and 80 mg orally once daily on Days 2 and 3 as part of a regimen that includes a 5-HT₃ antagonist with or without a corticosteroid.²

For patients who cannot swallow oral capsules, Emend for oral suspension can be used instead of Emend capsules. For pediatric patients 6 months to less than 12 years of age or pediatric and adult patients unable to swallow capsules, the recommended dose of Emend for oral suspension to be administered with a 5-HT₃ antagonist, with or without a corticosteroid, for the prevention of nausea and vomiting associated with administration of HEC or MEC is 3 mg/kg orally on Day 1 (maximum dose 125 mg) and 2 mg/kg orally on Days 2 and 3 (maximum dose 80 mg). Dosing of Emend for oral suspension is based on weight, to a maximum of 125 mg on Day 1 and 80 mg on Days 2 and 3. Dosing in pediatric patients less than 6 kg is not recommended. After preparation, the final concentration of Emend for oral suspension is 25 mg/ml.²

Emend 150 mg injection is administered on Day 1 only as an infusion over 20 -30 minutes initiated approximately 30 minutes prior to chemotherapy; Emend for injection is not administered on Days 2 and 3. Emend for injection should be administered in conjunction with a corticosteroid and a 5-HT3 antagonist.³

The recommended dosage of Cinvanti in adults for the prevention of nausea and vomiting associated with HEC is 130 mg intravenously over 30 minutes approximately 30 minutes prior to chemotherapy on Day 1 only. Cinvanti should be administered in conjunction with dexamethasone and a 5-HT3 antagonist. The recommended dosage of Cinvanti in adults for the prevention of nausea and vomiting associated with MEC is 100 mg administered intravenously over 30 minutes approximately 30 minutes prior to chemotherapy on Day 1 only. Cinvanti should be administered with dexamethasone and a 5-HT3 antagonist. Oral aprepitant 80 mg should be administered on Days 2 and 3.¹

Patients who receive multiday chemotherapy are at risk for both acute and delayed nausea/vomiting based on the emetogenic potential of the individual chemotherapy agents administered on any given day and their sequence. Acute and delayed emesis may overlap after the initial day of chemotherapy until the last day of chemotherapy. The period of risk for delayed emesis after chemotherapy administration has concluded also depends on the specific regimen and the emetogenic potential of the last chemotherapy agent administered in the regimen. According to the National Comprehensive Cancer Network (NCCN) guidelines, substance P/neurokinin-1 (NK-1) receptor antagonists, such as aprepitant, may be used for multiday regimens that are likely to be moderately or highly emetogenic and associated with significant risk for delayed nausea and emesis. If the oral aprepitant regimen is chosen, limited data exist to support administration of aprepitant on days 4 and 5 after multiday chemotherapy.⁷

The limit is designed to allow for the prevention of acute or delayed onset nausea and vomiting associated with chemotherapy at the recommended dose of Emend or Cinvanti. The limit allows a quantity sufficient for four chemotherapy cycles per month (i.e., one chemotherapy cycle every week).

The recommended oral dosage for the prevention of postoperative nausea and vomiting (PONV) is Emend 40 mg within three hours prior to induction of anesthesia. The safety and effectiveness of Emend have not been established for the prevention of postoperative nausea and vomiting in pediatric patients.² Since repeated use of general anesthesia carries inherent risks and patients need time to heal/recover following surgical procedures, the quantity for approval was determined based upon the assumption of an average of at least 30 days between surgical procedures utilizing anesthesia. Emend capsules are the only dosage formulation that is indicated for PONV. Cinvanti is not indicated for PONV. Therefore, this criteria does not provide coverage of Emend suspension, Emend for injection or Cinvanti for the prevention of postoperative nausea and vomiting.

The initial limit for Varubi allows a quantity sufficient for two chemotherapy cycles per month (i.e., one chemotherapy cycle every 2 weeks).⁴ Varubi may be administered at no less than 2 week intervals; therefore, no additional quantities are available through this post limit criteria. If the patient is requesting more than the initial quantity limit of Varubi, the claim will reject with a message indicating that quantity limits are exceeded.

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3. Emend for injection [package insert]. Whitehouse Station, NJ: Merck and Co., Inc; August 2017.
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Reviewed: Medical Affairs: (MM) 06/2006, 07/2006; (WF) 04/2007, 04/2008, 03/2009, 03/2010; (KP) 04/2011, 02/2012; (LS) 01/2013; (KP) 01/2014, (SES) 01/2015; (DHR) 01/2016; (LMS) 01/2017; (JG) 12/2017; (LMS) 01/2018
External Review: 08/2005; 08/2006, 08/2007, 08/2008, 08/2009, 08/2010, 08/2011, 04/2012, 06/2013, 04/2014, 04/2015, 04/2016, 04/2017, 04/2018

CRITERIA FOR APPROVAL

- | | | | |
|---|--|-----|----|
| 1 | Is the requested drug being prescribed for the prevention of nausea and vomiting associated with highly or moderately emetogenic chemotherapy?
[If no, then skip to question 3.] | Yes | No |
| 2 | Will the requested drug be used in combination with other antiemetic agents?
[If yes, then skip to question 5.].
[If no, then no further questions.] | Yes | No |
| 3 | Is the requested drug being prescribed for the prevention of postoperative nausea and vomiting? | Yes | No |
| 4 | Is this request for Emend capsules? | Yes | No |
| 5 | Does the patient require use of MORE than any of the following: A) 4 vials per 28 days of Cinvanti, B) 16 capsules per 28 days of Emend 80 mg, C) 4 capsules per 28 days of Emend 125 mg, D) 4 packs per 28 days of Emend Tri-pack, E) 12 kits per 28 days of Emend 125 mg for Oral Suspension, F) 4 vials per 28 days of Emend 150 mg injection, G) 6 capsules per 6 months of Emend 40 mg? | Yes | No |

[RPh Note: If yes, then deny and enter a partial approval per Post Limit Quantity Chart.]

Mapping Instructions

	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Go to 3	
2.	Go to 5	Deny	Your plan covers this drug when you will take this drug with another drug to prevent nausea and vomiting caused by chemotherapy. Your use of this drug does not meet the requirement. This is based on the information we have.
3.	Go to 4	Deny	Your plan covers this drug when you meet one of these conditions: - You have nausea or vomiting from certain types of chemotherapy - You have nausea or vomiting from surgery Your use of this drug does not meet the requirement. This is based on the information we have.
4.	Go to 5	Deny	Your plan covers this drug when you meet all of these conditions: - You have nausea or vomiting from surgery - This request is for Emend capsules

			Your use of this drug does not meet these requirements. This is based on the information we have.
5.	Deny RPh Note: For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.	Approve, 6 months **See Post Limit Quantity Chart	<p>You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to:</p> <ul style="list-style-type: none"> - 4 vials per 28 days of Cinvanti - 16 capsules per 28 days of Emend 80 mg - 4 capsules per 28 days of Emend 125 mg - 4 packs per 28 days of Emend Tri-pack - 12 kits per 28 days of Emend 125 mg for Oral Suspension - 4 vials per 28 days of Emend 150 mg injection - 6 capsules per 6 months of Emend 40 mg <p>You have been approved for the maximum quantity that your plan covers for a duration of 6 months. Your request for additional quantities of the requested drug and strength has been denied.</p>

POST LIMIT QUANTITY

Drug

Quantities to approve

Cinvanti 130 mg Vial

4 vials / 21 days

Emend 80 mg Capsules

16 capsules / 21 days

Emend 125 mg Capsules

4 capsules / 21 days

Emend Tri-pack (contains one 125mg and two 80mg)

4 packs / 21 days

Emend 125 mg for Oral Suspension (Single-Dose Kit)

12 kits / 21 days

Emend 150 mg Injection

4 vials / 21 days

Emend 40 mg capsule

6 capsules / 6 months

**** This drug is indicated for short-term acute use; therefore, the mail limit will be the same as the retail limit. The duration of 21 days is used for a 28-day fill period.***

SPECIALTY GUIDELINE MANAGEMENT

EMFLAZA (deflazacort)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Emflaza is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients 2 years of age and older.

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

- A. Laboratory confirmation of DMD diagnosis by genetic testing.
- B. Chart documentation of weight gain/obesity or persistent psychiatric/behavioral issues with previous prednisone treatment.

III. CRITERIA FOR INITIAL APPROVAL

Duchenne Muscular Dystrophy

Authorization of 6 months may be granted for treatment of DMD when all of the following criteria are met:

- A. The diagnosis of DMD was confirmed by genetic testing demonstrating a mutation in the *DMD* gene.
- B. The member is 2 years of age or older.
- C. The member has tried prednisone and experienced unmanageable and clinically significant weight gain/obesity or psychiatric/behavioral issues (e.g., abnormal behavior, aggression, irritability).
 - 1. For weight gain/obesity: body mass index is in the overweight or obese category while receiving treatment with prednisone (refer to Appendix for weight status categories for children and adults).
 - 2. For psychiatric/behavioral issues: psychiatric/behavioral issues persisted beyond the first 6 weeks of treatment with prednisone.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members requesting continuation of therapy when all of the following criteria are met:

- A. The member meets initial authorization criteria.
- B. The member is receiving a clinical benefit from Emflaza therapy, such as improvement or stabilization of muscle strength or pulmonary function.

V. APPENDIX

Body Mass Index Percentile and Weight Status Category for Children 2 Through 19 Years of Age

Body Mass Index Percentile Range	Weight Status
Less than the 5th percentile	Underweight
5th percentile to less than the 85th percentile	Normal or Healthy Weight
85th to less than the 95th percentile	Overweight
Equal to or greater than the 95th percentile	Obese

Body Mass Index and Weight Status Category for Adults (20 Years of Age and Older)

Body Mass Index	Weight Status
Below 18.5	Underweight
18.5 – 24.9	Normal or Healthy Weight
25.0 – 29.9	Overweight
30.0 and Above	Obese

VI. REFERENCES

1. Emflaza [package insert]. Northbrook, IL: Marathon Pharmaceuticals, LLC; June 2019.
2. Bushby K, Finkel R, Birnkrant DJ, et al. Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis and pharmacological and psychosocial management. *Lancet Neurol.* 2010;9:77-93.
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4. Griggs RC, Miller JP, Greenberg CR, et al. Efficacy and safety of deflazacort vs prednisone and placebo for Duchenne muscular dystrophy. *Neurology.* 2016;87(20):2123-2131.
5. Centers for Disease Control and Prevention. Assessing Your Weight. <https://www.cdc.gov/healthyweight/assessing/bmi/> Accessed April 17, 2019.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME* (generic)

GLYXAMBI
(empagliflozin / linagliptin)

JARDIANCE
(empagliflozin)

SYNJARDY
(empagliflozin / metformin HCl)

SYNJARDY XR
(empagliflozin / metformin HCl extended-release)

TRIJARDY XR
(empagliflozin / linagliptin / metformin HCl extended-release)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

Ref # 1171-A

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Glyxambi

Glyxambi is a combination of empagliflozin and linagliptin indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both empagliflozin and linagliptin is appropriate.

Empagliflozin is indicated to reduce the risk of cardiovascular death in adults with type 2 diabetes mellitus and established cardiovascular disease. However, the effectiveness of Glyxambi on reducing the risk of cardiovascular death in adults with type 2 diabetes mellitus and cardiovascular disease has not been established.

Limitations of Use

Glyxambi is not recommended for patients with type 1 diabetes or for the treatment of diabetic ketoacidosis. Glyxambi has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at an increased risk for the development of pancreatitis while using Glyxambi.

Jardiance

Jardiance is indicated:

- as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus,
- to reduce the risk of cardiovascular death in adult patients with type 2 diabetes mellitus and established cardiovascular disease

Limitation of Use

Jardiance is not recommended for patients with type 1 diabetes or for the treatment of diabetic ketoacidosis.

Synjardy, Synjardy XR

Synjardy and Synjardy XR are a combination of empagliflozin and metformin hydrochloride indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both empagliflozin and metformin is appropriate.

Empagliflozin is indicated to reduce the risk of cardiovascular death in adults with type 2 diabetes mellitus and established cardiovascular disease. However, the effectiveness of Synjardy/Synjardy XR on reducing the risk of cardiovascular death in adults with type 2 diabetes mellitus and cardiovascular disease has not been established.

Limitation of Use

Synjardy/Synjardy XR is not recommended for patients with type 1 diabetes or for the treatment of diabetic ketoacidosis.

Trijardy XR

Trijardy XR is a combination of empagliflozin, linagliptin, and metformin hydrochloride (HCl) indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use

Trijardy XR is not recommended for patients with type 1 diabetes or for the treatment of diabetic ketoacidosis.

Trijardy XR has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at increased risk for development of pancreatitis while using Trijardy XR.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has been receiving the requested drug for at least 3 months
AND
 - The patient has demonstrated a reduction in A1c (hemoglobin A1c) since starting this therapy
OR
 - The request is for Jardiance (empagliflozin) for a patient who has established cardiovascular disease
- OR**
- Patient has the diagnosis of type 2 diabetes mellitus
AND
 - The patient has experienced an inadequate treatment response, intolerance, or contraindication to metformin
OR
 - The patient requires combination therapy **AND** has an A1c (hemoglobin A1c) of 7.5 percent or greater
OR
 - The request is for Jardiance (empagliflozin) for a patient who has established cardiovascular disease

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Jardiance (empagliflozin), Glyxambi (empagliflozin/linagliptin), Synjardy (empagliflozin/metformin), Synjardy XR (empagliflozin/metformin extended-release), and Trijardy XR (empagliflozin/linagliptin/metformin extended-release) are indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Jardiance is also indicated to reduce the risk of cardiovascular death in adults with type 2 diabetes mellitus and established cardiovascular disease.

Jardiance (empagliflozin) is indicated to reduce the risk of major adverse cardiovascular events (cardiovascular death, nonfatal myocardial infarction and nonfatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease (CVD). However, the effectiveness of empagliflozin combination products such as Glyxambi, Synjardy, and Synjardy XR on reducing the risk of cardiovascular death in adults with type 2 diabetes mellitus and cardiovascular disease has not been established.

Clinical guidelines from the American Diabetes Association and the American Association of Clinical Endocrinologists and American College of Endocrinology for the management of hyperglycemia in type 2 diabetes indicate that metformin monotherapy should be started at diagnosis of type 2 diabetes unless there are contraindications. Metformin is effective and safe, is inexpensive, and may reduce risk of cardiovascular events and death. In patients with contraindications or intolerance of metformin, initial therapy should be based on patient factors; consider a drug from another class.^{7,8}

The clinical guidelines also state that the A1c test is the major tool for assessing glycemic control and has strong predictive value for diabetes complications. Thus, A1c testing should be performed routinely in all patients with diabetes at initial assessment and as part of continuing care.²⁷ The guidelines set goals for therapeutic effectiveness which must be evaluated frequently (e.g., every 3 months) until stable, using multiple criteria, including A1c. Less frequent monitoring is acceptable once targets are achieved.^{7,8} Therefore, continued use of Glyxambi, Jardiance, Synjardy or Synjardy XR will be approved for patients who have demonstrated a reduction in A1c since starting Glyxambi, Jardiance, Synjardy, or Synjardy XR therapy for at least three months.

If the A1c target is not achieved after approximately 3 months and patient does not have atherosclerotic cardiovascular disease (ASCVD) or chronic kidney disease (CKD), consider a combination of metformin and one of the preferred six treatment options: sulfonylurea, thiazolidinedione, dipeptidyl peptidase 4 (DPP-4) inhibitors, sodium-glucose cotransporter 2 (SGLT2) inhibitors, (glucagon-like peptide 1) (GLP-1) receptor agonists, or basal insulin; the choice of which agent to add is based on drug-specific effects and patient factors. For patients in whom ASCVD, Heart Failure, or CKD predominates, the best choice for a second agent is a GLP-1 receptor agonist or SGLT2 inhibitor with demonstrated cardiovascular risk reduction, after consideration of drug-specific and patient factors.^{7,8}

In patients with an initial A1c of 7.5% or greater, or in patients who are unable to achieve their glycemic goals with monotherapy, combination therapy is recommended.⁸ Add-on therapy with empagliflozin plus linagliptin in patients on metformin (i.e., Trijardy XR) was evaluated in a double-blind, active-controlled study that compared the efficacy and safety of empagliflozin 10 or 25 mg in combination with linagliptin 5 mg, compared to the individual components. Patients with type 2 diabetes inadequately controlled on at least 1500 mg of metformin per day entered a single-blind placebo run-in period for 2 weeks. At the end of the run-in period, patients who remained inadequately controlled and had an HbA1c between 7 and 10% were randomized to one of five active-treatment arms of empagliflozin 10 mg or 25 mg, linagliptin 5 mg, or linagliptin in combination with 10 mg or 25 mg empagliflozin as a fixed dose combination tablet. At week 24, empagliflozin 10 mg or 25 mg used in combination with linagliptin 5 mg provided statistically significant improvement in HbA1c (p-value <0.0001) and FPG (p-value <0.001) compared to the individual components in patients who had been inadequately controlled on metformin.⁹

The EMPA-REG OUTCOME study compared the risk of experiencing a major adverse cardiovascular event (MACE) between empagliflozin and placebo. Coadministered antidiabetic medications were to be kept stable for the first 12 weeks of the trial. Thereafter, antidiabetic and atherosclerotic therapies could be adjusted, at the discretion of investigators, to ensure participants were treated according to the standard of care for these diseases.² Therefore, Jardiance will be approved for initial therapy and continuation of therapy for patients who have established cardiovascular disease.

REFERENCES

1. Glyxambi [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; October 2018.
2. Jardiance [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; October 2018.
3. Synjardy [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; October 2018.
4. Synjardy XR [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; October 2018.
5. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed June 2019. .
6. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed June 2019.
7. American Diabetes Association. Standards of Medical Care in Diabetes-2019: *Diabetes Care* January 2019;42(Supplement1).
8. Garber AJ, Abrahamson MJ, Barzilay JI, et al. Consensus Statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the Comprehensive Type 2 Diabetes Management Algorithm 2019, *Endocr Pract.* January 2019; 25 (No 1); 69-100.

9. Trijardy XR [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; January 2020.

Written by: UM Development (PL)
 Date Written: 08/2014
 Revised: (MS) 03/2015 (added Glyxambi, eGFR note), (DN/SE) 07/2015; (CT) 09/2015 (added Synjardy); (KM) 07/2016 (no clinical changes), 12/2016 (updated for new Jardiance indication); 01/2017 (added Synjardy XR), 07/2017, 07/2018; (DFW) 07/2019 (no clinical changes), 01/2020 (added Trijardy XR)
 Reviewed: Medical Affairs: (LB) 08/2014; (AD) 03/2015, (DNC) 07/2015; (LS) 09/2015; (ME) 12/2016, 01/2017; (SD) 07/2017; (ME) 07/2018, (CHART) 8/1/2019, 02/06/2020
 External Review: 08/2014, 10/2015, 10/2016, 10/2017, 10/2018, 10/2019, 02/2020 (FYI)

CRITERIA FOR APPROVAL

1	Has the patient been receiving the requested drug for at least 3 months? [If no, then skip to question 4.]	Yes	No
2	Has the patient demonstrated a reduction in A1c (hemoglobin A1c) since starting this therapy? [If yes, then no further questions.]	Yes	No
3	Is this request for Jardiance (empagliflozin)? [If yes, then skip to question 8.] [If no, then no further questions.]	Yes	No
4	Does the patient have a diagnosis of type 2 diabetes mellitus?	Yes	No
5	Has the patient experienced an inadequate treatment response, intolerance, or contraindication to metformin? [If yes, then no further questions.]	Yes	No
6	Does the patient require combination therapy AND have an A1c (hemoglobin A1c) of 7.5 percent or greater? [If yes, then no further questions.]	Yes	No
7	Is this request for Jardiance (empagliflozin)?	Yes	No
8	Does the patient have established cardiovascular disease?	Yes	No

Mapping Instructions

DENIAL REASONS – DO NOT USE FOR MEDICARE PART D

	Yes	No	
1.	Go to 2	Go to 4	
2.	Approve, 36 months	Go to 3	
3.	Go to 8	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet these conditions; - You have been receiving the requested drug for at least 3 months - You had a reduction in A1c (hemoglobin A1c) since starting this therapy Your request has been denied based on the information we have. [Short Description: No response to treatment]
4.	Go to 5	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have type 2 diabetes mellitus.

			<p>Your request has been denied based on the information we have.</p> <p>[Short Description: No approvable diagnosis]</p>
5.	Approve, 36 months	Go to 6	
6.	Approve, 36 months	Go to 7	
7.	Go to 8	Deny	<p>You do not meet the requirements of your plan.</p> <p>Your plan covers this drug when you meet any of these conditions:</p> <ul style="list-style-type: none"> - You have tried metformin and it did not work for you, or you cannot use it - You require combination therapy and you have an A1c (hemoglobin A1c) of 7.5 percent or greater <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No inadequate response, intolerance or contraindication to metformin, no confirmation of combination therapy requirement]</p>
8.	Approve, 36 months	Deny	<p>You do not meet the requirements of your plan.</p> <p>Your plan covers this drug when you meet any of these conditions:</p> <ul style="list-style-type: none"> - You have tried metformin and it did not work for you, or you cannot use it - You require combination therapy and you have an A1c (hemoglobin A1c) of 7.5 percent or greater - You have cardiovascular (heart) disease - You have been taking the requested drug for at least 3 months and you had a reduction in A1c (hemoglobin A1c) since starting this therapy <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No inadequate response, intolerance or contraindication to metformin, No confirmation of combination therapy requirement, Jardiance no confirmation of heart disease]</p>

SPECIALTY GUIDELINE MANAGEMENT

EMPLICITI (elotuzumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Empliciti is indicated in combination with lenalidomide and dexamethasone for the treatment of adult patients with multiple myeloma who have received one to three prior therapies.
2. Empliciti is indicated in combination with pomalidomide and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least two prior therapies including lenalidomide and a proteasome inhibitor.

B. Compendial Uses

Therapy for previously treated multiple myeloma for relapsed or progressive disease in combination with bortezomib and dexamethasone

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Multiple Myeloma

Authorization of 12 months may be granted for the treatment of multiple myeloma when all of the following criteria are met:

- A. The disease is relapsed or progressive
- B. The requested medication will be used in any of the following regimens:
 1. In combination with lenalidomide and dexamethasone in members who have received one to three prior therapies
 2. In combination with bortezomib and dexamethasone in members who have received at least one prior therapy
 3. In combination with pomalidomide and dexamethasone in members who have received at least two prior therapies, including an immunomodulatory agent and a proteasome inhibitor

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Empliciti [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; November 2018.

Reference number(s)
2330-A

2. The NCCN Drugs & Biologics Compendium 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 29, 2019.
3. The NCCN Clinical Practice Guidelines in Oncology Multiple Myeloma (Version 1.2019) 2018 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed March 29, 2019.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

EMSAM
(selegiline)

Status: CVS Caremark Criteria

Type: Initial Prior Authorization

Ref # 867-A

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Emsam (selegiline transdermal system) is a monoamine oxidase inhibitor (MAOI) indicated for the treatment of adults with major depressive disorder (MDD).

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for an adult patient for the treatment of major depressive disorder (MDD)
- AND**
- The patient experienced an inadequate treatment response, intolerance, or contraindication to any of the following antidepressants: A) bupropion, trazodone, mirtazapine, B) serotonin norepinephrine reuptake inhibitors (e.g., venlafaxine), C) selective serotonin reuptake inhibitors (e.g., citalopram, fluoxetine, fluvoxamine, paroxetine, sertraline), D) tricyclic or tetracyclic antidepressants (e.g., amitriptyline, nortriptyline)
- OR**
- The patient is unable to swallow oral formulations

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Emsam (selegiline transdermal system) is indicated for the treatment of adults with major depressive disorder (MDD).¹⁻³

For most patients, the effectiveness of antidepressant medications is generally comparable between classes and within classes of medications. Therefore, the initial selection of an antidepressant medication will largely be based on the anticipated side effects, the safety or tolerability of these side effects for the individual patient, pharmacological properties of the medication (e.g., half-life, actions on cytochrome P450 enzymes, other drug interactions), and additional factors such as medication response in prior episodes, cost, and patient preference. For most patients, a selective serotonin reuptake inhibitor (SSRI), serotonin norepinephrine reuptake inhibitor (SNRI), mirtazapine, or bupropion is optimal. Tricyclic and tetracyclic antidepressants are effective treatments for major depressive disorder and have comparable efficacy to other classes of antidepressants, including SSRIs, SNRIs, and monoamine oxidase inhibitors (MAOIs). Use of trazodone can be an advantage in patients with initial insomnia because the sedation associated with trazodone is greater than that with other non-TCA, non-MAOI antidepressants.⁴

In general, the use of monoamine oxidase inhibitors (MAOIs) should be restricted to patients who do not respond to other treatments because of their potential drug interactions and the necessity of dietary restrictions. There do not appear to be any significant differences in efficacy among the older MAOIs, although there are important individual differences in responsiveness, and these medications are not interchangeable. There are no comparative studies of the newer transdermal formulation of Emsam. Its efficacy has only been established relative to placebo, and clinical experience is limited.⁴ Emsam may be approved for patients who are unable to swallow oral formulations. Emsam may also be approved for patients who have had an inadequate treatment response, intolerance, or contraindication to any of the following antidepressants: selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), bupropion, mirtazapine, trazodone, or tricyclic/tetracyclic antidepressants.

REFERENCES

1. Emsam [package insert]. Morgantown, WV: Somerset Pharmaceuticals, Inc.; July 2017.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed March 2019.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed March 2019.
4. Gelenberg A, Freeman M, Markowitz J, et al. Practice Guideline for the Treatment of Patients With Major Depressive Disorder Third Edition (November 2010). <http://psychiatryonline.org/guidelines.aspx>. Accessed March 2019.

Written by: UM Development (SE)
 Date written: 12/2009
 Revised: (SE/CT) 09/2010 (CAS adapted); (CT) 08/2011, 06/2012; (PL) 10/2012 (extended duration), (TM) 05/2013; (CF) 05/2014, 05/2015; (CT) 05/2016; (RP) 05/2017; (KC) 05/2018; (CF) 03/2019 (removed BBW question)
 Reviewed: Medical Affairs (KP) 12/2009, (KP) 10/2010, 08/2011, 06/2012, 10/2012, (LB) 05/2013; (LMS) 05/2014; (DNC) 05/2015; (ME) 05/2016; (LMS) 05/2017; (DC) 05/2018; (CHART) 8/22/19
 External Review: 02/2010, 12/2010, 10/2011, 10/2012, 08/2013, 06/2014, 08/2014, 08/2015, 08/2016, 08/2017, 08/2018, 08/2019

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for an adult patient for the treatment of major depressive disorder (MDD)?	Yes	No
2	Has the patient experienced an inadequate treatment response, intolerance, or contraindication to any of the following antidepressants: A) bupropion, trazodone, mirtazapine, B) serotonin norepinephrine reuptake inhibitors (e.g., venlafaxine), C) selective serotonin reuptake inhibitors (e.g., citalopram, fluoxetine, fluvoxamine, paroxetine, sertraline), D) tricyclic or tetracyclic antidepressants (e.g., amitriptyline, nortriptyline)? [If yes, then no further questions.]	Yes	No
3	Is the patient unable to swallow oral formulations?	Yes	No

Mapping Instructions

DENIAL REASONS – DO NOT USE FOR MEDICARE PART D

	Yes	No	
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions: - You are an adult - You have major depressive disorder (MDD) Your request has been denied based on the information we have. [Short Description: No approvable diagnosis.]
2.	Approve, 36 months	Go to 3	
3.	Approve, 36 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet one of these conditions: -You tried another drug for major depressive disorder (MDD) first, but it did not work for you or you cannot use it - You are unable to swallow oral medications Your request has been denied based on the information we have. [Short Description: No inadequate response, intolerance, or contraindication to other antidepressants; no inability to take oral formulations.]

SPECIALTY GUIDELINE MANAGEMENT

ENBREL (etanercept)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Moderately to severely active rheumatoid arthritis (RA)
2. Moderately to severely active polyarticular juvenile idiopathic arthritis (pJIA) in patients aged 2 years or older
3. Active psoriatic arthritis (PsA)
4. Active ankylosing spondylitis (AS)
5. Moderate to severe chronic plaque psoriasis (PsO) in patients aged 4 years and older

B. Compendial Uses

1. Axial spondyloarthritis
2. Oligoarticular juvenile idiopathic arthritis
3. Reactive arthritis
4. Hidradenitis suppurativa, severe, refractory
5. Behcet's disease
6. Graft versus host disease

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Moderately to severely active rheumatoid arthritis (RA)**

1. Authorization of 12 months may be granted for members who have previously received a biologic or targeted synthetic DMARD (e.g., Rinvoq, Xeljanz) indicated for moderately to severely active rheumatoid arthritis.
2. Authorization of 12 months may be granted for treatment of moderately to severely active RA when any of the following criteria is met:
 - a. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to 20 mg/week).
 - b. Member has an intolerance or contraindication to methotrexate (see Appendix A)

B. **Moderately to severely active articular juvenile idiopathic arthritis**

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for moderately to severely active articular juvenile idiopathic arthritis.

2. Authorization of 12 months may be granted for the treatment of moderately to severely active articular juvenile idiopathic arthritis when any of the following criteria are met:
 - a. The member has had an inadequate response to methotrexate or another non-biologic DMARD administered at an adequate dose and duration.
 - b. The member has risk factors (See Appendix C) and the member also meets one of the following:
 - i. High-risk joints are involved (e.g., cervical spine, wrist, or hip).
 - ii. High disease activity.
 - iii. Are judged to be at high risk for disabling joint disease.

C. Active psoriatic arthritis (PsA)

Authorization of 12 months may be granted for treatment of active psoriatic arthritis (PsA).

D. Active ankylosing spondylitis (AS) and axial spondyloarthritis

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for active ankylosing spondylitis or axial spondyloarthritis.
2. Authorization of 12 months may be granted for treatment of active ankylosing spondylitis and axial spondyloarthritis when any of the following criteria is met:
 - a. Member has experienced an inadequate response to at least two non-steroidal anti-inflammatory drugs (NSAIDs).
 - b. Member has an intolerance or contraindication to two or more NSAIDs.

E. Moderate to severe chronic plaque psoriasis

1. Authorization of 12 months may be granted for members who have previously received Otezla or a biologic indicated for the treatment of moderate to severe chronic plaque psoriasis.
2. Authorization of 12 months may be granted for treatment of moderate to severe chronic plaque psoriasis when all of the following criteria are met:
 - a. At least 3% of body surface area (BSA) is affected OR crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
 - b. Member meets any of the following criteria:
 - i. Member has had an inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) or a pharmacologic treatment with methotrexate, cyclosporine or acitretin.
 - ii. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine and acitretin (see Appendix B).
 - iii. Member has severe psoriasis that warrants a biologic DMARD as first-line therapy (i.e. at least 10% of the body surface area (BSA) or crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected).

F. Reactive arthritis

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for reactive arthritis.
2. Authorization of 12 months may be granted for treatment of reactive arthritis when any of the following criteria is met:
 - a. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to 20 mg/week).
 - b. Member has an intolerance or contraindication to methotrexate (see Appendix A).

G. Hidradenitis suppurativa

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for the treatment of severe, refractory hidradenitis suppurativa.

2. Authorization of 12 months may be granted for treatment of severe, refractory hidradenitis suppurativa when either of the following is met:
 - a. Member has experienced an inadequate response to oral antibiotics for at least 90 days.
 - b. Member has an intolerance or contraindication to oral antibiotics.

H. Graft versus host disease

Authorization of 12 months may be granted for treatment of graft versus host disease when either of the following criteria is met:

1. Member has experienced an inadequate response to topical or systemic corticosteroids or immunosuppressive therapy (e.g., cyclosporine or mycophenolate mofetil).
2. Member has an intolerance or contraindication to topical or systemic corticosteroids and immunosuppressive therapy (e.g. cyclosporine, mycophenolate mofetil).

I. Behcet's disease

1. Authorization of 12 months may be granted for members who have previously received Otezla or a biologic indicated for the treatment of Behcet's disease.
2. Authorization of 12 months may be granted for the treatment of Behcet's disease when the member has had an inadequate response to at least one nonbiologic medication for Behcet's disease (e.g., apremilast, colchicine, systemic glucocorticoids, azathioprine).

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who are using Enbrel for an indication outlined in section II and who achieve or maintain positive clinical response with Enbrel as evidenced by low disease activity or improvement in signs and symptoms of the condition.

OTHER

For all indications: Member has had a documented negative TB test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic DMARDs or targeted synthetic DMARDs (e.g., Xeljanz), and repeated yearly for members with risk factors** for TB that are continuing therapy with biologics.

* If the screening testing for TB is positive, there must be documentation of further testing to confirm there is no active disease. Do not administer etanercept to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of etanercept.

** Risk factors for TB include: Persons with close contact to people with infectious TB disease; persons who have recently immigrated from areas of the world with high rates of TB (e.g., Africa, Asia, Eastern Europe, Latin America, Russia); children less than 5 years of age who have a positive TB test; groups with high rates of TB transmission (e.g., homeless persons, injection drug users, persons with HIV infection); persons who work or reside with people who are at an increased risk for active TB (e.g., hospitals, long-term care facilities, correctional facilities, homeless shelters).

For all indications: Member cannot use Enbrel concomitantly with any other biologic DMARD or targeted synthetic DMARD.

IV. APPENDICES

Appendix A: Examples of Contraindications to Methotrexate

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
4. Elevated liver transaminases
5. History of intolerance or adverse event
6. Hypersensitivity
7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
8. Myelodysplasia
9. Pregnancy or planning pregnancy
10. Renal impairment
11. Significant drug interaction

Appendix B: Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine or Acitretin.

1. Alcoholism, alcoholic liver disease, or other chronic liver disease
2. Breastfeeding
3. Drug interaction
4. Cannot be used due to risk of treatment-related toxicity
5. Pregnancy or planning pregnancy
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

APPENDIX C: Risk factors for articular juvenile idiopathic arthritis

1. Positive rheumatoid factor
2. Positive anti-cyclic citrullinated peptide antibodies
3. Pre-existing joint damage

V. REFERENCES

1. Enbrel [package insert]. Thousand Oaks, CA: Immunex Corporation; November 2017.
2. van der Heijde D, Ramiro S, Landewe R, et al. 2016 Update of the international ASAS-EULAR management recommendations for axial spondyloarthritis. *Ann Rheum Dis.* 2017;0:1-14.
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19. Tuberculosis (TB). TB risk factors. Centers for Disease Control and Prevention. Retrieved on 21 June 2019 from: <https://www.cdc.gov/tb/topic/basics/risk.htm>.

SPECIALTY GUIDELINE MANAGEMENT

ENDARI (L-glutamine oral powder)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Endari is indicated to reduce the acute complications of sickle cell disease in adult and pediatric patients 5 years of age and older.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Sickle cell disease, to reduce the acute complications

Authorization of 12 months may be granted for use in reducing the acute complications of sickle cell disease in members 5 years of age or older when any of the following criteria are met:

- A. The member experienced, at any time in the past, an inadequate response or intolerance to a trial of hydroxyurea.
- B. The member has a contraindication to hydroxyurea.
- C. The member will be using Endari with concurrent hydroxyurea therapy.

III. CONTINUATION OF THERAPY

Sickle cell disease, to reduce the acute complications

Authorization of 12 months may be granted for continued treatment when the member experienced a reduction in acute complications of sickle cell disease (e.g., reduction in the number of sickle cell crises, acute chest syndrome episodes, fever, occurrences of priapism, splenic sequestration) since initiating therapy with Endari.

IV. REFERENCES

1. Endari [package insert]. Torrance, CA: Emmaus Medical, Inc; July 2017.
2. Niihara Y, Miller ST, et al. A phase 3 trial of L-glutamine in sickle cell disease. *N Engl J Med*. 2018;379(3):226-235.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME (generic)	ENDARI (L-glutamine oral powder)
Status: CVS Caremark Criteria Type: Initial Prior Authorization	MDC Ref #2211-A

FDA-APPROVED INDICATION¹

Endari is indicated to reduce the acute complications of sickle cell disease in adult and pediatric patients 5 years of age and older.

CRITERIA FOR APPROVAL

1	Is Endari being requested to reduce the acute complications of sickle cell disease? [If no, no further questions.]	Yes	No
2	Is the patient 5 years of age or older?	Yes	No

Guidelines for Approval	
Duration of Approval	12 months
Set 1	
Yes to question(s)	No to question(s)
1	None
2	

Mapping Instructions		
	Yes	No
1	Go to 2	Deny
2	Approve, 12 months	Deny

RATIONALE

These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to ensure that patients follow selection elements noted in labeling and/or practice guidelines in order to decrease the potential for inappropriate utilization.

REFERENCES

1. Endari [package insert]. Torrance, CA: Emmaus Medical, Inc; July 2017.

DOCUMENT HISTORY:

Written: Specialty Clinical Development (DK) 10/2017
 Revised: IP 03/2018 (2018 version), TE 07/2018, TE 06/2019 (CMS)
 Reviewed: CDPR/GAD 07/2017, ME 07/2018
 External Review: 09/2017, 09/2018

SPECIALTY GUIDELINE MANAGEMENT

ENHERTU (fam-trastuzumab deruxtecan-nxki)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Breast Cancer

Enhertu is indicated for the treatment of patients with human epidermal growth factor receptor 2 (HER2)-positive, unresectable or metastatic breast cancer who have previously received treatment with two or more prior anti-HER2 based regimens in the metastatic setting.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of human epidermal growth factor receptor 2 (HER2) status is necessary to initiate the prior authorization review.

III. CRITERIA FOR INITIAL APPROVAL

Breast cancer

Authorization of 12 months may be granted for treatment of HER2-positive metastatic or unresectable breast cancer in members who have received two or more prior anti-HER2 based regimens in the metastatic setting.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for breast cancer when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Enhertu [package insert]. Basking Ridge, NJ: Daiichi Sankyo Inc.; December 2019.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME (generic)	ENHERTU (fam-trastuzumab deruxtecan-nxki)
Status: CVS Caremark Criteria Type: Initial Prior Authorization	MDC Ref # 3471-A

FDA-APPROVED INDICATIONS¹

Breast Cancer

Enhertu, as a single agent, is indicated for the treatment of patients with human epidermal growth factor receptor 2 (HER2)-positive, unresectable or metastatic breast cancer who have previously received treatment with two or more prior anti-HER2 based regimens in the metastatic setting.

CRITERIA FOR APPROVAL

1	Does the patient have a diagnosis of breast cancer? [If no, no further questions.]	Yes	No
2	Does the patient has unresectable or metastatic disease? [If no, no further questions.]	Yes	No
3	Does the patient have human epidermal growth factor receptor 2 (HER2)-positive disease? [If no, no further questions.]	Yes	No
4	Has the patient received treatment with two or more anti-human epidermal growth factor receptor 2 (HER2) based regimens in the metastatic setting?	Yes	No

Guidelines for Approval	
Duration of Approval	Approved for 12 months
Set 1	
Yes to questions (s)	No to question(s)
1	None
2	
3	
4	

Mapping Instructions	
	No
1. Go to 2	Deny
2. Go to 3	Deny
3. Go to 4	Deny
4. Approve, 12 months	Deny

RATIONALE

These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to ensure that patients follow selection elements noted in labeling and/or practice guidelines in order to decrease the potential for inappropriate utilization.

REFERENCES

1. Enhertu [package insert]. Basking Ridge, NJ: Daiichi Sankyo Inc.; December 2019.

DOCUMENT HISTORY

Created: Specialty Clinical Development (FS) 01/2020
Revised:
Reviewed: CDPR / MF 01/2020
External Review: 01/2020

SPECIALTY GUIDELINE MANAGEMENT

ENTYVIO (vedolizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

1. Adult patients with moderately to severely active ulcerative colitis (UC) who have had an inadequate response with, lost response to, or were intolerant to a tumor necrosis factor (TNF) blocker or immunomodulator; or had an inadequate response with, were intolerant to, or demonstrated dependence on corticosteroids:
 - inducing and maintaining clinical response
 - inducing and maintaining clinical remission
 - improving endoscopic appearance of the mucosa
 - achieving corticosteroid-free remission
2. Adult patients with moderately to severely active Crohn's disease (CD) who have had an inadequate response with, lost response to, or were intolerant to a TNF blocker or immunomodulator; or had an inadequate response with, were intolerant to, or demonstrated dependence on corticosteroids:
 - achieving clinical response
 - achieving clinical remission
 - achieving corticosteroid-free remission

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Moderately to severely active ulcerative colitis (UC)

1. Authorization of 12 months may be granted for members who have previously received a biologic or targeted synthetic DMARD (e.g., Xeljanz) indicated for moderately to severely active ulcerative colitis.
2. Authorization of 12 months may be granted for the treatment of moderately to severely active UC for members who had an inadequate response, intolerance or contraindication to at least one conventional therapy option (See Appendix A).
3. Authorization of 12 months may be granted for members who have been hospitalized for fulminant UC (e.g., continuous bleeding, severe toxic symptoms, including fever and anorexia).

B. Moderately to severely active Crohn's disease (CD)

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for the treatment of moderately to severely active Crohn's disease.

2. Authorization of 12 months may be granted for the treatment of moderately to severely active CD in members who had an inadequate response, intolerance or contraindication to at least one conventional therapy option (See Appendix B).
3. Authorization of 12 months may be granted for the treatment of fistulizing CD.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who are using Entyvio for an indication outlined in section II and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

For all indications: Member cannot use Entyvio concomitantly with any other biologic DMARD or targeted synthetic DMARD.

V. APPENDICES

Appendix A: Examples of Conventional Therapy Options for UC

1. Mild to moderate disease – induction of remission:
 - a. Oral mesalamine (e.g., Asacol, Asacol HD, Lialda, Pentasa), balsalazide, olsalazine
 - b. Rectal mesalamine (e.g., Canasa, Rowasa)
 - c. Rectal hydrocortisone (e.g., Colocort, Cortifoam)
 - d. Alternatives: prednisone, azathioprine, mercaptopurine, sulfasalazine
2. Mild to moderate disease – maintenance of remission:
 - a. Oral mesalamine, balsalazide, olsalazine, rectal mesalamine
 - b. Alternatives: azathioprine, mercaptopurine, sulfasalazine
3. Severe disease – induction of remission:
 - a. Prednisone, hydrocortisone IV, methylprednisolone IV
 - b. Alternatives: cyclosporine IV, tacrolimus, sulfasalazine
4. Severe disease – maintenance of remission:
 - a. Azathioprine, mercaptopurine
 - b. Alternative: sulfasalazine
5. Pouchitis: Metronidazole, ciprofloxacin
 - a. Alternative: rectal mesalamine

Appendix B: Examples of Conventional Therapy Options for CD

1. Mild to moderate disease – induction of remission:
 - a. Oral budesonide
 - b. Alternatives: metronidazole, ciprofloxacin, rifaximin
2. Mild to moderate disease – maintenance of remission:
 - a. Azathioprine, mercaptopurine
 - b. Alternatives: oral budesonide, methotrexate intramuscular (IM) or subcutaneous (SC), sulfasalazine
3. Moderate to severe disease – induction of remission:
 - a. Prednisone, methylprednisolone intravenously (IV)
 - b. Alternatives: methotrexate IM or SC
4. Moderate to severe disease – maintenance of remission:

Reference number(s)
2004-A

- a. Azathioprine, mercaptopurine
- b. Alternative: methotrexate IM or SC
- 5. Perianal and fistulizing disease – induction of remission
 - a. Metronidazole ± ciprofloxacin, tacrolimus
- 6. Perianal and fistulizing disease – maintenance of remission
 - a. Azathioprine, mercaptopurine
 - b. Alternative: methotrexate IM or SC

VI. REFERENCES

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4. Rubin DT, Ananthakrishnan AN, et al. 2019 ACG Clinical Guideline: Ulcerative Colitis in Adults. *Am J Gastroenterol*. 2019;114:384-413.

SPECIALTY GUIDELINE MANAGEMENT

EPCLUSA (sofosbuvir and velpatasvir)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Epclusa is indicated for the treatment of adult patients with chronic hepatitis C virus (HCV) genotype 1, 2, 3, 4, 5 or 6 infection:

- A. without cirrhosis or with compensated cirrhosis
- B. with decompensated cirrhosis for use in combination with ribavirin

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR APPROVAL

A. Chronic hepatitis C virus infection, without ribavirin

1. Genotype 1 infection

- a. Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who are treatment-naïve or who failed prior treatment with peginterferon alfa (PEG-IFN) and ribavirin (RBV) with or without an HCV protease inhibitor (boceprevir, simeprevir or telaprevir).
- b. Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who have genotype 1b infection and who failed prior treatment with non-NS5A inhibitor, sofosbuvir-containing regimen.

2. Genotype 2 infection

- a. Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who are treatment-naïve or who failed prior treatment with PEG-IFN and RBV.
- b. Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who failed prior treatment with sofosbuvir (Sovaldi) and ribavirin.

3. Genotype 3 infection

Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who are treatment-naïve or who failed prior treatment with PEG-IFN and RBV.

4. Genotype 4, 5 or 6 infection

Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who are treatment-naïve or who failed prior treatment with PEG-IFN and RBV with or without an HCV protease inhibitor (boceprevir, simeprevir or telaprevir).

5. Decompensated cirrhosis (Child Turcotte Pugh [CTP] class B or C)

Authorization of up to 24 weeks total may be granted for members with genotype 1, 2, 3, 4, 5 or 6 infection who have decompensated cirrhosis and documented anemia (baseline hemoglobin [Hgb] below 10 g/dL) or RBV ineligibility (see Section IV).

B. Chronic hepatitis C virus infection, in combination with ribavirin**1. Genotype 3 infection**

- a. Authorization of up to 12 weeks total may be granted for members with the Y93H substitution associated with velpatasvir resistance who are either of the following:
 - i. Treatment-naïve with compensated cirrhosis
 - ii. Failed prior treatment with PEG-IFN and RBV without cirrhosis
- b. Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV.

2. Decompensated cirrhosis (CTP class B or C)

- a. Authorization of up to 12 weeks total may be granted for members with genotype 1, 2, 3, 4, 5 or 6 infection and decompensated cirrhosis.
- b. Authorization of up to 24 weeks total may be granted for members with genotype 1, 2, 3, 4, 5 or 6 infection and decompensated cirrhosis who failed prior treatment with a sofosbuvir- or NS5A inhibitor-based regimen.

3. Recurrent HCV infection post liver transplantation

Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis or decompensated cirrhosis and recurrent HCV genotype 2 or 3 infection post liver transplantation.

C. HCV and HIV coinfection

Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in Section A or B above are met.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. APPENDIX: RIBAVIRIN INELIGIBILITY

RBV ineligibility is defined as one or more of the below:

- Intolerance to RBV
- Pregnant female or male whose female partner is pregnant
- Hemoglobinopathy
- Coadministration with didanosine
- History of significant or unstable cardiac disease

V. REFERENCES

1. Epclusa [package insert]. Foster City, CA: Gilead Sciences, Inc.; November 2017.
2. AASLD/IDSA/IAS–USA. Recommendations for testing, managing, and treating hepatitis C. <http://www.hcvguidelines.org>. Last changes made May 24, 2017. Accessed August 02, 2018.

SPECIALTY GUIDELINE MANAGEMENT

EPIDIOLEX (cannabidiol)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Epidiolex is indicated for the treatment of seizures associated with Lennox-Gastaut syndrome or Dravet syndrome in patients 2 years of age and older.

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review:

- For new starts only:
 - Prior and current antiepileptic therapy
 - Medical record documentation (i.e., chart notes or laboratory report) indicating the clinical assessments outlined in section IV have been performed.
- For new starts and continuation requests: Medical record documentation (i.e., chart notes, imaging report, or laboratory report) of electroencephalography (EEG), magnetic resonance imaging (MRI), or SCN1A gene mutation

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a neurologist.

IV. CRITERIA FOR INITIAL APPROVAL

Seizures associated with Lennox-Gastaut syndrome or Dravet syndrome

Authorization of 6 months may be granted for treatment of seizures associated with Lennox-Gastaut syndrome or Dravet syndrome when all of the following criteria are met:

- A. Member has a documented inadequate response to prior therapy with at least one anti-epileptic drug. Examples of antiepileptic drugs⁴⁻⁶:
 - For Lennox-Gastaut syndrome: clobazam, falmate, lamotrigine, levetiracetam, topiramate, rufinamide, valproate
 - For Dravet syndrome: clobazam, levetiracetam, stiripentol, topiramate, valproate
- B. Epidiolex will be used in combination with one or more anti-epileptic drugs.
- C. Member has received documented clinical assessments that include all of the following:
 1. EEG, MRI, or SCN1A gene mutation confirmed by genetic testing
 2. Age at seizure onset, seizure types, and frequency of episodes

3. Review of risk factors, other causes of seizures (e.g., other medical conditions and medications), family history, and developmental history

V. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who meets both of the following:

- A. Documentation of EEG, MRI, or SCN1A gene mutation confirmed by genetic testing has been submitted
- B. Member has achieved and maintained positive clinical response with Epidiolex therapy as evidenced by reduction in frequency or duration of seizures

VI. REFERENCES

1. Epidiolex [package insert]. Carlsbad, CA: Greenwich Biosciences, Inc.; November 2018.
2. National Institute for Health and Care Excellence (2012). Epilepsies: diagnosis and management. NICE Guideline [CG137]. Updated April 2018. Available at: <https://www.nice.org.uk/guidance/cg137>. Accessed December 7, 2018.
3. Wirrell EC, Laux L, Donner E, et al. Optimizing the Diagnosis and Management of Dravet Syndrome: Recommendations From a North American Consensus Panel. *Pediatric Neurology* 68 (2017) 18-34.
4. Devinsky O, Cross H, Laux L, et al. Trial of Cannabidiol for Drug-Resistant Seizures in the Dravet Syndrome. *N Engl J Med* 2017;376:2011-20.
5. Thiele EA, Marsh ED, French JA, et al. Cannabidiol in patients with seizures associated with Lennox-Gastaut syndrome (GWPCARE4): a randomised, double-blind, placebo-controlled phase 3 trial. *Lancet*;391:1085-96, Published online January 24, 2018. Available at: [http://dx.doi.org/10.1016/S0140-6736\(18\)30136-3](http://dx.doi.org/10.1016/S0140-6736(18)30136-3)
6. Epilepsy Foundation. LGS: Seizure Medications. Available at: <https://www.epilepsy.com/learn/types-epilepsy-syndromes/lennox-gastaut-syndrome-lgs/treatment/lgs-seizure-medications>. Accessed January 22, 2019.

SPECIALTY GUIDELINE MANAGEMENT

EPOGEN, PROCIT, RETACRIT (epoetin alfa)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Epoetin alfa is indicated for the treatment of anemia due to chronic kidney disease (CKD), including patients on dialysis and not on dialysis to decrease the need for red blood cell (RBC) transfusion.
2. Epoetin alfa is indicated for the treatment of anemia due to zidovudine administered at ≤ 4200 mg/week in HIV-infected patients with endogenous serum erythropoietin levels of ≤ 500 mUnits/mL.
3. Epoetin alfa is indicated for the treatment of anemia in patients with non-myeloid malignancies where anemia is due to the effect of concomitant myelosuppressive chemotherapy, and upon initiation, there is a minimum of two additional months of planned chemotherapy.
4. Epoetin alfa is indicated to reduce the need for allogeneic RBC transfusions among patients with perioperative hemoglobin > 10 to ≤ 13 g/dL who are at high risk for perioperative blood loss from elective, noncardiac, nonvascular surgery. Epoetin alfa is not indicated for patients who are willing to donate autologous blood preoperatively.

B. Compendial Uses

1. Symptomatic anemia in patients with myelodysplastic syndromes (MDS)
2. Anemia in congestive heart failure
3. Anemia in rheumatoid arthritis
4. Anemia due to hepatitis C treatment with ribavirin in combination with either interferon alfa or peginterferon alfa
5. Anemia in patients whose religious beliefs forbid blood transfusions
6. Symptomatic anemia in patients with primary myelofibrosis, post-polycythemia vera myelofibrosis, and post-essential thrombocythemia myelofibrosis
7. Cancer patients who are undergoing palliative treatment

All other indications are considered experimental/investigational and are not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Note: Requirements regarding pretreatment hemoglobin level exclude values due to a recent transfusion. All members must be assessed for iron deficiency anemia and have adequate iron stores or are receiving iron therapy before starting Epogen/Procrit/Retacrit. Members may not use Epogen/Procrit/Retacrit concomitantly with other erythropoiesis stimulating agents.

A. Anemia Due to CKD

Reference number(s)
1619-A

Authorization of 12 weeks may be granted for members with pretreatment hemoglobin < 10 g/dL.

B. Anemia Due to Myelosuppressive Chemotherapy

Authorization of 12 weeks may be granted for members with nonmyeloid malignancy with pretreatment hemoglobin < 10 g/dL

C. Anemia in MDS

Authorization of 12 weeks may be granted for members with pretreatment hemoglobin < 10 g/dL whose pretreatment serum EPO level is < 500 mU/mL.

D. Reduction of Allogeneic Red Blood Cell Transfusion in Patients Undergoing Elective, Noncardiac, Nonvascular Surgery

Authorization of 30 days may be granted for members scheduled to have an elective, noncardiac, nonvascular surgery when the pretreatment hemoglobin is ≤ 13 g/dL.

E. Anemia in Congestive Heart Failure (CHF)

Authorization of 12 weeks may be granted for members with pretreatment hemoglobin < 9 g/dL.

F. Anemia in Rheumatoid Arthritis (RA)

Authorization of 12 weeks may be granted for members with pretreatment hemoglobin < 10 g/dL.

G. Anemia Due to Hepatitis C Treatment

Authorization of 12 weeks may be granted for members with pretreatment hemoglobin < 10 g/dL who are receiving ribavirin in combination with either interferon alfa or peginterferon alfa.

H. Anemia Due to Zidovudine in HIV-infected Patients

Authorization of 12 weeks may be granted for members currently receiving zidovudine with pretreatment hemoglobin < 10 g/dL whose pretreatment serum EPO level is < 500 mU/mL.

I. Anemia in Members Whose Religious Beliefs Forbid Blood Transfusions

Authorization of 12 weeks may be granted for members with pretreatment hemoglobin < 10 g/dL.

J. Anemia in Primary Myelofibrosis (MF), Post-polycythemia Vera MF, and Post-Essential Thrombocythemia MF

Authorization of 12 weeks may be granted for members who meet ALL of the following criteria:

1. Pretreatment hemoglobin < 10 g/dL
2. Pretreatment serum erythropoietin level < 500 mU/mL

K. Anemia Due to Cancer

Authorization of 12 weeks may be granted for members who have cancer and are undergoing palliative treatment

III. CONTINUATION OF THERAPY

Note: Requirements regarding current hemoglobin level exclude values due to a recent transfusion. Members may not use Epogen/Procrit/Retacrit concomitantly with other erythropoiesis stimulating agents.

For all indications below: all members (including new members) requesting authorization for continuation of therapy after at least 12 weeks of ESA treatment must show a response with a rise in hemoglobin of ≥ 1 g/dL. Members who completed less than 12 weeks of ESA treatment and have not yet responded with a rise in

hemoglobin of ≥ 1 g/dL may be granted authorization of up to 12 weeks to allow for sufficient time to demonstrate a response.

A. Anemia Due to CKD

Authorization of 12 weeks may be granted for continuation of therapy when the current hemoglobin is ≤ 12 g/dL.

B. Anemia Due to Myelosuppressive Chemotherapy

Authorization of 12 weeks may be granted for the continuation of therapy in members with nonmyeloid malignancy with current hemoglobin is < 12 g/dL.

C. Anemia in MDS

Authorization of 12 weeks may be granted for continuation of treatment when the current hemoglobin is ≤ 12 g/dL

D. Anemia in CHF, RA

Authorization of 12 weeks may be granted for continuation of treatment when the current hemoglobin is ≤ 12 g/dL.

E. Anemia Due to Hepatitis C Treatment

Authorization of 12 weeks may be granted for continuation of treatment when the member meets ALL of the following criteria:

1. The member is receiving ribavirin in combination with either interferon alfa or peginterferon alfa
2. The current hemoglobin is ≤ 12 g/dL.

F. Anemia Due to Zidovudine in HIV-infected Patients

Authorization of 12 weeks may be granted for continuation of therapy in members receiving zidovudine when the current hemoglobin is ≤ 12 g/dL.

G. Anemia in Members Whose Religious Beliefs Forbid Blood Transfusions

Authorization of 12 weeks may be granted for continuation of treatment when the current hemoglobin is ≤ 12 g/dL.

H. Anemia in Primary Myelofibrosis, Post-polycythemia Vera Myelofibrosis, and Post-Essential Thrombocythemia Myelofibrosis

Authorization of 12 weeks may be granted for continuation of treatment when the current hemoglobin is ≤ 12 g/dL.

I. Anemia Due to Cancer

Authorization of 12 weeks may be granted for members who have cancer and are undergoing palliative treatment

IV. REFERENCES

1. Epogen [package insert]. Thousand Oaks, CA: Amgen Inc.; July 2018.
2. Procrit [package insert]. Horsham, PA: Janssen Products.; July 2018.
3. Retacrit [package insert]. Lake Forest, IL: Hospira Inc.; May 2018
4. National Comprehensive Cancer Network. The NCCN Drugs & Biologics Compendium. <http://www.nccn.org>. Accessed September 19, 2018.
5. Micromedex Solutions [database online]. Ann Arbor, MI: Truven Health Analytics Inc. Updated periodically. www.micromedexsolutions.com [available with subscription]. Accessed September 19, 2018.

Reference number(s)
1619-A

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SPECIALTY GUIDELINE MANAGEMENT

Flolan (epoprostenol for injection) Veletri (epoprostenol for injection) epoprostenol for injection (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Epoprostenol/Flolan/Veletri is indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group I) to improve exercise capacity. Studies establishing effectiveness included predominantly patients with NYHA Functional Class III-IV symptoms and etiologies of idiopathic or heritable PAH or PAH associated with connective tissue diseases.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Indefinite authorization may be granted for treatment of PAH when ALL of the following criteria are met:

- A. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
- B. PAH was confirmed by either criterion (1) or criterion (2) below:
 1. Pretreatment right heart catheterization with all of the following results:
 - i. mPAP \geq 25 mmHg
 - ii. PCWP \leq 15 mmHg
 - iii. PVR $>$ 3 Wood units
 2. For infants less than one year of age with any of the following conditions, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed:
 - i. Post cardiac surgery
 - ii. Chronic heart disease
 - iii. Chronic lung disease associated with prematurity
 - iv. Congenital diaphragmatic hernia

III. CONTINUATION OF THERAPY

Indefinite authorization may be granted for members with an indication listed in Section II who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

IV. APPENDIX

WHO Classification of Pulmonary Hypertension**1 PAH**

- 1.1 Idiopathic (PAH)
- 1.2 Heritable PAH
- 1.3 Drug- and toxin-induced PAH
- 1.4. PAH associated with:
 - 1.4.1 Connective tissue diseases
 - 1.4.2 HIV infection
 - 1.4.3 Portal hypertension
 - 1.4.4 Congenital heart diseases
 - 1.4.5 Schistosomiasis
- 1.5 PAH long-term responders to calcium channel blockers
- 1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement
- 1.7 Persistent PH of the newborn syndrome

2 PH due to left heart disease

- 2.1 PH due to heart failure with preserved LVEF
- 2.2 PH due to heart failure with reduced LVEF
- 2.3 Valvular heart disease
- 2.4 Congenital/acquired cardiovascular conditions leading to post-capillary PH

3 PH due to lung diseases and/or hypoxia

- 3.1 Obstructive lung disease
- 3.2 Restrictive lung disease
- 3.3 Other lung disease with mixed restrictive/obstructive pattern
- 3.4 Hypoxia without lung disease
- 3.5 Developmental lung disorders

4 PH due to pulmonary artery obstruction

- 4.1 Chronic thromboembolic PH
- 4.2 Other pulmonary artery obstructions
 - 4.2.1 Sarcoma (high or intermediate grade) or angiosarcoma
 - 4.2.2 Other malignant tumors
 - Renal carcinoma
 - Uterine carcinoma
 - Germ cell tumours of the testis
 - Other tumours
 - 4.2.3 Non-malignant tumours
 - Uterine leiomyoma
 - 4.2.4 Arteritis without connective tissue disease
 - 4.2.5 Congenital pulmonary artery stenosis
 - 4.2.6 Parasites
 - Hydatidosis

5 PH with unclear and/or multifactorial mechanisms

- 5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders
- 5.2 Systemic and metabolic disorders: Pulmonary Langerhans cell histiocytosis, Gaucher disease, glycogen storage disease, neurofibromatosis, sarcoidosis
- 5.3 Others: chronic renal failure with or without hemodialysis, fibrosing mediastinitis
- 5.4 Complex congenital heart disease

V. REFERENCES

1. Flolan [package insert]. Research Triangle Park, NC: GlaxoSmithKline; December 2018.

2. Veletri [package insert]. South San Francisco, CA: Actelion Pharmaceuticals US, Inc.; December 2018.
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SPECIALTY GUIDELINE MANAGEMENT

ERBITUX® (cetuximab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Squamous Cell Carcinoma of the Head and Neck (SCCHN)
Erbix is indicated:
 - a. In combination with radiation therapy for the initial treatment of locally or regionally advanced squamous cell carcinoma of the head and neck (SCCHN).
 - b. In combination with platinum-based therapy with fluorouracil for the first-line treatment of patients with recurrent locoregional disease or metastatic SCCHN.
 - c. As a single agent for the treatment of patients with recurrent or metastatic SCCHN for whom prior platinum-based therapy has failed.
2. K-Ras Wild-type, EGFR-expressing Colorectal Cancer (CRC)
Erbix is indicated for the treatment of K-Ras wild-type, epidermal growth factor receptor (EGFR)-expressing, metastatic colorectal cancer (mCRC) as determined by an FDA-approved test:
 - a. In combination with FOLFIRI (irinotecan, fluorouracil, leucovorin) for first-line treatment,
 - b. In combination with irinotecan in patients who are refractory to irinotecan-based chemotherapy,
 - c. As a single agent in patients who have failed oxaliplatin- and irinotecan-based chemotherapy or who are intolerant to irinotecan.

Limitations of Use:

Erbix is not indicated for treatment of Ras-mutant colorectal cancer or when the results of the Ras mutation tests are unknown.

B. Compendial Uses

1. Colorectal cancer
2. Squamous cell carcinoma of the head and neck
3. Occult primary head and neck cancer
4. Penile cancer
5. Squamous cell skin cancer
6. Non-small cell lung cancer

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

- A. Documentation of Ras wild-type status, where applicable.
- B. Documentation of EGFR expression, where applicable.

Reference number(s)
1892-A

III. CRITERIA FOR INITIAL APPROVAL

A. Colorectal Cancer

Authorization of 6 months may be granted for treatment of colorectal cancer, including small bowel adenocarcinoma, appendiceal carcinoma, and anal adenocarcinoma, for unresectable/inoperable, advanced, or metastatic disease when all of the following criteria are met:

1. The *RAS* (*KRAS* and *NRAS*) mutation status is negative (wild-type).
2. Member has not previously experienced clinical failure on panitumumab.

B. Squamous Cell Carcinoma of the Head and Neck

Authorization of 6 months may be granted for treatment of squamous cell carcinoma of the head and neck when any of the following criteria is met:

1. Disease is locally or regionally advanced, unresectable, recurrent, or metastatic.
2. Member is unfit for surgery.
3. Erbitux will be used in combination with radiation.

C. Occult Primary Head and Neck Cancer

Authorization of 6 months may be granted as a single agent for treatment of occult primary head and neck cancer for sequential chemoradiation.

D. Penile Cancer

Authorization of 6 months may be granted as a single agent for subsequent treatment of metastatic penile cancer.

E. Squamous Cell Skin Cancer

Authorization of 6 months may be granted for treatment of squamous cell skin cancer for inoperable positive regional lymph nodes, regional recurrence or distant metastases.

F. Non-Small Cell Lung Cancer (NSCLC)

Authorization of 6 months may be granted for subsequent treatment of recurrent, advanced or metastatic NSCLC when the following criteria are met:

1. Erbitux will be used in combination with afatinib.
2. Erbitux will be used in members with a known sensitizing EGFR mutation following disease progression on EGFR tyrosine kinase inhibitor therapy.

IV. CONTINUATION OF THERAPY

Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES

1. Erbitux [package insert]. Princeton, NJ: Bristol-Meyers Squibb Company; April 2019.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed July 11, 2019.

SPECIALTY GUIDELINE MANAGEMENT

ERIVEDGE (vismodegib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Erivedge is indicated for the treatment of adults with metastatic basal cell carcinoma, or with locally advanced basal cell carcinoma that has recurred following surgery or who are not candidates for surgery, and who are not candidates for radiation.

B. Compendial Uses

Nodal or distant metastatic basal cell carcinoma

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Basal Cell Carcinoma (BCC)

Authorization of 12 months may be granted for the treatment of locally advanced or metastatic basal cell carcinoma.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy for an indication outlined in Section II when there is no evidence of unacceptable toxicity or disease progression on the current regimen.

IV. REFERENCES

1. Erivedge [package insert]. South San Francisco, CA: Genentech USA Inc.; January 2019.
2. The NCCN Drugs & Biologics Compendium™ © 2018 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed October 24, 2018.
3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology® Basal Cell Skin Cancer (Version 1.2019). <https://www.nccn.org>. Accessed October 24, 2018.

SPECIALTY GUIDELINE MANAGEMENT

ERLEADA (apalutamide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

1. Erleada is indicated for the treatment of patients with non-metastatic castration-resistant prostate cancer.
2. Erleada is indicated for the treatment of patients with metastatic castration-sensitive prostate cancer.

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

Coverage will not be provided if the requested medication is used in combination with a second-generation oral anti-androgen (e.g., enzalutamide [Xtandi]) or an oral androgen metabolism inhibitor (e.g., abiraterone acetate [Zytiga]).

III. CRITERIA FOR INITIAL APPROVAL

1. Non-metastatic castration-resistant prostate cancer

Authorization of 12 months may be granted for treatment of non-metastatic castration-resistant prostate cancer when Erleada will be administered with a gonadotropin-releasing hormone (GnRH) analog or after bilateral orchiectomy.

2. Metastatic castration-sensitive prostate cancer

Authorization of 12 months may be granted for treatment of metastatic castration-sensitive prostate cancer when Erleada will be administered with a gonadotropin-releasing hormone (GnRH) analog or after bilateral orchiectomy.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES

1. Erleada [package insert]. Horsham, PA: Janssen Products, LP; September 2019.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

SEGLUROMET
(ertugliflozin / metformin HCl)

STEGLATRO
(ertugliflozin)

STEGLUJAN
(ertugliflozin / sitagliptin)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

Ref # 2454-A
Ref # 2455-A

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Segluromet

Segluromet is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus who are not adequately controlled on a regimen containing ertugliflozin or metformin, or in patients who are already treated with both ertugliflozin and metformin.

Limitations of Use

Segluromet is not recommended in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis.

Steglatro

Steglatro is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use

Steglatro is not recommended in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis.

Steglujan

Steglujan is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both ertugliflozin and sitagliptin is appropriate.

Limitations of Use

Steglujan is not recommended in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis.

Steglujan has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at increased risk for the development of pancreatitis while using Steglujan.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has been receiving the requested drug for at least 3 months AND has demonstrated a reduction in A1c (hemoglobin A1c) since starting this therapy

OR

- Patient has the diagnosis of type 2 diabetes mellitus

AND

- The patient has experienced an inadequate treatment response, intolerance, or contraindication to metformin

OR

- The patient requires combination therapy AND has an A1c (hemoglobin A1c) of 7.5 percent or greater

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Segluromet (ertugliflozin/metformin), Steglatro (ertugliflozin), and Steglujan (ertugliflozin/sitagliptin) are indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Clinical guidelines from the American Diabetes Association and the American Association of Clinical Endocrinologists and American College of Endocrinology for the management of hyperglycemia in type 2 diabetes indicate that metformin monotherapy should be started at diagnosis of type 2 diabetes unless there are contraindications. Metformin is effective and safe, is inexpensive, and may reduce risk of cardiovascular events and death. In patients with contraindications or intolerance of metformin, initial therapy should be based on patient factors; consider a drug from another class.^{6,7}

The clinical guidelines also state that the A1c test is the major tool for assessing glycemic control and has strong predictive value for diabetes complications. Thus, A1c testing should be performed routinely in all patients with diabetes at initial assessment and as part of continuing care. The guidelines set goals for therapeutic effectiveness which must be evaluated frequently (e.g., every 3 months) until stable, using multiple criteria, including A1c. Less frequent monitoring is acceptable once targets are achieved.^{6,7} Therefore, continued use of Segluromet, Steglatro, and Steglujan will be approved for patients who have demonstrated a reduction in A1c (hemoglobin A1c) since starting Segluromet, Steglatro, or Steglujan therapy for at least three months.

If the A1c target is not achieved after approximately 3 months and patient does not have atherosclerotic cardiovascular disease (ASCVD) or chronic kidney disease (CKD), consider a combination of metformin and one of the preferred six treatment options: sulfonylurea, thiazolidinedione, dipeptidyl peptidase 4 (DPP-4) inhibitors, sodium-glucose cotransporter 2 (SGLT2) inhibitors, (glucagon-like peptide 1) (GLP-1) receptor agonists, or basal insulin; the choice of which agent to add is based on drug-specific effects and patient factors. For patients in whom ASCVD, Heart Failure or CKD predominates, the best choice for a second agent is a GLP-1 receptor agonist or SGLT2 inhibitor with demonstrated cardiovascular risk reduction, after consideration of drug-specific and patient factors.^{6,7}

In patients with an initial A1c of 7.5% or greater, or in patients who are unable to achieve their glycemic goals with monotherapy, combination therapy is recommended.⁷

REFERENCES

1. Segluromet [package insert]. Whitehouse Station, NJ: Merck Sharpe & Dohme Corp.; October 2018.
2. Steglatro [package insert]. Whitehouse Station, NJ: Merck Sharpe & Dohme Corp.; October 2018.
3. Steglujan [package insert]. Whitehouse Station, NJ: Merck Sharpe & Dohme Corp.; October 2018.
4. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed June 2019.
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7. Garber AJ, Abrahamson MJ, Barzilay JI, et al. Consensus Statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the Comprehensive Type 2 Diabetes Management Algorithm 2019, *Endocr Pract.* January 2019; 25 (No 1);69-100.

Written by: UM Development (KM)
Date Written: 02/2018
Revised: 07/2018 (no clinical changes); (DFW) 07/2019 (no clinical changes/removed MDC designation from title/document)
Reviewed: Medical Affairs (GAD) 12/2017; (EPA) 01/2018. (CHART) 8/1/2019
External Review: 02/2018, 10/2018, 10/2019

CRITERIA FOR APPROVAL

- | | | | |
|---|--|-----|----|
| 1 | Has the patient been receiving the requested drug for at least 3 months?
[If no, then skip to question 3.] | Yes | No |
| 2 | Has the patient demonstrated a reduction in A1c (hemoglobin A1c) since starting this therapy?
[No further questions.] | Yes | No |
| 3 | Does the patient have a diagnosis of type 2 diabetes mellitus? | Yes | No |
| 4 | Has the patient experienced an inadequate treatment response, intolerance, or contraindication to metformin?
[If yes, then no further questions.] | Yes | No |
| 5 | Does the patient require combination therapy AND have an A1c (hemoglobin A1c) of 7.5 percent or greater? | Yes | No |

Mapping Instructions (2454-A)

	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Go to 3	
2.	Approve, 36 months	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you meet these conditions:</p> <ul style="list-style-type: none"> - You have been receiving the requested drug for at least 3 months - You had a reduction in A1c (hemoglobin A1c) since starting this therapy <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No response to treatment]</p>
3.	Go to 4	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you have type 2 diabetes mellitus. Your request has been denied based on the information we have.</p> <p>[Short Description: No approvable diagnosis]</p>
4.	Approve, 36 months	Go to 5	
5.	Approve, 36 months	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you meet any of these conditions:</p> <ul style="list-style-type: none"> - You have tried metformin and it did not work for you, or you cannot use it - You require combination therapy and you have an A1c (hemoglobin A1c) of 7.5 percent or greater <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No inadequate response, intolerance or contraindication to metformin, no confirmation of combination therapy requirement]</p>

Guidelines for Approval (2455-A)**Duration of Approval 12 Months**

Set 1		Set 2		Set 3	
Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)
1	None	3	1	3	1

2		4		5	4
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Mapping Instructions (2455-A)			
	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Go to 3	
2.	Approve, 12 months	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you meet these conditions:</p> <ul style="list-style-type: none"> - You have been receiving the requested drug for at least 3 months - You had a reduction in A1c (hemoglobin A1c) since starting this therapy <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No response to treatment]</p>
3.	Go to 4	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you have type 2 diabetes mellitus. Your request has been denied based on the information we have.</p> <p>[Short Description: No approvable diagnosis]</p>
4.	Approve, 12 months	Go to 5	
5.	Approve, 12 months	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you meet any of these conditions:</p> <ul style="list-style-type: none"> - You have tried metformin and it did not work for you, or you cannot use it - You require combination therapy and you have an A1c (hemoglobin A1c) of 7.5 percent or greater <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No inadequate response, intolerance or contraindication to metformin, no confirmation of combination therapy requirement]</p>

SPECIALTY GUIDELINE MANAGEMENT

ERWINAZE (asparaginase *Erwinia chrysanthemi*)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Erwinaze is indicated as a component of a multi-agent chemotherapeutic regimen for the treatment of patients with acute lymphoblastic leukemia (ALL) who have developed hypersensitivity to *E. coli*-derived asparaginase.

B. Compendial Uses

1. Extranodal natural killer/T-cell lymphoma, nasal type: as a component of multi-agent chemotherapeutic regimen
2. Lymphoblastic lymphoma (managed in the same manner as ALL)
3. Acute lymphoblastic leukemia (ALL) as induction therapy for adults aged 65 years and older as a component of multi-agent chemotherapeutic regimen, or as a substitute for pegaspargase in cases of systemic allergic reaction or anaphylaxis due to pegaspargase hypersensitivity
4. Pediatric acute lymphoblastic leukemia (ALL) as a substitute for pegaspargase in cases of systemic allergic reaction or anaphylaxis due to pegaspargase hypersensitivity

All other indications are considered experimental/investigational and are not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Acute Lymphoblastic Leukemia (ALL) and Lymphoblastic Lymphoma**

Authorization of 12 months may be granted for the treatment of ALL or lymphoblastic lymphoma when the requested medication will be used in conjunction with multi-agent chemotherapy and any of the following criteria is met:

1. The member has previously received and developed hypersensitivity to an *E. coli*-derived asparaginase (e.g., L-asparaginase, pegaspargase).
2. The requested medication will be used as induction therapy for members age 65 years and older.

B. **Extranodal Natural Killer/T-cell Lymphoma, nasal type**

Authorization of 12 months may be granted for the treatment of extranodal natural killer/T-cell lymphoma, nasal type when the requested medication is used in conjunction with multi-agent chemotherapy.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced disease progression or an unacceptable toxicity while on the current regimen.

IV. REFERENCES

1. Erwinaze [package insert]. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; March 2016.
2. National Comprehensive Cancer Network. The NCCN Drugs & Biologics Compendium. <http://www.nccn.org>. Accessed July 15, 2019.
3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Acute Lymphoblastic Lymphoma. Version 2.2019. http://www.nccn.org/professionals/physician_gls/pdf/all.pdf. Accessed July 15, 2019.
4. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Pediatric Acute Lymphoblastic Leukemia. Version 1.2020. https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf. Accessed July 15, 2019.
5. Erwinaze. Micromedex® (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: <https://www.micromedexsolutions.com>. Accessed July 15, 2019.

SPECIALTY GUIDELINE MANAGEMENT

ESBRIET (pirfenidone)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Esbriet is indicated for the treatment of idiopathic pulmonary fibrosis.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review (where applicable):

- A. Result of a chest high-resolution computed tomography (HRCT) study.
- B. If a lung biopsy is conducted, submit the associated pathology report.

III. CRITERIA FOR INITIAL APPROVAL

Idiopathic Pulmonary Fibrosis (IPF)

Authorization of 12 months may be granted for treatment of idiopathic pulmonary fibrosis when the member has undergone a diagnostic work-up which includes the following:

- A. Other known causes of interstitial lung disease (e.g., domestic and occupational environmental exposures, connective tissue disease, drug toxicity) have been excluded AND
- B. The member has completed a high-resolution computed tomography (HRCT) study of the chest or a lung biopsy which reveals a result consistent with the usual interstitial pneumonia (UIP) pattern, OR has completed an HRCT study of the chest which reveals a result other than the UIP pattern (e.g., probable UIP, indeterminate for UIP) and the diagnosis is supported by a lung biopsy. If a lung biopsy has not been previously conducted, the diagnosis is supported by a multidisciplinary discussion between a radiologist and pulmonologist who are experienced in IPF.

IV. CONTINUATION OF THERAPY

Idiopathic Pulmonary Fibrosis (IPF)

All members (including new members) requesting authorization for continuation of therapy may be granted an authorization of 12 months when the member is currently receiving treatment with Esbriet, excluding when Esbriet is obtained as samples or via manufacturer's patient assistance programs.

Reference number(s)
1881-A

V. OTHER

Note: If the member is a current smoker, they should be counseled on the harmful effects of smoking on pulmonary conditions and available smoking cessation options.

VI. REFERENCES

1. Esbriet [package insert]. South San Francisco, CA: Genentech USA, Inc.; October 2017.
2. Raghu G, Remy-Jardin M, Myers JL, et al. Diagnosis of Idiopathic Pulmonary Fibrosis. An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline. *Am J Respir Crit Care Med*. 2018 Sep 1;198(5):e44-e68.
3. Vancheri C, Kreuter M, Richeldi L, et al. Nintedanib with add-on pirfenidone in idiopathic pulmonary fibrosis: results of the Injourney trial. *Am J Respir Crit Care Med*. 2017 Sept 10. doi: 10.1164/rccm.201706-1301OC. [Epub ahead of print].

SPECIALTY GUIDELINE MANAGEMENT

EVENTITY (romosozumab-aqqg)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Eventity is indicated for the treatment of osteoporosis in postmenopausal women at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapy.

Limitations of Use: Limit duration of use to 12 monthly doses. If osteoporosis therapy remains warranted, continued therapy with an anti-resorptive agent should be considered.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Supporting chart notes or medical record indicating a history of fragility fractures, T-score, and FRAX fracture probability as applicable to section III.

III. CRITERIA FOR INITIAL APPROVAL

Postmenopausal osteoporosis treatment

Authorization of a total of 12 months may be granted to postmenopausal members with osteoporosis when ANY of the following criteria are met:

- A. Member has a history of fragility fractures
- B. Member has a pre-treatment T-score less than or equal to -2.5 OR member has osteopenia (i.e., pre-treatment T-score greater than -2.5 and less than -1) with a high pre-treatment FRAX fracture probability (See Appendix B) and meets ANY of the following criteria:
 1. Member has indicators of higher fracture risk (e.g., advanced age, frailty, glucocorticoid use, very low T-scores [less than or equal to -3.5], or increased fall risk)
 2. Member has failed prior treatment with or is intolerant to previous injectable osteoporosis therapy (e.g., zoledronic acid [Reclast], teriparatide [Forteo], denosumab [Prolia])
 3. Member has had an oral bisphosphonate trial of at least 1-year duration or there is a clinical reason to avoid treatment with an oral bisphosphonate (See Appendix A)

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria AND have received less than 12 monthly doses of Evenity.

V. APPENDIX

Appendix A. Clinical reasons to avoid oral bisphosphonate therapy

- Esophageal abnormality that delays emptying such as stricture of achalasia
- Active upper gastrointestinal problem (e.g., dysphagia, gastritis, duodenitis, erosive esophagitis, ulcers)
- Inability to stand or sit upright for at least 30 to 60 minutes
- Inability to take at least 30 to 60 minutes before first food, drink, or medication of the day
- Renal insufficiency (creatinine clearance <35 mL/min)
- History of intolerance to an oral bisphosphonate

Appendix B. WHO Fracture Risk Assessment Tool

- High FRAX fracture probability: 10 year major osteoporotic fracture risk $\geq 20\%$ or hip fracture risk $\geq 3\%$.
- 10-year probability; calculation tool available at: <https://www.sheffield.ac.uk/FRAX/>
- The estimated risk score generated with FRAX should be multiplied by 1.15 for major osteoporotic fracture and 1.2 for hip fracture if glucocorticoid treatment is greater than 7.5 mg per day.

VI. REFERENCES

1. Evenity [package insert]. Thousand Oaks, CA: Amgen; April 2019.
2. Bisphosphonates. *Drug Facts and Comparisons*. Facts & Comparisons [database online]. St. Louis, MO: Wolters Kluwer Health Inc; March 21, 2019. Accessed April 10, 2019.
3. Cosman F, de Beur SJ, LeBoff MS, et al. National Osteoporosis Foundation. Clinician's guide to prevention and treatment of osteoporosis. *Osteoporos Int*. 2014;25(10): 2359-2381.
4. Jeremiah MP, Unwin BK, Greenwald MH, et al. Diagnosis and management of osteoporosis. *Am Fam Physician*. 2015;92(4):261-268.
5. Watts NB, Bilezikian JP, Camacho PM, et al. American Association of Clinical Endocrinologists medical guidelines for clinical practice for the diagnosis and treatment of postmenopausal osteoporosis. *Endocr Pract*. 2016;22 (Suppl 4):1-42.
6. ACOG Practice Bulletin Number 129: Osteoporosis. *Obstet Gynecol*. 2012;120(3):718-734.
7. National Institute for Health and Care Excellence. Osteoporosis Overview. Last updated February 2018. Available at: <http://pathways.nice.org.uk/pathways/osteoporosis>. Accessed April 10, 2019.
8. Treatment to prevent osteoporotic fractures: an update. Department of Health and Human Services, Agency for Healthcare Research and Quality. 2012; Publication No. 12-EHC023-EF. Available at <https://www.effectivehealthcare.ahrq.gov/lbd.cfm>.
9. FRAX® WHO fracture risk assessment tool. © World Health Organization Collaborating Centre for Metabolic Bone Diseases: University of Sheffield, UK. Available at: <https://www.sheffield.ac.uk/FRAX/>. Accessed April 10, 2019.
10. Fink HA, Gordon G, Buckley L, et al. 2017 American College of Rheumatology Guidelines for the Prevention and Treatment of Glucocorticoid-Induced Osteoporosis. *Arthritis Care Res*. 2017;69:1521-1537.
11. Ensrud KE, Crandall CJ. Osteoporosis. *Ann Intern Med* 2017;167(03):ITC17–ITC32.

SPECIALTY GUIDELINE MANAGEMENT

EXONDYS 51 (eteplirsen)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Exondys 51 is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the *DMD* gene that is amenable to exon 51 skipping.

This indication is approved under accelerated approval based on an increase in dystrophin in skeletal muscle observed in some patients treated with Exondys 51. A clinical benefit of Exondys 51 has not been established. Continued approval for this indication may be contingent upon verification of a clinical benefit in confirmatory trials.

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
Laboratory confirmation of DMD diagnosis with a *DMD* gene mutation that is amenable to exon 51 skipping (refer to examples in Appendix)

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a physician who specializes in treatment of DMD.

IV. CRITERIA FOR INITIAL APPROVAL

Duchenne Muscular Dystrophy

Authorization of 6 months may be granted for treatment of DMD when all of the following criteria are met:

1. Genetic testing was conducted to confirm the diagnosis of DMD and to identify the specific type of *DMD* gene mutation.
2. The *DMD* gene mutation is amenable to exon 51 skipping (refer to examples in Appendix).
3. Treatment with Exondys 51 is initiated before the age of 14.
4. Member is able to achieve an average distance of at least 180 meters while walking independently over 6 minutes.

V. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members requesting continuation of therapy when the member has demonstrated a response to therapy as evidenced by remaining ambulatory (e.g., able to walk with or without assistance, not wheelchair dependent).

VI. APPENDIX

Examples of *DMD* gene mutations (exon deletions) amenable to exon 51 skipping

1. Deletion of exon 50
2. Deletion of exon 52
3. Deletion of exons 45-50
4. Deletion of exons 47-50
5. Deletion of exons 48-50
6. Deletion of exons 49-50

VII. REFERENCES

1. Exondys 51 [package insert]. Cambridge, MA: Sarepta Therapeutics, Inc.; October 2018.
2. Mendell JR, Rodino-Klapac LR, Sahenk Z, et al. Eteplirsén for the treatment of Duchenne muscular dystrophy. *Ann Neurol*. 2013;74(5):637-47.
3. Cirak S, Arechavala-Gomeza V, Guglieri M, et al. Exon skipping and dystrophin restoration in patients with Duchenne muscular dystrophy after systemic phosphorodiamidate morpholino oligomer treatment: an open-label, phase 2, dose-escalation study. *Lancet*. 2011;378(9791):595-605.
4. Mendell JR, Goemans N, Lowes LP, et al; Eteplirsén Study Group and Telethon Foundation DMD Italian Network. Longitudinal effect of eteplirsén versus historical control on ambulation in Duchenne muscular dystrophy. *Ann Neurol*. 2016;79(2):257-271.
5. Randeree L, Eslick GD. Eteplirsén for paediatric patients with Duchenne muscular dystrophy: A pooled-analysis. *J Clin Neurosci*. 2018;49:1-6.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME EYLEA
(Generic) (aflibercept)

Status: CVS/Caremark Criteria
Type: Initial Prior Authorization

MDC
Ref #811-A

FDA-APPROVED INDICATIONS¹

Eylea is indicated for the treatment of patients with: neovascular (wet) age-related macular degeneration, macular edema following retinal vein occlusion, diabetic macular edema, and diabetic retinopathy.

CRITERIA FOR APPROVAL

1	Does the patient have a diagnosis of wet age-related macular degeneration? [If yes, no further questions.]	Yes	No
2	Does the patient have a diagnosis of macular edema following retinal vein occlusion? [If yes, no further questions.]	Yes	No
3	Does the patient have a diagnosis of diabetic macular edema? [If yes, no further questions.]	Yes	No
4	Does the patient have a diagnosis of diabetic retinopathy?	Yes	No

Guidelines for Approval

Duration of Approval		12 Months	
Set 1: AMD		Set 2: Macular edema RVO	
Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)
1	None	2	1
Set 3: DME		Set 4: Diabetic retinopathy	
Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)
3	1	4	1
	2		2
			3

Internal Use Only – Mapping Instructions

	Yes	No
1.	Approve, 12 months	Go to 2
2.	Approve, 12 months	Go to 3
3.	Approve, 12 months	Go to 4
4.	Approve, 12 months	Deny

RATIONALE

These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to ensure that patients follow selection elements noted in labeling and/or practice guidelines in order to decrease the potential for inappropriate utilization.

REFERENCES

1. Eylea [package insert]. Tarrytown, NY: Regeneron Pharmaceuticals, Inc.; May 2019.

DOCUMENT HISTORY

Written by:	Specialty Clinical Development (WH) 02/2013
Revised:	WH 09/2013 (CMS), KF 07/2014 (label update DME), KF 09/2014 (CMS), KF 11/2014 (label update RVO), TS 03/2015 (label update DR), TS 08/2015 (CMS), PK 02/2016, TS 06/2016 (CMS), PK 07/2017 (CMS), TE 02/2018, KF 05/2019 (label update), TE 06/2019 (CMS)
Reviewed:	CDPR/DNC 02/2013, 01/2014, 08/2014; LCB 11/2014, LMS 03/2015, LCB 02/2016, SD 02/2017, LMS 02/2018, EPA 05/2019
External Review:	06/2013, 04/2014, 06/2015, 04/2016, 05/2017, 05/2018

SPECIALTY GUIDELINE MANAGEMENT

EYLEA (aflibercept)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

- A. Diabetic macular edema
- B. Diabetic retinopathy
- C. Neovascular (wet) age-related macular degeneration
- D. Macular edema following retinal vein occlusion

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Diabetic Macular Edema

Authorization of 6 months may be granted for treatment of diabetic macular edema.

B. Diabetic Retinopathy

Authorization of 6 months may be granted for treatment of diabetic retinopathy.

C. Neovascular (Wet) Age-Related Macular Degeneration

Authorization of 6 months may be granted for treatment of neovascular (wet) age-related macular degeneration.

D. Macular Edema Following Retinal Vein Occlusion

Authorization of 6 months may be granted for treatment of macular edema following retinal vein occlusion.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment of an indication listed in Section II for members who have demonstrated a positive clinical response to therapy (e.g., improvement or maintenance in best corrected visual acuity [BCVA] or visual field, or a reduction in the rate of vision decline or the risk of more severe vision loss).

IV. REFERENCES

1. Eylea [package insert]. Tarrytown, NY: Regeneron Pharmaceuticals; August 2019.
2. American Academy of Ophthalmology Retinal/Vitreous Panel. Preferred Practice Pattern® Guidelines. Age-Related Macular Degeneration. San Francisco, CA: American Academy of Ophthalmology; 2015. Available at: <https://www.aao.org/preferred-practice-pattern/age-related-macular-degeneration-ppp-2015>

Reference number(s)
2024-A

3. American Academy of Ophthalmology Retinal/Vitreous Panel. Preferred Practice Pattern® Guidelines. Diabetic Retinopathy. San Francisco, CA: American Academy of Ophthalmology; 2017. Available at: <https://www.aao.org/preferred-practice-pattern/diabetic-retinopathy-ppp-updated-2017>
4. American Academy of Ophthalmology Retinal/Vitreous Panel. Preferred Practice Pattern® Guidelines. Retinal Vein Occlusions. San Francisco, CA: American Academy of Ophthalmology; 2015. Available at: <https://www.aao.org/preferred-practice-pattern/retinal-vein-occlusions-ppp-2015>

SPECIALTY GUIDELINE MANAGEMENT

FABRAZYME (agalsidase beta)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Fabrazyme is indicated for use in patients with Fabry disease. Fabrazyme reduces globotriaosylceramide (GL-3) deposition in capillary endothelium of the kidney and certain other cell types.

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: alpha-galactosidase enzyme assay or genetic testing results supporting diagnosis. In the case of obligate carriers, the documentation must be submitted for the parent.

III. CRITERIA FOR INITIAL APPROVAL

Fabry disease

Authorization for 12 months may be granted for treatment of Fabry disease when both of the following criteria are met:

- A. The diagnosis of Fabry disease was confirmed by enzyme assay demonstrating a deficiency of alpha-galactosidase enzyme activity or by genetic testing, or the member is a symptomatic obligate carrier.
- B. Fabrazyme will not be used in combination with Galafold.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for Fabry disease who are responding to therapy (e.g., reduction in plasma globotriaosylceramide [GL-3] or GL-3 inclusions).

V. REFERENCES

1. Fabrazyme [package insert]. Cambridge, MA: Genzyme Corporation; December 2018.
2. Desnick RJ, Brady RO. Fabry disease in childhood. *J Pediatr.* 2004;144(5 Suppl):S20-S26.
3. Biegstraaten M, Arngimsson R, Barbey F, et al. Recommendations for initiation and cessation of enzyme replacement therapy in patients with Fabry disease: the European Fabry Working Group consensus document. *Orphanet J Rare Dis.* 2015; 1036.
4. Desnick RJ, Brady R, Barranger J, et al. Fabry disease, an under-recognized multisystemic disorder: expert recommendations for diagnosis, and enzyme replacement therapy. *Ann Intern Med.* 2003; 138(4):338.

Reference number
2054-A

5. Sirrs, S, Bichet DG, Iwanochko RM, et al. Canadian Fabry disease treatment guidelines 2016.

SPECIALTY GUIDELINE MANAGEMENT

REBINYN (coagulation factor IX [recombinant], glycoPEGylated)

IDELVION (coagulation factor IX [recombinant], albumin fusion protein)

ALPROLIX (coagulation factor IX [recombinant], Fc fusion protein)

BENEFIX, IXINITY, RIXUBIS (coagulation factor IX [recombinant])

ALPHANINE SD, MONONINE (coagulation factor IX [human])

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Hemophilia B

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Hemophilia B

Indefinite authorization may be granted for treatment of hemophilia B.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Alprolix [package insert]. Cambridge, MA: Biogen Idec Inc.; June 2018.
2. BeneFix [package insert]. Philadelphia, PA: Wyeth Pharmaceuticals Inc.; June 2016.
3. Ixinity [package insert]. Berwyn, PA: Aptevio BioTherapeutics LLC, April 2018.
4. Rixubis [package insert]. Lexington, MA: Baxalta US Inc.; May 2018.
5. AlphaNine SD [package insert]. Los Angeles, CA: Grifols Biologicals Inc.; June 2018.
6. Mononine [package insert]. Kankakee, IL: CSL Behring LLC; April 2016.

Reference number(s)
1944-A

7. Idelvion [package insert]. Kankakee, IL: CSL Behring LLC; May 2018
8. Rebinyn [package insert]. DK-2880 Bagsvaerd, Denmark: Novo Nordisk A/S; May 2017.
9. Srivastava A, Brewer A, Street A, et al. Guidelines for the management of hemophilia. *Haemophilia: The Official Journal Of The World Federation Of Hemophilia* [serial online]. January 2013;19(1):e1-e47. Available from: MEDLINE Complete, Ipswich, MA. Accessed December 18, 2018.
10. National Hemophilia Foundation. MASAC recommendations concerning products licensed for the treatment of hemophilia and other bleeding disorders. Revised April 2018. MASAC Document # 253. Accessed December 18, 2018.

SPECIALTY GUIDELINE MANAGEMENT

REBINYN (coagulation factor IX [recombinant], glycoPEGylated)

IDELVION (coagulation factor IX [recombinant], albumin fusion protein)

ALPROLIX (coagulation factor IX [recombinant], Fc fusion protein)

BENEFIX, IXINITY, RIXUBIS (coagulation factor IX [recombinant])

ALPHANINE SD, MONONINE (coagulation factor IX [human])

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Hemophilia B

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Hemophilia B

Indefinite authorization may be granted for treatment of hemophilia B.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Alprolix [package insert]. Waltham, MA: Bioverativ Therapeutics Inc.; July 2019.
2. BeneFIX [package insert]. Philadelphia, PA: Wyeth Pharmaceuticals Inc.; July 2019.
3. Ixinity [package insert]. Seattle, WA: Aptevo BioTherapeutics LLC, December 2018.
4. Rixubis [package insert]. Lexington, MA: Baxalta US Inc.; May 2018.
5. AlphaNine SD [package insert]. Los Angeles, CA: Grifols Biologicals LLC; June 2018.
6. Mononine [package insert]. Kankakee, IL: CSL Behring LLC; December 2018.

Reference number(s)
1944-A

7. Idelvion [package insert]. Kankakee, IL: CSL Behring LLC; October 2019.
8. Rebinyn [package insert]. DK-2880 Bagsvaerd, Denmark: Novo Nordisk A/S; June 2017.
9. Srivastava A, Brewer AK, Mauser-Bunschoten EP, et al. Guidelines for the management of hemophilia. *Haemophilia*. 2013;19(1):e1-e47.
10. National Hemophilia Foundation. MASAC recommendations concerning products licensed for the treatment of hemophilia and other bleeding disorders. Revised April 2018. MASAC Document #253. Accessed December 3, 2019.

Reference number(s)
1941-A
1949-A

SPECIALTY GUIDELINE MANAGEMENT

BEBULIN, PROFILNINE (factor IX complex [human])

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Hemophilia B

B. Compendial Uses

1. Bleeding due to low levels of liver-dependent coagulation factors
2. Factor X deficiency (Bebulin only)
3. Factor II deficiency (Profilnine only)

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

1. Hemophilia B

Indefinite authorization may be granted for treatment of hemophilia B.

2. Bleeding Due to Low Levels of Liver-dependent Coagulation Factors

Indefinite authorization may be granted for treatment of bleeding due to low levels of liver-dependent coagulation factors.

3. Factor X Deficiency

Indefinite authorization of Bebulin may be granted for treatment of factor X deficiency.

4. Factor II Deficiency

Indefinite authorization of Profilnine may be granted for treatment of factor II deficiency.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Bebulin [package insert]. Westlake Village, CA: Baxalta US Inc.; September 2015.

Reference number(s)
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2. Profilnine [package insert]. Los Angeles, CA: Grifols Biologicals, Inc.; March 2017.
3. Micromedex Solutions [database online]. Ann Arbor, MI: Truven Health Analytics Inc. Updated periodically. www.micromedexsolutions.com [available with subscription]. Accessed December 11, 2018.
4. National Hemophilia Foundation. MASAC recommendations concerning products licensed for the treatment of hemophilia and other bleeding disorders. Revised April 2018. MASAC Document # 253. Accessed December 18, 2018.
5. Brown DL, Kouides PA. Diagnosis and treatment of inherited factor X deficiency. *Haemophilia*. 2008;14:1176-1182.

Reference number(s)
1941-A
1949-A

SPECIALTY GUIDELINE MANAGEMENT

BEBULIN, PROFILNINE (factor IX complex [human])

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Hemophilia B

B. Compendial Uses

1. Bleeding due to low levels of liver-dependent coagulation factors
2. Factor X deficiency (Bebulin only)
3. Factor II deficiency (Profilnine only)

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

1. Hemophilia B

Indefinite authorization may be granted for treatment of hemophilia B.

2. Bleeding Due to Low Levels of Liver-dependent Coagulation Factors

Indefinite authorization may be granted for treatment of bleeding due to low levels of liver-dependent coagulation factors.

3. Factor X Deficiency

Indefinite authorization of Bebulin may be granted for treatment of factor X deficiency.

4. Factor II Deficiency

Indefinite authorization of Profilnine may be granted for treatment of factor II deficiency.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Bebulin [package insert]. Westlake Village, CA: Baxalta US Inc.; September 2015.

Reference number(s)
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1949-A

2. Profilnine [package insert]. Los Angeles, CA: Grifols Biologicals, LLC; June 2018.
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Reference number(s)
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1938-A
1946-A
1939-A
1945-A
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SPECIALTY GUIDELINE MANAGEMENT

FACTOR VIII CONCENTRATES

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

Table: Factor VIII Concentrates and Covered Uses

Brand	Generic	FDA-Approved Indication(s)	Compendial Indication(s)
<i>Recombinant Factor VIII Concentrates</i>			
Advate	antihemophilic factor [recombinant]	Hemophilia A	Acquired Hemophilia A
Afstyla	antihemophilic factor [recombinant], single chain	Hemophilia A	
Helixate FS	antihemophilic factor [recombinant]	Hemophilia A	Acquired Hemophilia A
Kogenate FS	antihemophilic factor [recombinant]	Hemophilia A	Acquired Hemophilia A
Kovaltry	antihemophilic factor [recombinant]	Hemophilia A	
Novoeight	antihemophilic factor [recombinant]	Hemophilia A	
Nuwiq	antihemophilic factor [recombinant]	Hemophilia A	
Recombinate	antihemophilic factor [recombinant]	Hemophilia A	Acquired Hemophilia A
Xyntha	antihemophilic factor [recombinant]	Hemophilia A	Acquired Hemophilia A
<i>Extended Half-life Recombinant Factor VIII Concentrate</i>			
Adynovate	antihemophilic factor [recombinant], PEGylated	Hemophilia A	
Eloctate	antihemophilic factor [recombinant], Fc fusion protein	Hemophilia A	
Jivi	antihemophilic factor [recombinant], PEGylated-aucI	Hemophilia A	
<i>Human Plasma-Derived Factor VIII Concentrates</i>			
Hemofil M Monoclate-P	antihemophilic factor [human] monoclonal antibody purified	Hemophilia A	Acquired Hemophilia A
<i>Human Plasma-Derived Factor VIII Concentrates That Contain Von Willebrand Factor</i>			
Alphanate Humate-P	antihemophilic factor/von Willebrand factor complex [human]	Hemophilia A, von Willebrand Disease	Acquired Hemophilia A, Acquired von Willebrand Syndrome

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Koate	antihemophilic factor [human]	Hemophilia A	Acquired Hemophilia A, von Willebrand Disease
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All other indications are considered experimental/investigational and not medically necessary.

CRITERIA FOR INITIAL APPROVAL

A. Hemophilia A

Indefinite authorization of Advate, Adynovate, Afstyla, Alphanate, Eloctate, Helixate FS, Hemofil M, Humate-P, Koate, Kogenate FS, Kovaltry, Monoclate-P, Novoeight, Nuwiq, Recombinate or Xyntha may be granted for treatment of hemophilia A when either of the following criteria is met:

1. Member has mild disease (see Appendix A) and has had an insufficient response to desmopressin or a documented clinical reason for not using desmopressin (see Appendix B).
2. Member has moderate or severe disease (see Appendix A).

Indefinite authorization of Jivi may be granted for treatment of hemophilia A when both of the following criteria are met:

1. Member has previously received treatment for hemophilia A with a factor VIII product.
2. Member is ≥ 12 years of age.

B. Von Willebrand Disease

Indefinite authorization of Alphanate, Humate-P or Koate may be granted for treatment of vWD when any of the following criteria is met:

1. Member has type 1, 2A, 2M, or 2N vWD and has had an insufficient response to desmopressin or a documented clinical reason for not using desmopressin (see Appendix B).
2. Member has type 2B or type 3 vWD.

C. Acquired Hemophilia A

Indefinite authorization of Advate, Alphanate, Helixate FS, Hemofil M, Humate-P, Koate, Kogenate FS, Monoclate-P, Recombinate or Xyntha may be granted for treatment of acquired hemophilia A.

D. Acquired von Willebrand Syndrome

Indefinite authorization of Alphanate or Humate-P may be granted for treatment of acquired von Willebrand syndrome.

II. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

III. APPENDICES

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Appendix A: Classification of Hemophilia by Clotting Factor Level (% Activity) and Bleeding Episodes

Severity	Clotting Factor Level % activity*	Bleeding Episodes
Severe	<1%	Spontaneous bleeding episodes, predominantly into joints and muscles Severe bleeding with trauma, injury or surgery
Moderate	1% to 5%	Occasional spontaneous bleeding episodes Severe bleeding with trauma, injury or surgery
Mild	6% to 40%	Severe bleeding with serious injury, trauma or surgery

*Factor assay levels are required to determine the diagnosis and are of value in monitoring treatment response.

Appendix B: Clinical Reasons For Not Utilizing Desmopressin in Patients with Hemophilia A and Type 1, 2A, 2N and 2M vWD

- Age < 2 years
- Pregnancy
- Fluid/electrolyte imbalance
- High risk for cardiovascular or cerebrovascular disease (especially the elderly)
- Predisposition to thrombus formation
- Trauma requiring surgery
- Life-threatening bleed
- Contraindication or intolerance to desmopressin
- Severe type 1 von Willebrand disease

IV. REFERENCES

- Advate [package insert]. Westlake Village, CA: Baxter Healthcare Corporation; November 2016.
- Helixate FS [package insert]. Whippany, NJ: Bayer HealthCare LLC; May 2016.
- JIVI [package insert]. Whippany, NJ: Bayer HealthCare LLC; August 2018.
- Kogenate FS [package insert]. Whippany, NJ: Bayer HealthCare LLC; May 2016.
- Kogenate FS with BIO-SET [package insert]. Whippany, NJ: Bayer HealthCare LLC; May 2016.
- Kogenate FS with Vial Adapter [package insert]. Whippany, NJ: Bayer HealthCare LLC; May 2016.
- Kovaltry [package insert]. Whippany, NJ: Bayer Healthcare LLC; March 2016.
- Novoeight [package insert]. Plainsboro, NJ: Novo Nordisk Inc.; November 2018.
- Nuwiq [package insert]. Hoboken, NJ: Octapharma USA, Inc.; July 2017.
- Recombinant with 5 mL Sterile Water for Injection [package insert]. Westlake Village, CA: Baxter Healthcare Corporation; November 2015.
- Xyntha [package insert]. Philadelphia, PA: Wyeth Pharmaceuticals Inc.; October 2014.
- Xyntha Solufuse [package insert]. Philadelphia, PA: Wyeth Pharmaceuticals Inc.; October 2014.
- Adynovate [package insert]. Westlake Village, CA: Baxalta US Inc.; March 2017.
- Afstyla [package insert]. Marburg, Germany: CSL Behring GmbH. September 2017.
- Eloctate [package insert]. Cambridge, MA: Biogen Idec Inc.; December 2017.
- Hemofil M [package insert]. Westlake Village, CA: Baxalta US Inc.; March 2017.
- Monoclate-P [package insert]. Kankakee, IL: CSL Behring LLC; February 2014.
- Alphanate [package insert]. Los Angeles, CA: Grifols Biologicals Inc.; March 2017.
- Humate-P [package insert]. Kankakee, IL: CSL Behring LLC; September 2017.
- Koate [package insert]. Research Triangle Park, NC: Grifols Therapeutics Inc.; February 2016.

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26. National Hemophilia Foundation. MASAC recommendations concerning products licensed for the treatment of hemophilia and other bleeding disorders. Revised April 2018. MASAC Document # 253. Accessed December 12, 2018.
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28. *Acquired hemophilia*. World Federation of Hemophilia. <http://www1.wfh.org/publications/files/pdf-1186.pdf>. Accessed December 12, 2018.
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30. Franchini M, Mannucci PM. Acquired haemophilia A: a 2013 update. *Thromb Haemost*. 2013;110(6):1114-20.
31. National Hemophilia Foundation. Hemophilia A (Factor VIII Deficiency). Available at: <http://www.hemophilia.org/NHFWeb/MainPgs/MainNHF.aspx?menuid=180&contentid=45&rptname=bleeding>. Accessed December 12, 2018.
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1946-A
1939-A
1945-A
2688-A

SPECIALTY GUIDELINE MANAGEMENT

FACTOR VIII CONCENTRATES

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

Table: Factor VIII Concentrates and Covered Uses

Brand	Generic	FDA-Approved Indication(s)	Compendial Indication(s)
Recombinant Factor VIII Concentrates			
Advate	antihemophilic factor [recombinant]	Hemophilia A	Acquired Hemophilia A
Afstyla	antihemophilic factor [recombinant], single chain	Hemophilia A	
Helixate FS	antihemophilic factor [recombinant]	Hemophilia A	Acquired Hemophilia A
Kogenate FS	antihemophilic factor [recombinant]	Hemophilia A	Acquired Hemophilia A
Kovaltry	antihemophilic factor [recombinant]	Hemophilia A	
Novoeight	antihemophilic factor [recombinant]	Hemophilia A	
Nuwiq	antihemophilic factor [recombinant]	Hemophilia A	
Recombinate	antihemophilic factor [recombinant]	Hemophilia A	Acquired Hemophilia A
Xyntha	antihemophilic factor [recombinant]	Hemophilia A	Acquired Hemophilia A
Extended Half-life Recombinant Factor VIII Concentrate			
Adynovate	antihemophilic factor [recombinant], PEGylated	Hemophilia A	
Eloctate	antihemophilic factor [recombinant], Fc fusion protein	Hemophilia A	
Jivi	antihemophilic factor [recombinant], PEGylated-aucl	Hemophilia A	
Esperoct	antihemophilic factor [recombinant], Glycopegylated-exei	Hemophilia A	
Human Plasma-Derived Factor VIII Concentrates			
Hemofil M	antihemophilic factor [human]	Hemophilia A	Acquired Hemophilia A
Monoclate-P	monoclonal antibody purified		
Human Plasma-Derived Factor VIII Concentrates That Contain Von Willebrand Factor			

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Alphanate	antihemophilic factor/von Willebrand factor complex [human]	Hemophilia A, von Willebrand Disease	Acquired Hemophilia A, Acquired von Willebrand Syndrome
Humate-P			
Koate	antihemophilic factor [human]	Hemophilia A	Acquired Hemophilia A, von Willebrand Disease

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Hemophilia A

Indefinite authorization of Advate, Adynovate, Afstyla, Alphanate, Eloctate, Esperoct, Helixate FS, Hemofil M, Humate-P, Koate, Kogenate FS, Kovaltry, Monoclote-P, Novoeight, Nuwiq, Recombinate, or Xyntha may be granted for treatment of hemophilia A when either of the following criteria is met:

1. Member has mild disease (see Appendix A) and has had an insufficient response to desmopressin or a documented clinical reason for not using desmopressin (see Appendix B).
2. Member has moderate or severe disease (see Appendix A).

Indefinite authorization of Jivi may be granted for treatment of hemophilia A when BOTH of the following criteria are met:

1. Member has previously received treatment for hemophilia A with a factor VIII product.
2. Member is ≥ 12 years of age.

B. Von Willebrand Disease

Indefinite authorization of Alphanate, Humate-P, or Koate may be granted for treatment of VWD when any of the following criteria is met:

1. Member has type 1, 2A, 2M, or 2N VWD and has had an insufficient response to desmopressin or a documented clinical reason for not using desmopressin (see Appendix B).
2. Member has type 2B or type 3 VWD.

C. Acquired Hemophilia A

Indefinite authorization of Advate, Alphanate, Helixate FS, Hemofil M, Humate-P, Koate, Kogenate FS, Monoclote-P, Recombinate, or Xyntha or may be granted for treatment of acquired hemophilia A.

D. Acquired von Willebrand Syndrome

Indefinite authorization of Alphanate or Humate-P may be granted for treatment of acquired von Willebrand syndrome.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

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IV. APPENDICES

Appendix A: Classification of Hemophilia by Clotting Factor Level (% Activity) and Bleeding Episodes

Severity	Clotting Factor Level % activity*	Bleeding Episodes
Severe	<1%	Spontaneous bleeding episodes, predominantly into joints and muscles Severe bleeding with trauma, injury or surgery
Moderate	1% to 5%	Occasional spontaneous bleeding episodes Severe bleeding with trauma, injury or surgery
Mild	6% to 40%	Severe bleeding with serious injury, trauma or surgery

*Factor assay levels are required to determine the diagnosis and are of value in monitoring treatment response.

Appendix B: Clinical Reasons For Not Utilizing Desmopressin in Patients with Hemophilia A and Type 1, 2A, 2M and 2N VWD

- Age < 2 years
- Pregnancy
- Fluid/electrolyte imbalance
- High risk for cardiovascular or cerebrovascular disease (especially the elderly)
- Predisposition to thrombus formation
- Trauma requiring surgery
- Life-threatening bleed
- Contraindication or intolerance to desmopressin
- Severe type 1 von Willebrand disease

V. REFERENCES

- Advate [package insert]. Lexington, MA: Baxalta US Inc.; December 2018.
- Helixate FS [package insert]. Whippany, NJ: Bayer HealthCare LLC; May 2016.
- Jivi [package insert]. Whippany, NJ: Bayer HealthCare LLC; August 2018.
- Kogenate FS [package insert]. Whippany, NJ: Bayer HealthCare LLC; May 2016.
- Kogenate FS with BIO-SET [package insert]. Whippany, NJ: Bayer HealthCare LLC; May 2016.
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- Kovaltry [package insert]. Whippany, NJ: Bayer Healthcare LLC; March 2016.
- Novoeight [package insert]. Plainsboro, NJ: Novo Nordisk Inc.; November 2018.
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- Recombinant with 5 mL Sterile Water for Injection using BAXAJECT II [package insert]. Lexington, MA: Baxalta US Inc.; June 2018.
- Xyntha [package insert]. Philadelphia, PA: Wyeth Pharmaceuticals Inc.; August 2019.
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- Adynovate [package insert]. Lexington, MA: Baxalta US Inc.; May 2018.
- Afstyla [package insert]. Marburg, Germany: CSL Behring GmbH. September 2017R.
- Eloctate [package insert]. Waltham, MA: Bioverativ Therapeutics Inc.; September 2019.
- Hemofil M [package insert]. Lexington, MA: Baxalta US Inc.; June 2018.
- Monoclate-P [package insert]. Kankakee, IL: CSL Behring LLC; September 2018.
- Alphanate [package insert]. Los Angeles, CA: Grifols Biologicals Inc.; June 2018.
- Humate-P [package insert]. Marburg, Germany: CSL Behring GmbH; September 2017.

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25. Federici A, Budde U, Castaman G, Rand J, Tiede A. Current diagnostic and therapeutic approaches to patients with acquired von Willebrand syndrome: a 2013 update. *Semin Thromb Hemost*. 2013;39(2):191-201.
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27. National Hemophilia Foundation. MASAC recommendations concerning products licensed for the treatment of hemophilia and other bleeding disorders. Revised April 2018. MASAC Document # 253. <https://www.hemophilia.org/sites/default/files/document/files/masac253.pdf>. Accessed December 12, 2019.
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32. National Hemophilia Foundation. Hemophilia A (Factor VIII Deficiency). Available at: <http://www.hemophilia.org/NHFWeb/MainPgs/MainNHF.aspx?menuid=180&contentid=45&rptname=bleeding>. Accessed December 12, 2019.
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35. Reding MT, NG HJ, Poulsen LH, et al. Safety and efficacy of BAY 94-9027, a prolonged-half-life factor VIII. *Journal of thrombosis and Haemostasis*. 2017; 15: 411-9.
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SPECIALTY GUIDELINE MANAGEMENT

FARYDAK (panobinostat)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Farydak, in combination with bortezomib and dexamethasone, is indicated for the treatment of patients with multiple myeloma who have received at least 2 prior regimens, including bortezomib and an immunomodulatory agent. This indication is approved under accelerated approval based on progression free survival. Continued approval of this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

B. Compendial Uses

In combination with carfilzomib or in combination with dexamethasone and lenalidomide or in combination with dexamethasone and bortezomib for previously treated multiple myeloma for relapsed or progressive disease in patients who have received at least 2 prior regimens, including bortezomib and an immunomodulatory agent

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Multiple Myeloma

Authorization of 12 months may be granted for the treatment of relapsed or progressive multiple myeloma when the all of the following criteria are met:

- A. The member has received at least two prior regimens, including bortezomib and an immunomodulatory agent
- B. The requested medication will be used in any of the following regimens:
 1. In combination with bortezomib and dexamethasone
 2. In combination with lenalidomide and dexamethasone
 3. In combination with carfilzomib

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced intolerable adverse effects or disease progression while on the current regimen.

IV. REFERENCES

1. Farydak [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; June 2016.
2. The NCCN Drugs & Biologics Compendium 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 29, 2019.

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3. The NCCN Clinical Practice Guidelines in Oncology Multiple Myeloma (Version 1.2019) 2018 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed March 29, 2019.

SPECIALTY GUIDELINE MANAGEMENT

FASENRA (benralizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication¹

Fasenra is indicated for the add-on maintenance treatment of patients with severe asthma aged 12 years and older, and with an eosinophilic phenotype.

Limitations of Use:

- Not for treatment of other eosinophilic conditions
- Not for relief of acute bronchospasm or status asthmaticus

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Member's chart or medical record showing baseline eosinophil level (initial request only)

III. CRITERIA FOR INITIAL APPROVAL

Authorization of 6 months may be granted for treatment of asthma when all of the following criteria are met:

- A. Member is 12 years of age or older.
- B. Member has a baseline blood eosinophil count of at least 150 cells per microliter.
- C. Member has inadequate asthma control (e.g., hospitalization or emergency medical care visit within the past year) despite current treatment with both of the following medications at optimized doses:
 1. Inhaled corticosteroid
 2. Additional controller (long acting beta₂-agonist, leukotriene modifier, or sustained-release theophylline)
- D. Member will not use Fasenra as monotherapy.
- E. Member will not use Fasenra concomitantly with other biologics (e.g., Cinqair, Dupixent, Nucala, Xolair).

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for treatment of asthma when all of the following criteria are met:

- A. Member is 12 years of age or older.
- B. Asthma control has improved on Fasenra treatment as demonstrated by at least one of the following:
 1. A reduction in the frequency and/or severity of symptoms and exacerbations
 2. A reduction in the daily maintenance oral corticosteroid dose
- C. Member will not use Fasenra as monotherapy.

D. Member will not use Fasenra concomitantly with other biologics (e.g., Cinqair, Dupixent, Nucala, Xolair).

V. OTHER

Note: If the member is a current smoker, they should be counseled on the harmful effects of smoking on pulmonary conditions and available smoking cessation options.

VI. REFERENCES

1. Fasenra [package insert]. Wilmington, DE: AstraZeneca; October 2019.
2. Nair P, Wenzel S, Rabe K, et al. Oral glucocorticoid-sparing effect of benralizumab in severe asthma. *N Engl J Med*. 2017;376:2448-2458.
3. Global Initiative for Asthma (GINA). Global Strategy for Asthma Management and Prevention. 2018 update. <http://ginasthma.org/2018-gina-report-global-strategy-for-asthma-management-and-prevention/>. Accessed March 18, 2019.

SPECIALTY GUIDELINE MANAGEMENT

FASLODEX (fulvestrant) fulvestrant

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Faslodex is indicated for the treatment of:

- Hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced breast cancer in postmenopausal women not previously treated with endocrine therapy.
- HR-positive advanced breast cancer in postmenopausal women with disease progression following endocrine therapy.
- HR-positive, HER2-negative advanced or metastatic breast cancer in postmenopausal women in combination with ribociclib, as initial endocrine based therapy or following disease progression on endocrine therapy.
- HR-positive, HER2-negative advanced or metastatic breast cancer in combination with palbociclib or abemaciclib in women with disease progression after endocrine therapy

Compendial Indications

- Breast cancer: therapy for recurrent or stage IV hormone receptor-positive disease
- Ovarian cancer/Fallopian tube cancer/Primary peritoneal cancer/Epithelial ovarian cancer: recurrence therapy for low grade serous carcinoma
- Endometrial carcinoma
- Uterine sarcoma (low-grade endometrial stromal sarcoma and uterine leiomyosarcoma)

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Breast Cancer

Authorization of 12 months may be granted for treatment recurrent, advanced, or stage IV hormone receptor-positive breast cancer.

B. Ovarian cancer/Fallopian tube cancer/Primary peritoneal cancer/Epithelial ovarian cancer

Authorization of 12 months may be granted for treatment of recurrent low grade serous carcinoma.

C. Endometrial cancer

Authorization of 12 months may be granted for treatment of endometrial cancer.

Reference number(s)
2903-A

D. Uterine sarcoma

Authorization of 12 months may be granted for treatment of low-grade endometrial stromal sarcoma and uterine leiomyosarcoma.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for breast cancer, low grade serous carcinoma, endometrial cancer, low-grade endometrial stromal sarcoma or uterine leiomyosarcoma and who have not experienced disease progression or an unacceptable toxicity.

IV. REFERENCES

1. Faslodex [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; May 2019.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed August 16, 2019.

SPECIALTY GUIDELINE MANAGEMENT

FEIBA (anti-inhibitor coagulant complex [human])

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

- A. FDA-Approved Indication
Hemophilia A and hemophilia B with inhibitors
- B. Compendial Use
Acquired hemophilia A

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

- A. **Hemophilia A with Inhibitors**
Indefinite authorization may be granted for treatment of hemophilia A with inhibitors (see Appendix) when the inhibitor titer is ≥ 5 Bethesda units per milliliter (BU/mL) or if the patient has a history of an inhibitor titer ≥ 5 BU.
- B. **Hemophilia B with Inhibitors**
Indefinite authorization may be granted for treatment of hemophilia B with inhibitors (see Appendix) when the inhibitor titer is ≥ 5 Bethesda units per milliliter (BU/mL) or if the patient has a history of an inhibitor titer ≥ 5 BU.
- C. **Acquired Hemophilia A**
Indefinite authorization may be granted for treatment of acquired hemophilia A.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. APPENDIX

Appendix: Inhibitors - Bethesda Units (BU)

The presence of inhibitors is confirmed by a specific blood test called the Bethesda inhibitor assay.

- High-titer inhibitors:
 - ≥ 5 BU/mL
 - Inhibitors act strongly and quickly neutralize factor
- Low-titer inhibitors:
 - < 5 BU/mL
 - Inhibitors act weakly and slowly neutralize factor

V. REFERENCES

1. FEIBA [package insert]. Westlake Village, CA: Baxter Healthcare Corporation; October 2018.
2. AHFS DI (Adult and Pediatric) [database online]. Hudson, OH: Lexi-Comp, Inc.; https://online.lexi.com/lco/action/doc/retrieve/docid/essential_ashp/988283 [available with subscription]. Accessed December 18, 2018.
3. *Acquired hemophilia*. World Federation of Hemophilia. <http://www1.wfh.org/publications/files/pdf-1186.pdf>. Accessed December 18, 2018.
4. Huth-Kuhne A, Baudo F, Collins P, et al. International recommendations on the diagnosis and treatment of patients with acquired hemophilia A. *Haematologica*. 2009;94(4):566-75.
5. Franchini M, Mannucci PM. Acquired haemophilia A: a 2013 update. *Thromb Haemost*. 2013;110(6):1114-20.
6. National Hemophilia Foundation. MASAC recommendations concerning products licensed for the treatment of hemophilia and other bleeding disorders. Revised April 2018. MASAC Document # 253. Accessed December 18, 2018.
7. Srivastava A, Brewer A, Street A, et al. Guidelines for the management of hemophilia. *Haemophilia: The Official Journal Of The World Federation Of Hemophilia* [serial online]. January 2013;19(1):e1-e47. Available from: MEDLINE Complete, Ipswich, MA. Accessed December 18, 2018.
8. National Hemophilia Foundation. MASAC recommendations regarding prophylaxis with bypassing agents in patients with hemophilia and high titer inhibitors. MASAC Document #220. <https://www.hemophilia.org/sites/default/files/document/files/masac220.pdf>. Accessed December 18, 2018.

SPECIALTY GUIDELINE MANAGEMENT

FEIBA (anti-inhibitor coagulant complex [human])

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

- A. FDA-Approved Indication
Hemophilia A and hemophilia B with inhibitors
- B. Compendial Use
Acquired hemophilia A

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

- A. **Hemophilia A with Inhibitors**
Indefinite authorization may be granted for treatment of hemophilia A with inhibitors (see Appendix) when the inhibitor titer is ≥ 5 Bethesda units per milliliter (BU/mL) or if the patient has a history of an inhibitor titer ≥ 5 BU.
- B. **Hemophilia B with Inhibitors**
Indefinite authorization may be granted for treatment of hemophilia B with inhibitors (see Appendix) when the inhibitor titer is ≥ 5 Bethesda units per milliliter (BU/mL) or if the patient has a history of an inhibitor titer ≥ 5 BU.
- C. **Acquired Hemophilia A**
Indefinite authorization may be granted for treatment of acquired hemophilia A.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. APPENDIX

Appendix: Inhibitors - Bethesda Units (BU)

The presence of inhibitors is confirmed by a specific blood test called the Bethesda inhibitor assay.

- High-titer inhibitors:
 - ≥ 5 BU/mL
 - Inhibitors act strongly and quickly neutralize factor
- Low-titer inhibitors:
 - < 5 BU/mL
 - Inhibitors act weakly and slowly neutralize factor

V. REFERENCES

1. FEIBA [package insert]. Lexington, MA: Baxalta US Inc.; December 2018.
2. AHFS DI (Adult and Pediatric) [database online]. Hudson, OH: Lexi-Comp, Inc.; https://online.lexi.com/lco/action/doc/retrieve/docid/essential_ashp/988283 [available with subscription]. Accessed December 15, 2019.
3. *Acquired hemophilia*. World Federation of Hemophilia. <http://www1.wfh.org/publications/files/pdf-1186.pdf>. Accessed December 12, 2019.
4. Huth-Kuhne A, Baudo F, Collins P, et al. International recommendations on the diagnosis and treatment of patients with acquired hemophilia A. *Haematologica*. 2009;94(4):566-75.
5. Franchini M, Mannucci PM. Acquired haemophilia A: a 2013 update. *Thromb Haemost*. 2013;110(6):1114-20.
6. National Hemophilia Foundation. MASAC recommendations concerning products licensed for the treatment of hemophilia and other bleeding disorders. Revised April 2018. MASAC Document # 253. <https://www.hemophilia.org/sites/default/files/document/files/masac253.pdf>. Accessed December 12, 2019.
7. Srivastava A, Brewer A, Street A, et al. Guidelines for the management of hemophilia. *Haemophilia*. 2013;19(1):e1-e47.
8. National Hemophilia Foundation. MASAC recommendations regarding prophylaxis with bypassing agents in patients with hemophilia and high titer inhibitors. MASAC Document #220. <https://www.hemophilia.org/sites/default/files/document/files/masac220.pdf>. Accessed December 14, 2019.
9. Kruse-Jarres, R, Kempton CL, Baudo, F, et al. Acquired hemophilia A: Updated review of evidence and treatment guidance. *Am J Hematol*. 2017;92:695-705.

SPECIALTY GUIDELINE MANAGEMENT

FERRIPROX (deferiprone)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Transfusional iron overload due to thalassemia syndromes when current chelation therapy is inadequate

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

- A. Initial requests: pretreatment serum ferritin level
- B. Continuation requests: current serum ferritin level

III. CRITERIA FOR INITIAL APPROVAL

Transfusional Iron Overload

Authorization of 6 months may be granted for treatment of transfusional iron overload due to thalassemia syndromes when both of the following criteria are met:

- A. Pretreatment serum ferritin level is consistently greater than 1000 mcg/L.
- B. Dose of Ferriprox will not exceed 99 mg/kg per day.

IV. CONTINUATION OF THERAPY

Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when both of the following criteria are met:

- A. Member is experiencing benefit from therapy as evidenced by a decrease in serum ferritin levels as compared to pretreatment baseline.
- B. Serum ferritin level is not consistently below 500 mcg/L.

V. REFERENCES

1. Ferriprox [package insert]. Rockville, MD: ApoPharma USA, Inc.; May 2017.
2. Micromedex Solutions [database online]. Truven Health Analytics, Inc. Ann Arbor, MI. Available at: www.micromedexsolutions.com. Accessed October 15, 2018.
3. AHFS DI (Adult and Pediatric) [database online]. Lexi-Comp, Inc. Hudson, OH. Available at: http://online.lexi.com/lco/action/index/dataset/complete_ashp [available with subscription]. Accessed October 15, 2018.

Reference number(s)
1621-A

4. Clinical Pharmacology [Internet]. Elsevier. Tampa (FL). Available from: <http://www.clinicalpharmacology.com>. Accessed October 15, 2018.
5. Cappellini MD, Cohen A, Porter J, et al. Guidelines for the management of transfusion dependent thalassaemia (TDT) 3rd Edition [Internet]. *Thalassaemia International Federation* 2014;20:1-253.

SPECIALTY GUIDELINE MANAGEMENT

FIBRYGA (fibrinogen [human])

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Fibryga is indicated in adults and adolescents with congenital fibrinogen deficiency, including afibrinogenemia and hypofibrinogenemia, for the treatment of acute bleeding episodes.

Fibryga is not indicated for dysfibrinogenemia.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Fibrinogen Deficiency

Authorization of 1 month may be granted for treatment of acute bleeding episodes in members with a diagnosis of congenital fibrinogen deficiency, including afibrinogenemia and hypofibrinogenemia.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Fibryga [package insert]. Hoboken, NJ: Octapharma USA, Inc.; September 2017.

SPECIALTY GUIDELINE MANAGEMENT

FIRDAPSE (amifampridine)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Firdapse is indicated for the treatment of Lambert-Eaton myasthenic syndrome (LEMS) in adults.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of either of the following diagnostic tests is necessary to initiate prior authorization review:

- A. Electromyography (EMG)
- B. Anti-P/Q type voltage-gated calcium channel antibody test

III. EXCLUSIONS

Coverage will not be provided for members with a history of seizures.

IV. CRITERIA FOR INITIAL APPROVAL

Lambert-Eaton Myasthenic Syndrome (LEMS)

Authorization of 6 months may be granted for treatment of Lambert-Eaton myasthenic syndrome (LEMS) when all of the following criteria are met:

- A. Diagnosis is confirmed by either of the following:
 - 1. EMG showing compound muscle action potential (CMAP) that increased at least 2-fold after maximum voluntary contraction of the tested muscle
 - 2. A positive anti- P/Q type voltage-gated calcium channel antibody test
- B. Member has proximal muscle weakness
- C. For treatment-naïve members, the Quantitative Myasthenia Gravis (QMG) score is at least 5

V. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for LEMS who are responding to therapy (i.e., there is stability or improvement in symptoms relative to the natural course of LEMS).

Reference number(s)
2803-A

VI. REFERENCES

1. Firdapse [package insert]. Coral Gables, FL: Catalyst Pharmaceuticals, Inc.; November 2018.

SPECIALTY GUIDELINE MANAGEMENT

Firmagon (degarelix)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Firmagon is indicated for the treatment of advanced prostate cancer.

B. Compendial Uses

Prostate cancer

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of prostate cancer.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. REFERENCES

1. Firmagon [package insert]. Parsippany, NJ: Ferring Pharmaceuticals; October 2016.
2. The NCCN Drugs & Biologics Compendium® © 2018 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed October 11, 2018.
3. National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology: prostate cancer. Version 4.2018. http://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed October 11, 2018.

SPECIALTY GUIDELINE MANAGEMENT

FOLLISTIM AQ (follitropin beta injection) GONAL-F (follitropin alfa injection)

*Hereafter, follitropin will be used to describe all products

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Follistim AQ is indicated for:

1. Induction of ovulation and pregnancy in anovulatory infertile women in whom the cause of infertility is functional and not due to primary ovarian failure
2. Development of multiple follicles in ovulatory women participating in an assisted reproductive technology (ART) program
3. Pregnancy in normal ovulatory women undergoing controlled ovarian stimulation as part of an in vitro fertilization or intracytoplasmic sperm injection (ICSI) cycle
4. Induction of spermatogenesis in men with primary and secondary hypogonadotropic hypogonadism in whom the cause of infertility is not due to primary testicular failure

Gonal-f is indicated for:

1. Induction of ovulation and pregnancy in oligio-anovulatory women in whom the cause of infertility is functional and not due to primary ovarian failure.
2. Development of multiple follicles in ovulatory women as part of an ART cycle.
3. Induction of spermatogenesis in men with primary and secondary hypogonadotropic hypogonadism in whom the cause of infertility is not due to primary testicular failure.

All other indications are considered experimental/investigational and not medically necessary.

II. MEDICAL BENEFIT ALIGNMENT

Specialty Guideline Management coverage review will be bypassed for drug(s) being requested for a procedure that has been approved under a member's medical benefit plan. Such members will be exempt from the requirements in Sections IV and V. A medical authorization number and confirmation of the approved procedure(s) will be required.

NOTE: Some plans may opt-out of medical benefit alignment. Members receiving coverage under such plans must meet the requirements in Sections IV and V.

III. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review for hypogonadotropic hypogonadism: testosterone, FSH, and LH levels.

IV. CRITERIA FOR INITIAL APPROVAL

A. Follicle stimulation

Authorization of 12 months may be granted for members undergoing ovulation induction or assisted reproductive technology (ART) who meet any of the following criteria:

1. Member has completed three or more previous cycles of clomiphene, or
2. Member has a risk factor for poor ovarian response to clomiphene, or
3. Member has a contraindication or exclusion to clomiphene, or
4. Member is 37 years of age or older

B. Hypogonadotropic hypogonadism

Authorization of 12 months may be granted for treatment of hypogonadotropic hypogonadism in members who meet both of the following criteria:

1. Low pretreatment testosterone levels
2. Low or low-normal follicle stimulating hormone (FSH) or luteinizing hormone (LH) levels

V. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

VI. REFERENCES

1. Follistim AQ [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; December 2013.
2. Follistim AQ Cartridge [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; December 2014.
3. Gonal-f Multi-Dose [package insert]. Rockland, MA: EMD Serono, Inc.; December 2012.
4. Gonal-f RFF [package insert]. Rockland, MA: EMD Serono, Inc.; May 2018.
5. Gonal-f RFF Redi-ject [package insert]. Rockland, MA: EMD Serono, Inc.; May 2018.
6. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, CO. Available at: <http://www.micromedexsolutions.com> Accessed May 13, 2019.
7. Practice Committee of the American Society of Reproductive Medicine. Use of clomiphene citrate in infertile women: a committee opinion. *Fertil & Steril.* 2013;100:341-348.
8. American Association of Clinical Endocrinologists. Medical guidelines for clinical practice for the evaluation and treatment of hypogonadism in adult male patients – 2002 Update. *Endocr Pract.* 2002;8:439-456.

SPECIALTY GUIDELINE MANAGEMENT

FOLLISTIM AQ (follitropin beta injection) GONAL-F (follitropin alfa injection)

*Hereafter, follitropin will be used to describe all products

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Follistim AQ is indicated for:

1. Induction of ovulation and pregnancy in anovulatory infertile women in whom the cause of infertility is functional and not due to primary ovarian failure
2. Development of multiple follicles in ovulatory women participating in an assisted reproductive technology (ART) program
3. Pregnancy in normal ovulatory women undergoing controlled ovarian stimulation as part of an in vitro fertilization or intracytoplasmic sperm injection (ICSI) cycle
4. Induction of spermatogenesis in men with primary and secondary hypogonadotropic hypogonadism in whom the cause of infertility is not due to primary testicular failure

Gonal-f is indicated for:

1. Induction of ovulation and pregnancy in oligio-anovulatory women in whom the cause of infertility is functional and not due to primary ovarian failure.
2. Development of multiple follicles in ovulatory women as part of an ART cycle.
3. Induction of spermatogenesis in men with primary and secondary hypogonadotropic hypogonadism in whom the cause of infertility is not due to primary testicular failure.

All other indications are considered experimental/investigational and not medically necessary.

II. MEDICAL BENEFIT ALIGNMENT

Specialty Guideline Management coverage review will be bypassed for drug(s) being requested for a procedure that has been approved under a member's medical benefit plan. Such members will be exempt from the requirements in Sections IV and V. A medical authorization number and confirmation of the approved procedure(s) will be required.

NOTE: Some plans may opt-out of medical benefit alignment. Members receiving coverage under such plans must meet the requirements in Sections IV and V.

III. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review for hypogonadotropic hypogonadism: testosterone, FSH, and LH levels.

IV. CRITERIA FOR INITIAL APPROVAL

A. Follicle stimulation

Authorization of 12 months may be granted for members undergoing ovulation induction or assisted reproductive technology (ART) who meet any of the following criteria:

1. Member has completed three or more previous cycles of clomiphene, or
2. Member has a risk factor for poor ovarian response to clomiphene, or
3. Member has a contraindication or exclusion to clomiphene, or
4. Member is 37 years of age or older

B. Hypogonadotropic hypogonadism

Authorization of 12 months may be granted for treatment of hypogonadotropic hypogonadism in members who meet both of the following criteria:

1. Low pretreatment testosterone levels
2. Low or low-normal follicle stimulating hormone (FSH) or luteinizing hormone (LH) levels

V. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

VI. REFERENCES

1. Follistim AQ [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; December 2013.
2. Follistim AQ Cartridge [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; December 2014.
3. Gonal-f Multi-Dose [package insert]. Rockland, MA: EMD Serono, Inc.; December 2012.
4. Gonal-f RFF [package insert]. Rockland, MA: EMD Serono, Inc.; May 2018.
5. Gonal-f RFF Redi-ject [package insert]. Rockland, MA: EMD Serono, Inc.; May 2018.
6. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, CO. Available at: <http://www.micromedexsolutions.com> Accessed May 13, 2019.
7. Practice Committee of the American Society of Reproductive Medicine. Use of clomiphene citrate in infertile women: a committee opinion. *Fertil & Steril.* 2013;100:341-348.
8. American Association of Clinical Endocrinologists. Medical guidelines for clinical practice for the evaluation and treatment of hypogonadism in adult male patients – 2002 Update. *Endocr Pract.* 2002;8:439-456.

SPECIALTY GUIDELINE MANAGEMENT

FOLOTYN (pralatrexate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Treatment of patients with relapsed or refractory peripheral T-cell lymphoma (PTCL)

B. Compendial Uses

1. Adult T-cell leukemia/lymphoma (ATLL)
2. Mycosis fungoides/Sezary syndrome (MF/SS)
3. Primary cutaneous CD30+ T-cell lymphoproliferative disorders: cutaneous anaplastic large cell lymphoma (ALCL)
4. Extranodal NK/T-cell lymphoma, nasal type
5. Hepatosplenic gamma-delta T-cell lymphoma

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Peripheral T-cell lymphoma (PTCL)**

Authorization of 12 months may be granted for treatment of PTCL when used for relapsed or refractory disease.

B. **Adult T-cell leukemia/lymphoma (ATLL)**

Authorization of 12 months may be granted for treatment of ATLL when both of the following criteria are met:

1. Folutyn is used as a single agent.
2. Folutyn is used as second-line or subsequent therapy.

C. **Mycosis fungoides/Sezary syndrome (MF/SS)**

Authorization of 12 months may be granted for treatment of MF or SS.

D. **Primary cutaneous CD30+ T-cell lymphoproliferative disorders**

Authorization of 12 months may be granted for treatment of cutaneous anaplastic large cell lymphoma (ALCL) when Folutyn is used as a single agent.

E. **Extranodal NK/T-cell lymphoma, nasal type**

Authorization of 12 months may be granted for treatment of extranodal NK/T-cell lymphoma, nasal type when all of the following criteria are met:

1. Folutyn will be used as a single agent.

Reference number(s)
1702-A

2. Patient has relapsed or refractory disease.
3. Patient has had an inadequate response or contraindication to asparaginase-based therapy (e.g., pegaspargase).

F. Hepatosplenic Gamma-Delta T-cell lymphoma

Authorization of 12 months may be granted for treatment of hepatosplenic gamma-delta T-cell lymphoma when both of the following criteria are met:

1. Folutyn will be used as a single agent.
2. The patient has had two or more previous lines of chemotherapy.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced disease progression or an unacceptable toxicity.

IV. REFERENCES

1. Folutyn [package insert]. Westminster, CO: Allos Therapeutics, Inc.; May 2016.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed April 28, 2019.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

FORTAMET
(metformin extended-release)

GLUMETZA
(metformin extended-release)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

Ref # 1517-A

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Fortamet

Fortamet is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Glumetza

Glumetza is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has experienced an intolerance to generic Glucophage XR. The prescriber **MUST** submit chart notes or other documentation supporting date of trial and reason for intolerance to generic Glucophage XR.
- AND**
- Chart notes or other documentation supporting date of trial and reason for intolerance to generic Glucophage XR have been submitted to CVS Health

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Fortamet (metformin extended-release) and Glumetza (metformin extended-release) are indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

If the patient has experienced an intolerance to generic Glucophage XR, then the requested drug (brand or high cost generic) will be covered.

REFERENCES

1. Fortamet [package insert]. Florham Park, NJ: Shionogi, Inc.; November 2018.
2. Glumetza [package insert]. Bridgewater, NJ: Salix Pharmaceuticals; November 2018.
3. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed June 2019.
4. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed June 2019.

Written by: UM Development (RP)

Date Written: 09/2016

Revised: 11/2016 (rephrased question 2), 07/2017, 11/2017 (extended DOA), 07/2018 (no clinical changes), 03/2019 (no clinical changes);

Fortamet Glumetza 1517-A 07-2019.doc

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CRITERIA FOR APPROVAL

- | | | | |
|---|--|-----|----|
| 1 | Has the patient experienced an intolerance to generic Glucophage XR?
[If yes, then prescriber MUST submit chart notes or other documentation supporting date of trial and reason for intolerance to generic Glucophage XR.] | Yes | No |
|---|--|-----|----|

[Tech Note: Leave response as answered by prescriber. Verification of chart note will be addressed in question 2.]

- | | | | |
|---|--|-----|----|
| 2 | Have chart notes or other documentation supporting date of trial and reason for intolerance to generic Glucophage XR been submitted to CVS Health? | Yes | No |
|---|--|-----|----|

[Tech Note: MUST obtain a physical copy of chart notes or other documentation supporting date of trial and reason for intolerance to generic Glucophage XR. If the PA is worked over the phone, then the prescriber still MUST submit physical chart notes or other documentation. If a physical copy of documentation of date of trial and reason for intolerance to generic Glucophage XR is not received, then the PA should be denied.]

Mapping Instructions			
	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you have tried generic Glucophage XR and you cannot use it. Your request has been denied based on the information we have.</p> <p>[Short Description: No intolerance to generic Glucophage XR]</p>
2.	Approve, 36 months	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when your prescriber submits your chart notes or other documentation that supports your date of trial and reason for intolerance to generic Glucophage XR to CVS Health. Your request has been denied based on the information we have.</p> <p>[Short Description: Prescriber did not submit documentation to confirm intolerance to generic Glucophage XR]</p>

SPECIALTY GUIDELINE MANAGEMENT

FORTEO (teriparatide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

- A. Treatment of postmenopausal women with osteoporosis at high risk for fracture
- B. Increase of bone mass in men with primary or hypogonadal osteoporosis at high risk for fracture
- C. Treatment of men and women with glucocorticoid-induced osteoporosis at high risk for fracture

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Supporting chart notes or medical record indicating a history of fractures, T-score, and FRAX fracture probability as applicable to Section III.

III. CRITERIA FOR INITIAL APPROVAL

A. Postmenopausal osteoporosis

Authorization of a lifetime total of 24 months for parathyroid hormone analogs (e.g., abaloparatide or teriparatide) may be granted to postmenopausal members with osteoporosis when ANY of the following criteria are met:

1. Member has a history of fragility fractures
2. Member has a pre-treatment T-score less than or equal to -2.5 OR member has osteopenia (i.e., pre-treatment T-score greater than -2.5 and less than -1) with a high pre-treatment FRAX fracture probability (See Appendix B) and meets ANY of the following criteria:
 - a. Member has indicators of higher fracture risk (e.g., advanced age, frailty, glucocorticoid use, very low T-scores [less than or equal to -3.5], or increased fall risk)
 - b. Member has failed prior treatment with or is intolerant to previous injectable osteoporosis therapy (e.g., zoledronic acid [Reclast], denosumab [Prolia])
 - c. Member has had an oral bisphosphonate trial of at least 1-year duration or there is a clinical reason to avoid treatment with an oral bisphosphonate (See Appendix A)

B. Primary or hypogonadal osteoporosis in men

Authorization of a lifetime total of 24 months for parathyroid hormone analogs (e.g., abaloparatide or teriparatide) may be granted to male members with primary or hypogonadal osteoporosis when ANY of the following criteria are met:

1. Member has a history of an osteoporotic vertebral or hip fracture
2. Member meets criteria BOTH of the following criteria:
 - a. Member has a pre-treatment T-score less than or equal to -2.5 OR member has osteopenia (i.e., pre-treatment T-score greater than -2.5 and less than -1) with a high pre-treatment FRAX fracture probability (See Appendix B)
 - b. Member has had an oral bisphosphonate trial of at least 1-year duration OR there is a clinical reason to avoid treatment with an oral bisphosphonate (See Appendix A)

C. Glucocorticoid-induced Osteoporosis

Authorization of a lifetime total of 24 months for parathyroid hormone analogs (e.g., abaloparatide or teriparatide) may be granted for members with glucocorticoid-induced osteoporosis when ALL of the following criteria are met:

1. Member has had an oral bisphosphonate trial of at least 1-year duration OR there is a clinical reason to avoid treatment with an oral bisphosphonate (See Appendix A)
2. Member is currently receiving or will be initiating glucocorticoid therapy
3. Member meets ANY of the following criteria:
 - a. Member has a history of a fragility fracture
 - b. Member has a pre-treatment T-score less than or equal to -2.5
 - c. Member has osteopenia (i.e., pre-treatment T-score greater than -2.5 and less than -1) with a high pre-treatment FRAX fracture probability (See Appendix B)

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet ALL initial authorization criteria AND have received less than 24 months of total lifetime therapy with parathyroid hormone analogs (e.g., abaloparatide or teriparatide).

V. APPENDIX

Appendix A. Clinical reasons to avoid oral bisphosphonate therapy

- Esophageal abnormality that delays emptying such as stricture of achalasia
- Active upper gastrointestinal problem (e.g., dysphagia, gastritis, duodenitis, erosive esophagitis, ulcers)
- Inability to stand or sit upright for at least 30 to 60 minutes
- Inability to take at least 30 to 60 minutes before first food, drink, or medication of the day
- Renal insufficiency (creatinine clearance < 35 mL/min)
- History of intolerance to an oral bisphosphonate

Appendix B. WHO Fracture Risk Assessment Tool

- High FRAX fracture probability: 10 year major osteoporotic fracture risk \geq 20% or hip fracture risk \geq 3%.
- 10-year probability; calculation tool available at: <https://www.sheffield.ac.uk/FRAX/>
- The estimated risk score generated with FRAX should be multiplied by 1.15 for major osteoporotic fracture and 1.2 for hip fracture if glucocorticoid treatment is greater than 7.5 mg per day.

VI. REFERENCES

1. Forteo [package insert]. Indianapolis, IN: Eli Lilly and Company; October 2016.
2. Bisphosphonates. *Drug Facts and Comparisons*. Facts & Comparisons [database online]. St. Louis, MO: Wolters Kluwer Health Inc; March 21, 2019. Accessed April 10, 2019.

3. Cosman F, de Beur SJ, LeBoff MS, et al. National Osteoporosis Foundation. Clinician's guide to prevention and treatment of osteoporosis. *Osteoporos Int*. 2014;25(10): 2359-2381.
4. Jeremiah MP, Unwin BK, Greenwald MH, et al. Diagnosis and management of osteoporosis. *Am Fam Physician*. 2015;92(4):261-268.
5. Watts NB, Bilezikian JP, Camacho PM, et al. American Association of Clinical Endocrinologists medical guidelines for clinical practice for the diagnosis and treatment of postmenopausal osteoporosis. *Endocr Pract*. 2016;22 (Suppl 4):1-42.
6. ACOG Practice Bulletin Number 129: Osteoporosis. *Obstet Gynecol*. 2012;120(3):718-734.
7. National Institute for Health and Care Excellence. Osteoporosis Overview. Last updated February 2018. Available at: <http://pathways.nice.org.uk/pathways/osteoporosis>. Accessed April 10, 2019.
8. Treatment to prevent osteoporotic fractures: an update. Department of Health and Human Services, Agency for Healthcare Research and Quality. 2012; Publication No. 12-EHC023-EF. Available at www.effectivehealthcare.ahrq.gov/lbd.cfm.
9. Watts NB, Adler RA, Bilezikian JP, et al. Osteoporosis in men : an Endocrine Society clinical practice guideline. *J Clin Endocr Metab*. 2012;97(6):1802-1822.
10. Fink HA, Gordon G, Buckley L, et al. 2017 American College of Rheumatology Guidelines for the Prevention and Treatment of Glucocorticoid-Induced Osteoporosis. *Arthritis Care Res*. 2017;69:1521-1537.
11. FRAX® WHO fracture risk assessment tool. © World Health Organization Collaborating Centre for Metabolic Bone Diseases: University of Sheffield, UK. Available at: <https://www.sheffield.ac.uk/FRAX/>. Accessed April 10, 2019.
12. Ensrud KE, Crandall CJ. Osteoporosis. *Ann Intern Med* 2017;167(03):ITC17–ITC32.

SPECIALTY GUIDELINE MANAGEMENT

FASLODEX (fulvestrant) fulvestrant

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Faslodex is indicated for the treatment of:

- Hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced breast cancer in postmenopausal women not previously treated with endocrine therapy.
- HR-positive advanced breast cancer in postmenopausal women with disease progression following endocrine therapy.
- HR-positive, HER2-negative advanced or metastatic breast cancer in postmenopausal women in combination with ribociclib, as initial endocrine based therapy or following disease progression on endocrine therapy.
- HR-positive, HER2-negative advanced or metastatic breast cancer in combination with palbociclib or abemaciclib in women with disease progression after endocrine therapy

Compendial Indications

- Breast cancer: therapy for recurrent or stage IV hormone receptor-positive disease
- Ovarian cancer/Fallopian tube cancer/Primary peritoneal cancer/Epithelial ovarian cancer: recurrence therapy for low grade serous carcinoma
- Endometrial carcinoma
- Uterine sarcoma (low-grade endometrial stromal sarcoma and uterine leiomyosarcoma)

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of hormone receptor (HR) status is necessary to initiate the prior authorization review, where applicable.

III. CRITERIA FOR INITIAL APPROVAL

A. Breast Cancer

Authorization of 12 months may be granted for treatment recurrent, advanced, or stage IV HR-positive breast cancer.

B. Ovarian cancer/Fallopian tube cancer/Primary peritoneal cancer/Epithelial ovarian cancer

Authorization of 12 months may be granted for treatment of recurrent low grade serous carcinoma.

C. Endometrial cancer

Authorization of 12 months may be granted for treatment of endometrial cancer.

D. Uterine sarcoma

Authorization of 12 months may be granted for treatment of low-grade endometrial stromal sarcoma and uterine leiomyosarcoma.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for breast cancer, low grade serous carcinoma, endometrial cancer, low-grade endometrial stromal sarcoma or uterine leiomyosarcoma and who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES

1. Faslodex [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; November 2019.
2. The NCCN Drugs & Biologics Compendium® © 2020 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed January 9, 2020.

SPECIALTY GUIDELINE MANAGEMENT

FUZEON (enfuviride)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Fuzeon in combination with other antiretroviral agents is indicated for the treatment of human immunodeficiency virus (HIV)-1 infection in treatment-experienced patients with evidence of HIV-1 replication despite ongoing antiretroviral therapy.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Human immunodeficiency virus (HIV)-1

Authorization of 12 months may be granted for treatment of HIV-1 infection when either of the following criteria are met:

- A. The member has viremia despite 3 or more prior months of therapy with at least one appropriate regimen used to treat HIV.
- B. The member has viremia and documented resistance or intolerance to at least one appropriate regimen used to treat HIV.

III. CONTINUATION OF THERAPY

Authorization for continuation of therapy for 12 months may be granted for treatment of HIV-1 infection when the member has had a positive or stable virologic response to Fuzeon.

IV. REFERENCES

1. Fuzeon [package insert]. South San Francisco, CA: Genentech USA, Inc.; August 2019.
2. Micromedex Solutions [electronic version]. Truven Health Analytics, Greenwood Village, Colorado, USA. Available at: <http://www.micromedexsolutions.com>. Accessed December 11, 2019.
3. Clinical Pharmacology [database online]. Atlanta, GA: Elsevier, Inc.; 2019. <https://www.clinicalkey.com/pharmacology>. Accessed December 11, 2019.
4. Lexicomp Online®, AHFS® Drug Information, Hudson, Ohio: Wolters Kluwer Clinical Drug Information, Inc.; <http://online.lexi.com> Accessed December 11, 2019.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

FYCOMPA
(perampanel)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

Ref # 887-A

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Partial Onset Seizures:

Fycompa is indicated for the treatment of partial-onset seizures with or without secondarily generalized seizures in patients with epilepsy 4 years of age and older.

Primary Generalized Tonic-Clonic Seizures:

Fycompa is indicated as adjunctive therapy for the treatment of primary generalized tonic-clonic seizures in patients with epilepsy 12 years of age and older.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for one of the following: A) Treatment of partial-onset seizures in a patient 4 years of age or older with epilepsy or B) Adjunctive therapy for the treatment of primary generalized tonic-clonic seizures in a patient 12 years of age or older with epilepsy

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines.

Fycompa (perampanel) is indicated for the treatment of partial-onset seizures with or without secondarily generalized seizures in patients with epilepsy 4 years of age and older, or as adjunctive therapy for the treatment of primary generalized tonic-clonic seizures in patients with epilepsy 12 years of age and older.

REFERENCES

1. Fycompa [package insert]. Woodcliff Lake, NJ: Eisai Inc.; September 2018.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed May 2019.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed May 2019.

Written by: UM Development (SE/BMS)
Date Written: 10/2012
Revised: (SE) 05/2013, 05/2014, 05/2015, 06/2015; (KM) 05/2016 (no clinical changes), (SE) 05/2017; (KM) 08/2017 (updated indication); (KC) 05/2018 (no clinical changes), 10/2018 (updated indication), 05/2019 (no clinical changes)
Reviewed: Medical Affairs: (LMS) 11/2012, (DNC) 05/2013, 05/2014, 05/2015, 06/2015, (LMS) 05/2017, (TP) 08/2017; (ME) 10/2018
External Review: 01/2013, 02/2013, 10/2013, 10/2014, 10/2015, 10/2016, 10/2017, 10/2018, 10/2019

Fycompa 887-A 05-2019_7-10-20.doc

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CRITERIA FOR APPROVAL

- | | | | |
|---|---|-----|----|
| 1 | Is the requested drug being prescribed for one of the following: A) Treatment of partial-onset seizures in a patient 4 years of age or older with epilepsy or B) Adjunctive therapy for the treatment of primary generalized tonic-clonic seizures in a patient 12 years of age or older with epilepsy? | Yes | No |
|---|---|-----|----|

Mapping Instructions

	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Approve, 36 months	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you meet any of these conditions:</p> <ul style="list-style-type: none">- You have epilepsy, you are 4 years or older, and you are using Fycompa (perampanel) to treat partial-onset seizures- You have epilepsy, you are 12 years or older, and you are using Fycompa (perampanel) along with another seizure drug to treat primary generalized tonic-clonic seizures <p>Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]</p>

SPECIALTY GUIDELINE MANAGEMENT

GALAFOLD (migalastat)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Galafold is indicated for the treatment of adults with a confirmed diagnosis of Fabry disease and an amenable galactosidase alpha gene (*GLA*) variant based on in vitro assay data.

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: alpha-galactosidase enzyme assay or genetic testing results supporting diagnosis. In the case of obligate carriers, the documentation must be submitted for the parent.

III. CRITERIA FOR INITIAL APPROVAL

Fabry disease with an amenable galactosidase alpha gene (*GLA*) variant

Authorization of 12 months may be granted for treatment of Fabry disease with an amenable galactosidase alpha gene (*GLA*) variant when all of the following criteria are met:

- A. The diagnosis of Fabry disease was confirmed by enzyme assay demonstrating a deficiency of alpha-galactosidase enzyme activity or by genetic testing, or the member is a symptomatic obligate carrier; and
- B. Member has an amenable galactosidase alpha gene (*GLA*) variant based on in vitro assay data; and
- C. Galafold will not be used in combination with Fabrazyme.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for Fabry disease with an amenable galactosidase alpha gene (*GLA*) variant who are responding to therapy (e.g., reduction in plasma globotriaosylceramide [GL-3] or GL-3 inclusions).

V. REFERENCES

1. Galafold [package insert]. Cranbury, NJ: Amicus Therapeutics U.S., Inc.; June 2019.
2. Desnick RJ, Brady RO. Fabry disease in childhood. *J Pediatr.* 2004;144(5 Suppl):S20-S26.
3. Biegstraaten M, Arnglimsson R, Barbey F, et al. Recommendations for initiation and cessation of enzyme replacement therapy in patients with Fabry disease: the European Fabry Working Group consensus document. *Orphanet J Rare Dis.* 2015; 1036.

Reference number
2650-A

4. Desnick RJ, Brady R, Barranger J, et al. Fabry disease, an under-recognized multisystemic disorder: expert recommendations for diagnosis, and enzyme replacement therapy. *Ann Intern Med.* 2003; 138(4):338.
5. Sirrs, S, Bichet DG, Iwanochko RM, et al. Canadian Fabry disease treatment guidelines 2016.

SPECIALTY GUIDELINE MANAGEMENT

Intramuscular Immune Globulin:

GamaSTAN® (Immune Globulin [Human]) GamaSTAN® S/D (Immune Globulin [Human])

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

- A. Pre- or post-exposure prophylaxis of hepatitis A
- B. Postexposure prophylaxis/modification of measles (rubeola) in susceptible persons
- C. Postexposure prophylaxis of varicella in immunosuppressed patients when varicella-zoster immune globulin is not available
- D. Postexposure prophylaxis of rubella during pregnancy

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Prophylaxis of hepatitis A

Authorization of 1 month may be granted for prophylaxis of hepatitis A when one of the following criteria is met:

1. Member was exposed to hepatitis A virus within the past 2 weeks (eg, household contact, sexual contact, and child care center or classroom contact with an infected person), OR
2. Member is at high risk for hepatitis A exposure (examples of populations at high risk for hepatitis A are travelers to and workers in countries of high endemicity of infection and illicit drug users).

B. Prophylaxis of measles (rubeola)

Authorization of 1 month may be granted for prophylaxis of measles in unvaccinated members who have not had measles previously and were exposed to measles within the past 6 days.

C. Prophylaxis of varicella

Authorization of 1 month may be granted for prophylaxis of varicella when all of the following criteria are met:

1. Member was exposed to varicella within the past 10 days
2. Member is at high risk for severe varicella (eg, immunocompromised persons, newborns/infants, pregnant women)
3. Varicella zoster immune globulin (eg, Varizig®) is not available

D. Prophylaxis of rubella

Reference number(s)
2067-A

Authorization of 1 month may be granted for prophylaxis of rubella when both of the following criteria are met:

1. Member was recently exposed to rubella
2. Member is currently pregnant

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. GAMASTAN [package insert]. Research Triangle Park, NC: Grifols Therapeutics, Inc.; February 2018.
2. GamaSTAN S/D [package insert]. Research Triangle Park, NC: Grifols Therapeutics, Inc.; June 2017.
3. Nelson NP, Link-Gelles R, Hofmeister MG, et al. Update: Recommendations of the Advisory Committee on Immunization Practices for Use of Hepatitis A Vaccine for Postexposure Prophylaxis and for Preexposure Prophylaxis for International Travel. *MMWR Morb Mortal Wkly Rep* 2018;67:1216–1220.
4. Centers for Disease Control and Prevention. Prevention of Measles, Rubella, Congenital Rubella Syndrome, and Mumps, 2013. Summary Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR*. 2013;62(4).
5. Centers for Disease Control and Prevention Health Information for International Travel (Yellow Book). Varicella (Chickenpox). <https://wwwnc.cdc.gov/travel/yellowbook/2018/infectious-diseases-related-to-travel/varicella-chickenpox>. Accessed June 11, 2019.

SPECIALTY GUIDELINE MANAGEMENT

GAMIFANT (emapalumab-lzsg)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Gamifant is indicated for the treatment of adult and pediatric (newborn and older) patients with primary hemophagocytic lymphohistiocytosis (HLH) with refractory, recurrent or progressive disease or intolerance with conventional HLH therapy.

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review: medical record documentation (i.e., chart notes or laboratory report) confirming the diagnosis of HLH with the presence of the following: A) a mutation in one of the genes listed under III.B.1 or B) clinical signs and symptoms listed under III.B.2.

III. CRITERIA FOR INITIAL APPROVAL

Primary HLH

Authorization of 6 months may be granted for treatment of primary HLH when all of the following criteria are met:

- A. Member has refractory, recurrent or progressive disease or intolerance with conventional HLH therapy.
- B. Member's diagnosis of primary HLH was confirmed by either of the following:
 1. Mutation in one of the following genes: PRF1, UNC13D, STX11 and STXBP2
 2. Presence of at least 5 of the following:
 - a. Fever
 - b. Splenomegaly
 - c. Cytopenias (affecting at least 2 of 3 lineages in the peripheral blood: hemoglobin less than 9 g/dL [hemoglobin less than 10 g/dL in infants younger than 4 weeks], platelets less than 100,000/microliter, neutrophils less than 1,000/microliter)
 - d. Hypertriglyceridemia (fasting triglyceride greater than or equal to 265 mg/dL) or hypofibrinogenemia (less than or equal to 150 mg/dL)
 - e. Hemophagocytosis in bone marrow or spleen or lymph nodes or liver with no evidence of malignancy
 - f. Low or absent natural killer (NK) cell activity
 - g. Ferritin greater than or equal to 500 ng/mL
 - h. Soluble CD25 (soluble IL-2 receptor alpha) level greater than or equal to 2400 U/mL, or above age-adjusted, laboratory-specific normal levels (defined as 2 standard deviation from the mean)

- C. Possible causes of secondary or acquired forms of HLH (e.g., autoimmune disease, persistent infection, malignancy, or loss of inhibitory immune mechanisms) have been ruled out.
- D. Member has been evaluated for tuberculosis (TB) risk factors and has undergone pretreatment screening for latent TB with the purified protein derivative (PPD) skin test or interferon gamma release assay.
- E. If member has a positive test result or is at risk for TB, prophylactic treatment for TB must be initiated before starting therapy.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for primary HLH who have achieved or maintained positive clinical response.

V. REFERENCES

1. Gamifant [package insert]. Waltham, MA: Sobi, Inc.; November 2018.
2. Henter JL, Horne A, Arico M et al. HLH-2004: diagnostic and therapeutic guidelines for hemophagocytic lymphohistiocytosis. *Pediatr Blood Cancer*. 2007;48:124-131.
3. Allen CE and McClain KL. *Hematology Am Soc Hematol Educ Program*. 2015;2015:177-82.
4. Janka, G.E. and E.M. Schneider, Modern management of children with haemophagocytic lymphohistiocytosis. *Br J Haematol*, 2004. 124(1): p. 4-14.

SPECIALTY GUIDELINE MANAGEMENT

GATTEX (teduglutide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Gattex is indicated for the treatment of adult and pediatric patients 1 year of age and older with short bowel syndrome (SBS) who are dependent on parenteral support.

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review:

- A. For initial authorization of adult patients greater than or equal to 18 years of age: chart notes supporting the use of parenteral nutrition/IV fluids 3 times a week for 12 months and current volume of parenteral support in liters per week.
- B. For initial authorization of pediatric patient's less than 18 years of age: chart notes supporting the use of parenteral nutrition/IV fluids to account for at least 30% of caloric and/or fluid/electrolyte needs.
- C. For continuation of treatment: chart notes supporting the continued use of parenteral nutrition/IV fluids and current volume of parenteral support in liters per week.
- D. For continuation of treatment for patients who were previously on parenteral nutrition and have been weaned off parenteral nutrition/IV fluids while on Gattex therapy: chart notes supporting the volume of parenteral support in liters per week required at baseline.

III. CRITERIA FOR INITIAL APPROVAL

Short bowel syndrome (SBS)

- A. Authorization of 6 months may be granted for treatment of short bowel syndrome in adult members greater than or equal to 18 years of age who have been dependent on parenteral nutrition and/or intravenous fluids for at least 12 months and the patient receives intravenous nutrition/fluids at least 3 times a week.
- B. Authorization of 6 months may be granted for treatment of short bowel syndrome in pediatric member's less than 18 years of age who are receiving intravenous nutrition/fluids to account for at least 30% of caloric and/or fluid/electrolyte needs.

IV. CONTINUATION OF THERAPY

Short bowel syndrome (SBS)

- A. Patient remains dependent on parenteral nutrition and/or intravenous fluids and whose requirement for parenteral support has decreased by at least 20% from baseline while on Gattex therapy.
- B. Patient who was previously dependent on parenteral nutrition and/or intravenous fluids and has been able to wean off the requirement for parenteral support while on Gattex therapy.

V. REFERENCES

1. Gattex [package insert]. Lexington, MA: Shire-NPS Pharmaceuticals, Inc.; May 2019.
2. Jeppesen PB, Pertkiewicz M, Messing B, et al. Teduglutide reduces need for parenteral support among patients with short bowel syndrome with intestinal failure. *Gastroenterology*. 2012; 143(6):1473-1481.
3. Schwartz LK, O'Keefe SJD, Fujioka K, et al. Long-term teduglutide for the treatment of patients with intestinal failure associated with short bowel syndrome. *Clin Transl Gastroenterol*. 2016; 7:e142.

SPECIALTY GUIDELINE MANAGEMENT

GAZYVA (obinutuzumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Chronic Lymphocytic Leukemia (CLL)
Gazyva, in combination with chlorambucil, is indicated for the treatment of patients with previously untreated CLL.
2. Follicular Lymphoma
 - a. Gazyva, in combination with bendamustine followed by Gazyva monotherapy, is indicated for the treatment of patients with follicular lymphoma who relapsed after, or are refractory to, a rituximab-containing regimen.
 - b. Gazyva, in combination with chemotherapy followed by Gazyva monotherapy in patients achieving at least a partial remission, is indicated for the treatment of adult patients with previously untreated stage II bulky, III or IV follicular lymphoma.

B. Compendial Uses

1. Chronic lymphocytic leukemia
2. Small lymphocytic lymphoma (SLL) (managed in the same manner as CLL)
3. Follicular lymphoma
4. Gastric MALT lymphoma, second-line or subsequent therapy in combination with bendamustine for recurrent or progressive disease, maintenance therapy, or substitute for rituximab in patients experiencing rare complications from rituximab
5. Non-gastric MALT lymphoma, second-line or subsequent therapy in combination with bendamustine for refractory or progressive disease, maintenance therapy, or substitute for rituximab in patients experiencing rare complications from rituximab
6. Nodal marginal zone lymphoma, second-line or subsequent therapy in combination with bendamustine for refractory or progressive disease, maintenance therapy, or substitute for rituximab in patients experiencing rare complications from rituximab
7. Splenic marginal zone lymphoma, second-line (if prior treatment with rituximab) or subsequent therapy in combination with bendamustine for recurrent disease, maintenance therapy, or substitute for rituximab in patients experiencing rare complications from rituximab
8. Histologic transformation of marginal zone lymphoma to diffuse large B-cell lymphoma substitute for rituximab in patients experiencing rare complications from rituximab
9. Mantle cell lymphoma, substitute for rituximab in patients experiencing rare complications from rituximab
10. Diffuse large B-cell lymphoma, substitute for rituximab in patients experiencing rare complications from rituximab
11. High-grade B-cell lymphomas, substitute for rituximab in patients experiencing rare complications from rituximab
12. Burkitt lymphoma, substitute for rituximab in patients experiencing rare complications from rituximab

13. AIDS-related B-cell lymphomas, substitute for rituximab in patients experiencing rare complications from rituximab
14. Post-transplant lymphoproliferative disorders, substitute for rituximab in patients experiencing rare complications from rituximab
15. Castleman's disease, substitute for rituximab in patients experiencing rare complications from rituximab

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Chronic Lymphocytic Leukemia (CLL) and Small Lymphocytic Lymphoma (SLL)

Authorization of 6 months may be granted for the treatment of CLL/SLL.

B. Follicular Lymphoma (FL)

Authorization of 6 months, up to 30 months total, may be granted for the treatment of follicular lymphoma when any of the following criteria are met:

1. The requested medication will be used in combination with CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) regimen, CVP (cyclophosphamide, vincristine and prednisone) regimen, or bendamustine.
2. The requested medication will be used as maintenance therapy
3. The requested medication will be used as a substitute for rituximab in members experiencing rare complications from rituximab such as mucocutaneous reactions including paraneoplastic pemphigus, Stevens-Johnson syndrome, lichenoid dermatitis, vesiculobullous dermatitis, and toxic epidermal necrolysis.

C. Gastric MALT Lymphoma, Non-gastric MALT Lymphoma, Nodal and Splenic Marginal Zone Lymphoma

Authorization of 6 months may be granted for the treatment of gastric MALT lymphoma, non-gastric MALT lymphoma, nodal marginal zone lymphoma, or splenic marginal zone lymphoma when any of the following criteria are met:

1. The requested medication will be used as second-line or subsequent therapy in combination with bendamustine.
2. The requested medication be used as maintenance therapy when the member has been previously treated with the requested medication and bendamustine.
3. The requested medication is used as a substitute for rituximab in members experiencing rare complications from rituximab such as mucocutaneous reactions including paraneoplastic pemphigus, Stevens-Johnson syndrome, lichenoid dermatitis, vesiculobullous dermatitis, and toxic epidermal necrolysis.

D. Histologic Transformation of Marginal Zone Lymphoma to Diffuse Large B-Cell Lymphoma, Mantle Cell Lymphoma, Diffuse Large B-Cell Lymphoma, High-Grade B-Cell Lymphomas, Burkitt Lymphoma, AIDS-Related B-Cell Lymphomas, Post-Transplant Lymphoproliferative Disorders, and Castleman's Disease

Authorization of 6 months may be granted for the treatment of histologic transformation of marginal zone lymphoma to diffuse large B-cell lymphoma, mantle cell lymphoma, diffuse large B-cell lymphoma, high-grade B-cell lymphomas, Burkitt lymphoma, AIDS-related B-cell lymphomas, post-transplant lymphoproliferative disorders, or Castleman's disease when the requested medication is used as a substitute for rituximab in members experiencing rare complications from rituximab such as mucocutaneous reactions including paraneoplastic pemphigus, Stevens-Johnson syndrome, lichenoid dermatitis, vesiculobullous dermatitis, and toxic epidermal necrolysis.

III. CONTINUATION OF THERAPY

A. Follicular Lymphoma (FL)

Authorization of 12 months, up to 30 months total, may be granted for continued treatment in members requesting reauthorization for follicular lymphoma who have not experienced disease progression or an unacceptable toxicity while on the current regimen.

B. All other indications

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced disease progression or an unacceptable toxicity while on the current regimen.

IV. REFERENCES

1. Gazyva [package insert]. South San Francisco, CA: Genentech, Inc.; November 2017.
2. National Comprehensive Cancer Network. The NCCN Drugs & Biologics Compendium. <http://www.nccn.org>. Accessed July 09, 2019.
3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. Version 5.2019. https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf. Accessed July 09, 2019.
4. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: B-Cell Lymphomas. Version 4.2019. https://www.nccn.org/professionals/physician_gls/pdf/b-cell_blocks.pdf. Accessed July 09, 2019.

SPECIALTY GUIDELINE MANAGEMENT

Gemzar (gemcitabine) gemcitabine (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Ovarian cancer
In combination with carboplatin for the treatment of patients with advanced ovarian cancer that has relapsed at least 6 months after completion of platinum-based therapy
2. Breast cancer
In combination with paclitaxel for the first-line treatment of patients with metastatic breast cancer after failure of prior anthracycline-containing adjuvant chemotherapy, unless anthracyclines were clinically contraindicated
3. Non-small cell lung cancer
In combination with cisplatin for the first-line treatment of patients with inoperable, locally advanced (Stage IIIA or IIIB), or metastatic (Stage IV) non-small cell lung cancer (NSCLC)
4. Pancreatic cancer
As first-line treatment for patients with locally advanced (nonresectable Stage II or Stage III) or metastatic (Stage IV) adenocarcinoma of the pancreas. Gemzar or gemcitabine is indicated for patients previously treated with fluorouracil.

B. Compendial Uses

1. Bladder cancer, primary carcinoma of the urethra, upper genitourinary tract tumors, transitional cell carcinoma of the urinary tract, urothelial carcinoma of the prostate, non-urothelial and urothelial cancer with variant histology
2. Bone cancer
 - a. Ewing's sarcoma family of tumors
 - b. Osteosarcoma
3. Breast cancer
4. Head and neck cancers (including very advanced head and neck cancer and cancer of the nasopharynx)
5. Hepatobiliary and biliary tract cancer
 - a. Extrahepatic cholangiocarcinoma
 - b. Intrahepatic cholangiocarcinoma
 - c. Gallbladder cancer
 - d. Ampullary cancer
6. Hodgkin lymphoma
 - a. Classic Hodgkin lymphoma
 - b. Nodular lymphocyte-predominant Hodgkin lymphoma
7. Kidney cancer
8. Malignant pleural mesothelioma
9. Non-small cell lung cancer (NSCLC)

10. Occult primary tumors (cancer of unknown primary)
11. Ovarian cancer, fallopian tube cancer, and primary peritoneal cancer: epithelial ovarian cancer, fallopian tube cancer, and primary peritoneal cancer
12. Pancreatic adenocarcinoma
13. Small cell lung cancer (SCLC)
14. Soft tissue sarcoma
 - a. Extremity/superficial trunk, head/neck
 - b. Retroperitoneal/intra-abdominal
 - c. Angiosarcoma
 - d. Rhabdomyosarcoma
15. Testicular cancer
16. Thymomas and thymic carcinomas
17. Uterine neoplasms (including uterine sarcoma and uterine leiomyosarcoma)
18. AIDS-Related Kaposi Sarcoma
19. Primary cutaneous lymphomas
 - a. Mycosis fungoides/Sezary syndrome
 - b. Primary cutaneous CD30+ T-Cell lymphoproliferative disorders
20. T-Cell lymphomas
 - a. Peripheral T-Cell lymphomas
 - b. Adult T-Cell leukemia/lymphoma
 - c. Extranodal NK/T-Cell lymphoma, nasal type
 - d. Hepatosplenic Gamma-Delta T-Cell lymphoma
21. Gestational trophoblastic neoplasia
22. B-Cell lymphomas
 - a. Follicular lymphoma (grade 1-2)
 - b. Histologic transformation of marginal zone lymphoma to diffuse large B-Cell lymphoma
 - c. Mantle cell lymphoma
 - d. Diffuse large B-Cell lymphoma
 - e. High-Grade B-Cell lymphomas
 - f. Burkitt lymphoma
 - g. AIDS-Related B-Cell lymphomas
 - h. Post-Transplant lymphoproliferative disorders
23. Cervical cancer

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Pancreatic Adenocarcinoma

Authorization of 6 months may be granted for the treatment of pancreatic adenocarcinoma.

B. Breast Cancer

Authorization of 6 months may be granted for the treatment of recurrent or metastatic breast cancer.

C. Hepatobiliary and Biliary Tract Cancer

Authorization of 6 months may be granted for the treatment of hepatobiliary and biliary tract cancer (including intrahepatic and extrahepatic cholangiocarcinoma, gallbladder cancer, and ampullary cancer).

D. Ovarian Cancer, Fallopian Tube Cancer, and Primary Peritoneal Cancer

Epithelial Ovarian Cancer, Fallopian Tube Cancer, and Primary Peritoneal Cancer

Authorization of 6 months may be granted for the treatment of advanced, persistent, or recurrent epithelial ovarian cancer, fallopian tube cancer, and primary peritoneal cancer.

E. Non-Small Cell Lung Cancer (NSCLC)

Authorization of 6 months may be granted for the treatment of NSCLC.

F. Bladder Cancer, Primary Carcinoma of the Urethra, Upper Genitourinary Tract Tumors, Transitional Cell Carcinoma of the Urinary Tract, Urothelial Carcinoma of the Prostate, and Non-Urothelial and Urothelial cancer with Variant Histology

Authorization of 6 months may be granted for the treatment of bladder cancer, primary carcinoma of the urethra, upper genitourinary tract tumors, transitional cell carcinoma of the urinary tract, urothelial carcinoma of the prostate, and non-urothelial and urothelial cancer with variant histology.

G. Small Cell Lung Cancer (SCLC)

Authorization of 6 months may be granted for the treatment of SCLC.

H. Soft Tissue Sarcoma

Authorization of 6 months may be granted for treatment of soft tissue sarcoma (including extremity/superficial trunk, head/neck, retroperitoneal/intra-abdominal, angiosarcoma, and rhabdomyosarcoma).

I. Bone Cancer

1. Ewing's Sarcoma

Authorization of 6 months may be granted for treatment of relapsed, progressive, or metastatic Ewing's sarcoma.

2. Osteosarcoma

Authorization of 6 months may be granted for treatment of relapsed/refractory or metastatic osteosarcoma.

J. Head and Neck Cancer

Authorization of 6 months may be granted for the treatment of head and neck cancer (including very advanced head and neck cancer and cancer of the nasopharynx).

K. Hodgkin Lymphoma

1. Classic Hodgkin Lymphoma

Authorization of 6 months may be granted for the treatment of classic Hodgkin lymphoma.

2. Nodular Lymphocyte-Predominant Hodgkin Lymphoma

Authorization of 6 months may be granted for the treatment of progressive, relapsed, or refractory nodular lymphocyte-predominant Hodgkin lymphoma.

L. Kidney Cancer

Authorization of 6 months may be granted for the treatment of relapsed or metastatic kidney cancer.

M. Malignant Pleural Mesothelioma

Authorization of 6 months may be granted for the treatment of malignant pleural mesothelioma.

N. Occult Primary Tumors (cancer of unknown primary)

Authorization of 6 months may be granted for the treatment of occult primary tumors.

O. Testicular Cancer

Authorization of 6 months may be granted for the treatment of testicular cancer.

P. Thymomas and Thymic Carcinomas

Authorization of 6 months may be granted for the treatment of thymomas and thymic carcinomas.

Q. Uterine Neoplasms

Authorization of 6 months may be granted for the treatment of uterine neoplasms (including uterine sarcoma and uterine leiomyosarcoma).

R. AIDS-Related Kaposi Sarcoma

Authorization of 6 months may be granted for the treatment of AIDS-Related Kaposi Sarcoma.

S. Primary Cutaneous Lymphomas

Authorization of 6 months may be granted for the treatment of primary cutaneous lymphomas (including mycosis fungoides/Sézary syndrome and primary cutaneous CD30+ T-Cell lymphoproliferative disorders).

T. T-Cell Lymphomas

Authorization of 6 months may be granted for the treatment of T-Cell lymphomas (including peripheral T-Cell lymphomas, adult T-Cell leukemia/lymphoma, hepatosplenic gamma-delta T-Cell lymphoma, and extranodal NKT/T-Cell lymphoma, nasal type).

U. Gestational Trophoblastic Neoplasia

Authorization of 6 months may be granted for the treatment of gestational trophoblastic neoplasia in members when either of the following criteria are met:

1. Member has recurrent or progressive intermediate trophoblastic tumor (placental site trophoblastic tumor or epithelioid trophoblastic tumor) following treatment with a platinum/etoposide-containing regimen; or
2. Member has methotrexate-resistant high-risk disease

V. B-Cell Lymphomas

Authorization of 6 months may be granted for the treatment of B-Cell lymphomas (including follicular lymphoma [grade 1-2], histologic transformation of marginal zone lymphoma to diffuse large B-Cell lymphoma, mantle cell lymphoma, diffuse large B-Cell lymphoma, high-grade B-Cell lymphomas, Burkitt lymphoma, AIDS-Related B-Cell lymphomas, and post-transplant lymphoproliferative disorders).

W. Cervical Cancer

Authorization of 6 months may be granted treatment of cervical cancer in members when either of the following criteria are met:

1. The disease is recurrent or persistent; or
2. Gemcitabine will be used in combination with cisplatin as neoadjuvant therapy.

III. CONTINUATION OF THERAPY

Reference number(s)
2040-A

Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who are experiencing clinical benefit to therapy or who have not experienced an unacceptable toxicity.

IV. **REFERENCES**

1. Gemzar [package insert]. Indianapolis, IN: Eli Lilly and Company; May 2019.
2. Gemcitabine [package insert]. Lake Forest, IL: Hospira, Inc.; June 2019.
3. The NCCN Drugs & Biologics Compendium 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed July 07, 2019.
4. Micromedex Solutions [database online]. Ann Arbor, MI: Truven Health Analytics Inc. Updated periodically. www.micromedexsolutions.com [available with subscription]. Accessed (July 2019).
5. Lexicomp [database online]. Hudson, OH: Lexi-Comp, Inc.; http://online.lexi.com/lco/action/index/dataset/complete_ashp [available with subscription]. Accessed (July 2019).
6. AHFS DI (Adult and Pediatric) [database online]. Hudson, OH: Lexi-Comp, Inc.; http://online.lexi.com/lco/action/index/dataset/complete_ashp [available with subscription]. Accessed (July 2019).

SPECIALTY GUIDELINE MANAGEMENT

GILENYA (fingolimod)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication: Gilenya is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in patients 10 years of age and older.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Relapsing forms of multiple sclerosis

Authorization of 12 months may be granted to members who have been diagnosed with a relapsing form of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse).

B. Clinically isolated syndrome

Authorization of 12 months may be granted to members for the treatment of clinically isolated syndrome of multiple sclerosis.

III. CONTINUATION OF THERAPY

For all indications: Authorization of 12 months may be granted to members who are experiencing disease stability or improvement while receiving Gilenya.

IV. OTHER CRITERIA

Members will not use Gilenya concomitantly with other medications used for the treatment of multiple sclerosis, excluding Ampyra.

V. REFERENCE

1. Gilenya [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; August 2019.

SPECIALTY GUIDELINE MANAGEMENT

GILOTRIF (afatinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. EGFR Mutation-Positive, Metastatic Non-Small Cell Lung Cancer
 Gilotrif is indicated for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have non-resistant epidermal growth factor receptor (EGFR) mutations as detected by an FDA-approved test.
2. Previously Treated, Metastatic Squamous NSCLC
 Gilotrif is indicated for the treatment of patients with metastatic squamous NSCLC progressing after platinum-based chemotherapy.

B. Compendial Uses

1. NSCLC, recurrent, advanced or metastatic sensitizing EGFR mutation-positive
2. Recurrent brain metastases from EGFR sensitizing mutation-positive NSCLC
3. Non-nasopharyngeal head and neck cancer

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: For NSCLC, EGFR mutation testing results (where applicable).

III. CRITERIA FOR INITIAL APPROVAL

A. **Non-Small Cell Lung Cancer (NSCLC)**

1. Authorization of 12 months may be granted for treatment of recurrent, advanced or metastatic NSCLC (including brain metastases from NSCLC) when the member has sensitizing EGFR mutation-positive disease.
2. Authorization of 12 months may be granted for treatment of metastatic squamous NSCLC progressing after platinum-based chemotherapy.

B. **Head and Neck Cancer**

Authorization of 12 months may be granted for treatment of non-nasopharyngeal head and neck cancer following disease progression on or after platinum-containing chemotherapy.

Reference number(s)
1658-A

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced an unacceptable toxicity.

V. REFERENCES

1. Gilotrif [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; January 2018.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed March 18, 2019.
3. The NCCN Clinical Practice Guidelines in Oncology® Non-Small Cell Lung Cancer (Version 3.2019).© 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 18, 2019.
4. The NCCN Clinical Practice Guidelines in Oncology® Central Nervous System Cancers Version 1.2019. ©2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 18, 2019.
5. The NCCN Clinical Practice Guidelines in Oncology® Head and Neck Cancers Version 1.2019. ©2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 18, 2019.

SPECIALTY GUIDELINE MANAGEMENT

GIVLAARI (givosiran)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Givlaari is an aminolevulinate synthase 1-directed small interfering RNA indicated for the treatment of adults with acute hepatic porphyria (AHP).

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
Elevated porphobilinogen (PBG) in the urine confirmed by a PBG quantitative, random urine test, or an elevated porphyrin level (plasma or fecal).

III. CRITERIA FOR INITIAL APPROVAL

Acute Hepatic Porphyria

Authorization of 12 months may be granted for treatment of acute hepatic porphyria when all of the following criteria are met:

1. The member is actively symptomatic
2. The member has an elevated urine porphobilinogen (PBG), or an elevated porphyrin level (plasma or fecal).

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment of an indication listed in Section III for members who are experiencing benefit from therapy while receiving Givlaari.

V. REFERENCES

1. Givlaari [package insert]. Cambridge, MA: Alnylam Pharmaceuticals; November 2019.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME **GIVLAARI**
(generic) **(givosiran)**

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

MDC
Ref # 3419-A

FDA-APPROVED INDICATIONS

Givlaari is an aminolevulinate synthase 1-directed small interfering RNA indicated for the treatment of adults with acute hepatic porphyria (AHP).

CRITERIA FOR APPROVAL

1	Does the patient have a diagnosis of acute hepatic porphyria?	Yes	No
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Guidelines for Approval	
Duration of Approval	12 months
Set 1: Acute hepatic porphyria	
Yes to question(s)	No to question(s)
1	None

Mapping Instructions	
	Yes No
1. Approve, 12 months	Deny

RATIONALE

These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to ensure that patients follow selection elements noted in labeling and/or practice guidelines in order to decrease the potential for inappropriate utilization.

REFERENCES

1. Givlaari [package insert]. Cambridge, MA: Alnylam Pharmaceuticals; November 2019.

DOCUMENT HISTORY

Created: Specialty Clinical Development (AS) 11/2019
 Revised:
 Reviewed: CDPR / AN 12/2019
 External Review:

SPECIALTY GUIDELINE MANAGEMENT

GENOTROPIN (somatropin)
HUMATROPE (somatropin)
NORDITROPIN (somatropin)
NUTROPIN AQ (somatropin)
OMNITROPE (somatropin)
SAIZEN (somatropin)
ZOMACTON (somatropin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no contraindications or exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Pediatric patients with growth failure due to any of the following:
 - a. Growth hormone (GH) deficiency
 - b. Turner syndrome
 - c. Noonan syndrome
 - d. Small for gestational age (SGA)
 - e. Prader-Willi syndrome
 - f. Chronic kidney disease (CKD)
 - g. Short stature homeobox-containing gene (SHOX) deficiency
2. Adults with childhood-onset or adult-onset GH deficiency

B. Compendial Uses

1. Human immunodeficiency virus (HIV)-associated wasting/cachexia
2. Short bowel syndrome (SBS)
3. Growth failure associated with any of the following:
 - a. Cerebral palsy
 - b. Congenital adrenal hyperplasia
 - c. Cystic fibrosis
 - d. Russell-Silver syndrome

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review for both initial and continuation of therapy requests (where applicable):

- A. Medical records supporting the diagnosis of neonatal GH deficiency
- B. Pretreatment growth hormone provocative test result(s) (laboratory report or medical record documentation)
- C. Pretreatment and/or current IGF-1 level (laboratory report or medical record documentation)*

Reference number(s)
1742-A

- D. The following laboratory test reports must be provided:
 - 1. Diagnostic karyotype results in Turner syndrome
 - 2. Diagnostic genetic test results in Prader-Willi syndrome
 - 3. Diagnostic molecular or genetic test results in SHOX deficiency
- E. The following information must be provided for all continuation of therapy requests:
 - 1. Total duration of treatment (approximate duration is acceptable)
 - 2. Date of last dose administered
 - 3. Approving health plan/pharmacy benefit manager
 - 4. Date of prior authorization/approval
 - 5. Prior authorization approval letter

* IGF-1 levels vary based on the laboratory performing the analysis. Laboratory-specific values must be provided to determine whether the value is within the normal range.

III. INITIAL CRITERIA FOR APPROVAL

A. Pediatric GH Deficiency

Authorization of 12 months may be granted to members with pediatric GH deficiency when EITHER criteria 1. or 2. below is met:

- 1. Member is a neonate or was diagnosed with GH deficiency as a neonate. Medical records must be available to support the diagnosis of neonatal GH deficiency (e.g., hypoglycemia with random GH level, evidence of multiple pituitary hormone deficiency, chart notes, or magnetic resonance imaging [MRI] results).
- 2. Member meets ALL of the following:
 - a. Member has EITHER:
 - i. Two pretreatment pharmacologic provocative GH tests with both results demonstrating a peak GH level < 10 ng/mL, OR
 - ii. A documented pituitary or CNS disorder (refer to Appendix A) and a pretreatment IGF-1 level > 2 standard deviations (SD) below the mean
 - b. For members < 2.5 years of age at initiation of treatment, the pretreatment height is > 2 SD below the mean and growth velocity is slow
 - c. For members ≥ 2.5 years of age at initiation of treatment:
 - i. Pretreatment height is > 2 SD below the mean and 1-year height velocity is > 1 SD below the mean, OR
 - ii. Pretreatment 1-year height velocity is > 2 SD below the mean
 - d. Epiphyses are open

B. Small for Gestational Age

Authorization of 12 months may be granted to members born SGA when ALL of the following criteria are met:

- 1. Member meets at least one of the following:
 - a. Birth weight < 2500 g at gestational age > 37 weeks
 - b. Birth weight or length less than 3rd percentile for gestational age
 - c. Birth weight or length ≥ 2 SD below the mean for gestational age
- 2. Pretreatment age is ≥ 2 years
- 3. Member failed to manifest catch-up growth by age 2 (i.e., pretreatment height > 2 SD below the mean)
- 4. Epiphyses are open

C. Turner Syndrome

Authorization of 12 months may be granted to members with Turner syndrome when ALL of the following criteria are met:

1. Diagnosis was confirmed by karyotyping
2. Patient's pretreatment height is less than the 5th percentile for age
3. Epiphyses are open

D. Growth Failure Associated with Chronic Kidney Disease, Cerebral Palsy, Congenital Adrenal Hyperplasia, Cystic Fibrosis, and Russell-Silver Syndrome

Authorization of 12 months may be granted to members with CKD, cerebral palsy, congenital adrenal hyperplasia, cystic fibrosis, or Russell-Silver syndrome when ALL of the following criteria are met:

1. For members < 2.5 years of age at initiation of treatment, the pretreatment height is > 2 SD below the mean and growth velocity is slow
2. For members ≥ 2.5 years of age at initiation of treatment:
 - a. Pretreatment height is > 2 SD below the mean and 1-year height velocity is > 1 SD below the mean, OR
 - b. Pretreatment 1-year height velocity is > 2 SD below the mean
3. Epiphyses are open

E. Prader-Willi Syndrome

Authorization of 12 months may be granted to members with Prader-Willi syndrome when the diagnosis was confirmed by genetic testing demonstrating any of the following:

1. Deletion in the chromosomal 15q11.2-q13 region
2. Maternal uniparental disomy in chromosome 15
3. Imprinting defects or translocations involving chromosome 15

F. Noonan Syndrome

Authorization of 12 months may be granted to members with Noonan syndrome when ALL of the following criteria are met:

1. Pretreatment height is > 2 SD below the mean and 1-year height velocity is > 1 SD below the mean OR pretreatment 1-year height velocity is > 2 SD below the mean
2. Epiphyses are open

G. Short Stature Homeobox-Containing Gene Deficiency

Authorization of 12 months may be granted to members with SHOX deficiency when ALL of the following criteria are met:

1. The diagnosis of SHOX deficiency was confirmed by molecular or genetic analyses
2. Pretreatment height is > 2 SD below the mean and 1-year height velocity is > 1 SD below the mean OR pretreatment 1-year height velocity is > 2 SD below the mean
3. Epiphyses are open

H. Adult GH Deficiency

Authorization of 12 months may be granted to members with adult GH deficiency when ANY of the following criteria is met:

1. Member has had 2 pretreatment pharmacologic provocative GH tests and both results demonstrated GH levels < 5 ng/mL, unless the agent is Macrilen in which case a GH level of less than 2.8 ng/ml confirms the presence of adult GHD
2. Member has had 1 pretreatment pharmacologic provocative GH test that demonstrated a GH level < 5 ng/mL AND has a pretreatment IGF-1 level that is low for age and gender, unless the agent is Macrilen in which case a GH level of less than 2.8 ng/ml confirms the presence of adult GHD
3. Member has a structural abnormality of the hypothalamus or pituitary (refer to Appendix A) and ≥ 3 documented pituitary hormone deficiencies (refer to Appendix B)
4. Member has childhood-onset GH deficiency and a congenital abnormality of the hypothalamus or pituitary (refer to Appendix A)

I. **HIV-Associated Wasting/Cachexia**

Authorization of 12 weeks may be granted to members with HIV-associated wasting or cachexia when ALL of the following criteria are met:

1. Member has tried and had a suboptimal response to alternative therapies (e.g., cyproheptadine, dronabinol, megestrol acetate or testosterone if hypogonadal) unless the member has a contraindication or intolerance to alternative therapies
2. Member is currently on antiretroviral therapy
3. Pretreatment BMI is < 18.5 kg/m² (see Appendix C)

J. **Short Bowel Syndrome**

Authorization of a lifetime total of 8 weeks may be granted to members with short bowel syndrome who depend on intravenous parenteral nutrition when GH will be used in conjunction with optimal management of SBS.

IV. **CONTINUATION OF THERAPY**

A. **Pediatric GH Deficiency, Turner Syndrome, Noonan Syndrome, CKD, SGA, SHOX deficiency, Congenital Adrenal Hyperplasia, Cerebral Palsy, Cystic Fibrosis, and Russell-Silver Syndrome**

Authorization of 12 months may be granted for continuation of therapy when ALL of the following criteria are met:

1. Epiphyses are open (confirmed by X-ray or X-ray is not available)
2. Member's growth rate is > 2 cm/year unless there is a documented clinical reason for lack of efficacy (e.g., on treatment less than 1 year, nearing final adult height/late stages of puberty)

B. **Prader-Willi Syndrome**

Authorization of 12 months may be granted for continuation of therapy when the member's body composition and psychomotor function have improved or stabilized in response to GH therapy.

C. **Adult GH Deficiency**

Authorization of 12 months may be granted for continuation of therapy when all criteria for initial authorization are met (refer to Section III.H. above).

D. **HIV-Associated Wasting/Cachexia**

Authorization of 12 weeks may be granted for continuation of therapy when ALL of the following criteria are met:

1. Member is currently on antiretroviral therapy.
2. Current BMI is < 27 kg/m² (see Appendix C).

V. **APPENDICES**

A. **Appendix A: Examples of Hypothalamic/Pituitary/CNS Disorders**

1. Congenital genetic abnormalities
 - a. Known mutations in growth-hormone-releasing hormone (GHRH) receptor, GH gene, GH receptor, or pituitary transcription factors
2. Congenital structural abnormalities
 - a. Optic nerve hypoplasia/septo-optic dysplasia
 - b. Agenesis of corpus callosum
 - c. Empty sella syndrome
 - d. Ectopic posterior pituitary
 - e. Pituitary aplasia/hypoplasia

- f. Pituitary stalk defect
- g. Anencephaly or prosencephaly
- h. Other mid-line defects
- i. Vascular malformations
3. Acquired structural abnormalities (or causes of hypothalamic/pituitary damage)
 - a. CNS tumors/neoplasms (e.g., craniopharyngioma, glioma, pituitary adenoma)
 - b. Cysts (Rathke cleft cyst or arachnoid cleft cyst)
 - c. Surgery
 - d. Radiation
 - e. Chemotherapy
 - f. CNS infections
 - g. CNS infarction (e.g., Sheehan's syndrome)
 - h. Inflammatory lesions (e.g., autoimmune hypophysitis)
 - i. Infiltrative lesions (e.g., sarcoidosis, histiocytosis)
 - j. Head trauma/traumatic brain injury
 - k. Aneurysmal subarachnoid hemorrhage

B. Appendix B: Pituitary Hormones (Other than Growth Hormone)

1. Adrenocorticotrophic hormone (ACTH)
2. Antidiuretic hormone (ADH)
3. Follicle stimulating hormone (FSH)
4. Luteinizing hormone (LH)
5. Thyroid stimulating hormone (TSH)
6. Prolactin

C. Appendix C: Calculation of BMI

BMI =	$\frac{\text{Weight (pounds)} \times 703}{[\text{Height (inches)}]^2}$	OR	$\frac{\text{Weight (kg)}}{[\text{Height (m)}]^2}$
BMI classification:	Underweight		< 18.5 kg/m ²
	Normal weight		18.5 – 24.9 kg/m ²
	Overweight		25 – 29.9 kg/m ²
	Obesity (class 1)		30 – 34.9 kg/m ²
	Obesity (class 2)		35 – 39.9 kg/m ²
	Extreme obesity		≥ 40 kg/m ²

VI. REFERENCES

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ENHANCED SPECIALTY GUIDELINE MANAGEMENT

HAEGARDA (C1 Esterase Inhibitor Subcutaneous [Human])

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Routine prophylaxis to prevent Hereditary Angioedema (HAE) attacks in adolescent and adult patients

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

- A. C4 levels and C1 inhibitor functional and antigenic protein levels
- B. F12, angiopoietin-1 or plasminogen gene mutation testing, if applicable
- C. Chart notes confirming family history of angioedema, if applicable

III. CRITERIA FOR APPROVAL

Authorization of 12 months may be granted for prevention of hereditary angioedema attacks when Haegarda will not be used in combination with Cinryze or Takhzyro and either of the following criteria is met:

- A. Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing.
 - 1. C1 inhibitor (C1-INH) antigenic level below the lower limit of normal as defined by the laboratory performing the test; or
 - 2. Normal C1-INH antigenic level and a low C1-INH functional level (functional C1-INH less than 50% or C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test)
- B. Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
 - 1. Member has an F12, angiopoietin-1, or plasminogen gene mutation as confirmed by genetic testing, or
 - 2. Member has a documented family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine (e.g., cetirizine) for at least one month.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy when all of the following criteria are met:

- A. Member meets the criteria for initial approval.
- B. Member has experienced reduction in frequency, severity, and/or duration of attacks since starting treatment.

V. REFERENCES

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SPECIALTY GUIDELINE MANAGEMENT

HALAVEN (eribulin mesylate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Halaven is indicated for the treatment of patients with metastatic breast cancer who have previously received at least two chemotherapeutic regimens for the treatment of metastatic disease. Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting.
2. Halaven is indicated for the treatment of patients with unresectable or metastatic liposarcoma who have received a prior anthracycline-containing regimen.

B. Compendial Uses

1. Breast cancer
 - a. Recurrent or stage IV (M1) human epidermal growth factor receptor 2 (HER2)-negative breast cancer
 - b. Recurrent or stage IV (M1) human epidermal growth factor receptor 2 (HER2)-positive breast cancer
2. Soft tissue sarcoma
 - a. Angiosarcoma
 - b. Retroperitoneal/intra-abdominal soft tissue sarcoma
 - c. Pleomorphic rhabdomyosarcoma
 - d. Extremity/superficial trunk, head/neck
3. Uterine sarcoma

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: HER2 status testing results (where applicable).

III. CRITERIA FOR INITIAL APPROVAL

A. **Breast Cancer**

Authorization of 12 months may be granted for treatment of recurrent or metastatic breast cancer when any of the following criteria is met:

1. Halaven will be used as a single agent for human epidermal growth factor receptor 2 (HER2)-negative disease; or
2. Halaven will be used in combination with trastuzumab for human epidermal growth factor receptor 2 (HER2)-positive disease.

Reference number(s)
1893-A

B. Soft Tissue Sarcoma

Authorization of 12 months may be granted for treatment of any of the following types of soft tissue sarcoma, as single-agent palliative therapy:

1. Liposarcoma
2. Angiosarcoma
3. Pleomorphic rhabdomyosarcoma
4. Retroperitoneal/intra-abdominal soft tissue sarcoma
5. Extremity/superficial trunk, head/neck

C. Uterine Sarcoma

Authorization of 12 months may be granted for treatment of recurrent or metastatic uterine sarcoma.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication in Section III who are experiencing clinical benefit to therapy or who have not experienced an unacceptable toxicity.

V. REFERENCES

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SPECIALTY GUIDELINE MANAGEMENT

HARVONI (ledipasvir and sofosbuvir)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Harvoni is indicated for the treatment of:

1. Adult patients with chronic hepatitis C virus (HCV):
 - a. genotype 1, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis
 - b. genotype 1 infection with decompensated cirrhosis, for use in combination with ribavirin
 - c. genotype 1 or 4 infection who are liver transplant recipients without cirrhosis or with compensated cirrhosis, in combination with ribavirin
2. Pediatric patients 12 years of age and older or weighing at least 35 kg with HCV genotype 1, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR APPROVAL

A. Chronic hepatitis C virus infection, without ribavirin

1. Genotype 1 infection

- a. Authorization of up to 12 weeks total may be granted for treatment-naïve members with compensated cirrhosis.
- b. Authorization of up to 12 weeks total may be granted for treatment-naïve members without cirrhosis who have HIV co-infection, are African American, are less than 18 years of age, or have pre-treatment HCV RNA greater than or equal to 6 million IU/mL.
- c. Authorization of up to 8 weeks total may be granted for treatment-naïve members without cirrhosis who have pre-treatment HCV RNA below 6 million IU/mL and are HIV-uninfected and non-African American.
- d. Authorization of up to 12 weeks total may be granted for members without cirrhosis who failed prior treatment with peginterferon alfa (PEG-IFN) and ribavirin (RBV) with or without an HCV protease inhibitor (telaprevir, boceprevir, or simeprevir).
- e. Authorization of up to 24 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV with or without an HCV protease inhibitor.

2. Genotype 4 infection

Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who are treatment-naïve or who failed prior treatment with PEG-IFN and RBV with or without an HCV protease inhibitor.

3. Genotype 5 infection

Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who are treatment-naïve or who failed prior treatment with PEG-IFN and RBV with or without an HCV protease inhibitor.

4. Genotype 6 infection

Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who are treatment-naïve or who failed prior treatment with PEG-IFN and RBV with or without an HCV protease inhibitor.

5. Decompensated cirrhosis (CTP class B or C)

Authorization of up to 24 weeks total may be granted for members with HCV genotype 1, 4, 5 or 6 infection and documented anemia (baseline Hgb below 10 g/dL) or RBV ineligibility (see Section IV).

6. Kidney transplant recipients

Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who have HCV genotype 1 or 4 infection.

B. Chronic hepatitis C virus infection, in combination with ribavirin

1. Genotype 1 infection

- Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV with or without an HCV protease inhibitor.
- Authorization of up to 12 weeks total may be granted for members without cirrhosis who failed prior treatment with sofosbuvir (Sovaldi) plus RBV with or without PEG-IFN.

2. Genotype 4 infection

Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV with or without an HCV protease inhibitor.

3. Decompensated cirrhosis (CTP class B or C)

- Authorization of up to 12 weeks total may be granted for members with HCV genotype 1, 4, 5 or 6 infection.
- Authorization of up to 24 weeks total may be granted for members with HCV genotype 1, 4, 5 or 6 infection who failed prior treatment with a sofosbuvir-based regimen (eg, sofosbuvir and RBV, sofosbuvir plus PEG-IFN and RBV, sofosbuvir plus simeprevir with or without RBV).
- Authorization of up to 12 weeks total may be granted for members with recurrent HCV genotype 1, 4, 5 or 6 infection post liver transplantation and decompensated cirrhosis (see section B.4 below).

4. Recurrent HCV infection post liver transplantation

Authorization of up to 12 weeks total may be granted for members with recurrent HCV genotype 1, 4, 5 or 6 infection post liver transplantation.

C. HCV and HIV coinfection

Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in Section A or B above are met.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. APPENDIX: RIBAVIRIN INELIGIBILITY

RBV ineligibility is defined as one or more of the below:

- Intolerance to RBV
- Pregnant female or male whose female partner is pregnant
- Hemoglobinopathy
- Coadministration with didanosine
- History of significant or unstable cardiac disease

V. REFERENCES

1. Harvoni [package insert]. Foster City, CA: Gilead Sciences; November 2017.
2. AASLD/IDSA/IAS–USA. Recommendations for testing, managing, and treating hepatitis C. <http://www.hcvguidelines.org>. Last changes made May 24, 2018. Accessed August 02, 2018.

SPECIALTY GUIDELINE MANAGEMENT

NOVAREL (chorionic gonadotropin) PREGNYL (chorionic gonadotropin) OVIDREL (choriogonadotropin alfa) chorionic gonadotropin

*Hereafter, hCG will be used to describe all products

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Novarel and Pregnyl are indicated for:

1. Prepubertal cryptorchidism not due to anatomic obstruction
2. Selected cases of hypogonadotropic hypogonadism (hypogonadism secondary to a pituitary deficiency) in males
3. Induction of ovulation and pregnancy in the anovulatory, infertile woman in whom the cause of anovulation is secondary and not due to primary ovarian failure, and who has been appropriately pretreated with human menotropins

Ovidrel is indicated for:

1. Induction of final follicular maturation and early luteinization in infertile women who have undergone pituitary desensitization and who have been appropriately pretreated with follicle stimulating hormones as part of an assisted reproductive technology (ART) program such as in vitro fertilization and embryo transfer
2. Induction of ovulation and pregnancy in anovulatory infertile patients in whom the cause of infertility is functional and not due to primary ovarian failure

B. Compendial Uses

1. Prepubertal cryptorchidism
2. Hypogonadotropic hypogonadism in males
3. Infertility, luteal phase support

All other indications are considered experimental/investigational and not medically necessary.

II. MEDICAL BENEFIT ALIGNMENT

Specialty Guideline Management coverage review will be bypassed for drug(s) being requested for a procedure that has been approved under a member's medical benefit plan. Such members will be exempt from the requirements in Sections IV and V. A medical authorization number and confirmation of the approved procedure(s) will be required.

Reference number(s)
1925-A, 1926-A

NOTE: Some plans may opt-out of medical benefit alignment. Members receiving coverage under such plans must meet the requirements in Sections IV and V.

III. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review for hypogonadotropic hypogonadism: testosterone, FSH, and LH levels.

IV. CRITERIA FOR INITIAL APPROVAL

A. Induction of oocyte maturation and/or release

Authorization of 12 months may be granted for members undergoing ovulation induction or assisted reproductive technology (ART).

B. Prepubertal cryptorchidism

Authorization of 6 months may be granted for treatment of prepubertal cryptorchidism.

C. Hypogonadotropic hypogonadism

Authorization of 12 months may be granted for treatment of hypogonadotropic hypogonadism in members who meet both of the following criteria:

1. Low pretreatment testosterone levels
2. Low or low-normal follicle stimulating hormone (FSH) or luteinizing hormone (LH) levels

V. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

VI. REFERENCES

1. Novarel [package insert]. Parsippany, NJ: Ferring Pharmaceuticals Inc.; May 2018.
2. Pregnyl [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; January 2015.
3. Ovidrel [package insert]. Rockland, MA: EMD Serono, Inc.; June 2018.
4. Chorionic Gonadotropin for Injection [package insert]. Lake Zurich, IL: Fresenius Kabi; February 2016.
5. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, CO. Available at: <http://www.micromedexsolutions.com> Accessed May 14, 2019.
6. Nosarka S, Kruger T, Siebert I, et al. Luteal phase support in in vitro fertilization: meta-analysis of randomized trials. *Gynecol Obstet Invest.* 2005;60:67-74.
7. American Association of Clinical Endocrinologists. Medical guidelines for clinical practice for the evaluation and treatment of hypogonadism in adult male patients – 2002 Update. *Endocr Pract.* 2002;8:439-456.

SPECIALTY GUIDELINE MANAGEMENT

NOVAREL (chorionic gonadotropin) PREGNYL (chorionic gonadotropin) OVIDREL (choriogonadotropin alfa) chorionic gonadotropin

*Hereafter, hCG will be used to describe all products

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Novarel and Pregnyl are indicated for:

1. Prepubertal cryptorchidism not due to anatomic obstruction
2. Selected cases of hypogonadotropic hypogonadism (hypogonadism secondary to a pituitary deficiency) in males
3. Induction of ovulation and pregnancy in the anovulatory, infertile woman in whom the cause of anovulation is secondary and not due to primary ovarian failure, and who has been appropriately pretreated with human menotropins

Ovidrel is indicated for:

1. Induction of final follicular maturation and early luteinization in infertile women who have undergone pituitary desensitization and who have been appropriately pretreated with follicle stimulating hormones as part of an assisted reproductive technology (ART) program such as in vitro fertilization and embryo transfer
2. Induction of ovulation and pregnancy in anovulatory infertile patients in whom the cause of infertility is functional and not due to primary ovarian failure

B. Compendial Uses

1. Prepubertal cryptorchidism
2. Hypogonadotropic hypogonadism in males
3. Infertility, luteal phase support

All other indications are considered experimental/investigational and not medically necessary.

II. MEDICAL BENEFIT ALIGNMENT

Specialty Guideline Management coverage review will be bypassed for drug(s) being requested for a procedure that has been approved under a member's medical benefit plan. Such members will be exempt from the requirements in Sections IV and V. A medical authorization number and confirmation of the approved procedure(s) will be required.

Reference number(s)
1925-A, 1926-A

NOTE: Some plans may opt-out of medical benefit alignment. Members receiving coverage under such plans must meet the requirements in Sections IV and V.

III. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review for hypogonadotropic hypogonadism: testosterone, FSH, and LH levels.

IV. CRITERIA FOR INITIAL APPROVAL

A. Induction of oocyte maturation and/or release

Authorization of 12 months may be granted for members undergoing ovulation induction or assisted reproductive technology (ART).

B. Prepubertal cryptorchidism

Authorization of 6 months may be granted for treatment of prepubertal cryptorchidism.

C. Hypogonadotropic hypogonadism

Authorization of 12 months may be granted for treatment of hypogonadotropic hypogonadism in members who meet both of the following criteria:

1. Low pretreatment testosterone levels
2. Low or low-normal follicle stimulating hormone (FSH) or luteinizing hormone (LH) levels

V. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

VI. REFERENCES

1. Novarel [package insert]. Parsippany, NJ: Ferring Pharmaceuticals Inc.; May 2018.
2. Pregnyl [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; January 2015.
3. Ovidrel [package insert]. Rockland, MA: EMD Serono, Inc.; June 2018.
4. Chorionic Gonadotropin for Injection [package insert]. Lake Zurich, IL: Fresenius Kabi; February 2016.
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SPECIALTY GUIDELINE MANAGEMENT

HEMLIBRA (emicizumab-kxwh)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Hemlibra is indicated for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adult and pediatric patients ages newborn and older with hemophilia A (congenital factor VIII deficiency) with or without factor VIII inhibitors

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of hemophilia A (congenital factor VIII deficiency).

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain reduction in the frequency of bleeding episodes.

IV. REFERENCES

1. Hemlibra [package insert]. South San Francisco, CA: Genentech, Inc.; October 2018.
2. Oldenburg J, Mahlangu JN, Kim B, et al. Emicizumab Prophylaxis in Hemophilia A with Inhibitors. *N Engl J Med*. 2017; 377:809-818.
3. A Study of Emicizumab Administered Subcutaneously (SC) in Pediatric Participants With Hemophilia A and Factor VIII (FVIII) Inhibitors (HAVEN 2). *ClinicalTrials.gov* [Internet]. Bethesda (MD): National Library of Medicine (US). June 10, 2016. Identifier: NCT02795767. Available at <https://clinicaltrials.gov/ct2/show/NCT02795767>. Accessed November 20, 2017.
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6. National Hemophilia Foundation. MASAC recommendations concerning products licensed for the treatment of hemophilia and other bleeding disorders. Revised April 2018. MASAC Document #253. Available at <https://www.wfh.org/en/resources/wfh-treatment-guidelines>. Accessed December 18, 2018.
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SPECIALTY GUIDELINE MANAGEMENT

HEMLIBRA (emicizumab-kxwh)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Hemlibra is indicated for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adult and pediatric patients ages newborn and older with hemophilia A (congenital factor VIII deficiency) with or without factor VIII inhibitors.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of hemophilia A (congenital factor VIII deficiency).

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain reduction in the frequency of bleeding episodes.

IV. REFERENCES

1. Hemlibra [package insert]. South San Francisco, CA: Genentech, Inc.; October 2018.
2. Oldenburg J, Mahlangu JN, Kim B, et al. Emicizumab Prophylaxis in Hemophilia A with Inhibitors. *N Engl J Med*. 2017; 377:809-818.
3. A Study of Emicizumab Administered Subcutaneously (SC) in Pediatric Participants With Hemophilia A and Factor VIII (FVIII) Inhibitors (HAVEN 2). *ClinicalTrials.gov* [Internet]. Bethesda (MD): National Library of Medicine (US). June 10, 2016. Identifier: NCT02795767. Available at <https://clinicaltrials.gov/ct2/show/NCT02795767>. Accessed December 15, 2019.
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5. Kruse-Jarres R, Kempton CL, Baudo F, et al. Acquired hemophilia A: Updated review of evidence and treatment guidance. *Am J Hematol*. 2017;92:695–705.
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SPECIALTY GUIDELINE MANAGEMENT

HERCEPTIN HYLECTA (trastuzumab and hyaluronidase-oysk)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

- A. Herceptin Hylecta is indicated for adjuvant treatment of adults with HER2 overexpressing node positive or node negative (ER/PR negative or with one high risk feature) breast cancer:
 - 1. As part of a treatment regimen consisting of doxorubicin, cyclophosphamide, and either paclitaxel or docetaxel
 - 2. As part of a treatment regimen with docetaxel and carboplatin
 - 3. As a single agent following multi-modality anthracycline based therapy
- B. Herceptin Hylecta is indicated in adults:
 - 1. In combination with paclitaxel for first-line treatment of HER2-overexpressing metastatic breast cancer
 - 2. As a single agent for treatment of HER2-overexpressing breast cancer in patients who have received one or more chemotherapy regimens for metastatic disease

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of human epidermal growth factor receptor 2 (HER2) status is necessary to initiate the prior authorization review.

III. CRITERIA FOR APPROVAL

Breast Cancer

- A. Authorization of up to 12 months may be granted for adjuvant treatment of HER2-positive breast cancer.
- B. Authorization of 12 months may be granted for treatment of HER2-positive recurrent or metastatic breast cancer.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy for an indication outlined in section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen. Adjuvant treatment of breast cancer will be approved for a total of 12 months of therapy.

V. REFERENCES

1. Herceptin Hylecta [package insert]. South San Francisco, CA: Genentech, Inc.; February 2019.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed August 20, 2019.

SPECIALTY GUIDELINE MANAGEMENT

HERCEPTIN (trastuzumab) OGIVRI (trastuzumab-dkst) KANJINTI (trastuzumab-anns)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Adjuvant breast cancer
Treatment of human epidermal growth factor receptor 2 (HER2)-overexpressing node positive or node negative (estrogen receptor (ER)/progesterone receptor (PR) negative or with one high risk feature) breast cancer:
 - a. As part of a treatment regimen consisting of doxorubicin, cyclophosphamide, and either paclitaxel or docetaxel
 - b. As part of a treatment regimen with docetaxel and carboplatin
 - c. As a single agent following multi-modality anthracycline based therapy
2. Metastatic breast cancer
 - a. In combination with paclitaxel for first-line treatment of HER2-overexpressing metastatic breast cancer
 - b. As a single agent for treatment of HER2-overexpressing breast cancer in patients who have received one or more chemotherapy regimens for metastatic disease
3. Metastatic gastric cancer
In combination with cisplatin and capecitabine or 5-fluorouracil, for the treatment of patients with HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma, who have not received prior treatment for metastatic disease

B. Compendial Uses

1. HER2-positive breast cancer
 - a. Neoadjuvant therapy
 - b. Treatment of recurrent or stage IV (M1) disease
2. Intra-cerebrospinal fluid (CSF) treatment for leptomeningeal metastases from breast cancer
3. HER2- positive esophageal and esophagogastric junction cancer
4. HER2- positive advanced and recurrent uterine serous carcinoma
5. HER2- positive salivary gland tumor

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of human epidermal growth factor receptor 2 (HER2) status is necessary to initiate the prior authorization review, where applicable.

III. CRITERIA FOR INITIAL APPROVAL

A. Breast Cancer

1. Authorization of up to 12 months may be granted for neoadjuvant treatment of HER2-positive breast cancer as part of a complete treatment regimen.
2. Authorization of up to 12 months may be granted for adjuvant treatment of HER2-positive breast cancer.
3. Authorization of 12 months may be granted for treatment of HER2-positive recurrent or metastatic breast cancer.
4. Authorization of 12 months may be granted for intra-CSF treatment for leptomeningeal metastases from breast cancer.

B. Esophageal, Gastric, or Gastroesophageal Junction Cancer

Authorization of 12 months may be granted for treatment of HER2-positive esophageal, gastric, or gastroesophageal junction cancer in combination with chemotherapy.

C. Uterine Serous Carcinoma

Authorization of 12 months may be granted for treatment of HER2-positive advanced and recurrent uterine serous carcinoma in combination with carboplatin and paclitaxel.

D. Salivary Gland Tumor

Authorization of 12 months may be granted for treatment of recurrent HER2-positive salivary gland tumors with distant metastases.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy for an indication outlined in section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen. Adjuvant and neoadjuvant treatment of breast cancer will be approved for a total of 12 months of therapy.

V. REFERENCES

1. Herceptin [package insert]. South San Francisco, CA: Genentech, Inc.; November 2018.
2. Kanjinti [package insert]. Thousand Oaks, CA: Amgen, Inc.; June 2019.
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4. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed August 13, 2019.
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SPECIALTY GUIDELINE MANAGEMENT

HETLIOZ (tasimelteon)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Hetlitz is indicated for the treatment of Non-24-Hour Sleep-Wake Disorder (Non-24).

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Non-24-Hour Sleep-Wake Disorder

Authorization of 6 months may be granted for treatment of Non-24-Hour Sleep-Wake Disorder when all of the following criteria are met:

- A. The member has a diagnosis of total blindness in both eyes (e.g., nonfunctioning retinas).
- B. The member is not able to perceive light in either eye.
- C. The member is experiencing difficulty initiating sleep, difficulty awakening in the morning, or excessive daytime sleepiness.

III. CONTINUATION OF THERAPY

Non-24-Hour Sleep-Wake Disorder

Authorization of 12 months may be granted for treatment of Non-24-Hour Sleep-Wake Disorder when all of the following criteria are met:

- A. The member has a diagnosis of total blindness in both eyes (e.g., nonfunctioning retinas).
- B. The member is not able to perceive light in either eye.
- C. The member is experiencing increased total nighttime sleep and/or decreased daytime nap duration.

IV. REFERENCES

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2. Auger, Robert R, Burgess, Helen J, et al. Clinical Practice Guideline for the Treatment of Intrinsic Circadian Rhythm Sleep-Wake Disorders: Advanced Sleep-Wake Phase Disorder (ASWPD), Delayed Sleep-Wake Phase Disorder (DSWPD), Non-24-Hour Sleep-Wake Rhythm Disorder (N24SWD), and Irregular Sleep-Wake Rhythm Disorder (ISWRD). An Update for 2015: An American Academy of Sleep Medicine Clinical Practice Guideline. *J Clin Sleep Med*. 2015 Oct;11(10):1199-236.

SPECIALTY GUIDELINE MANAGEMENT

HUMIRA (adalimumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately to severely active RA.
2. Reducing signs and symptoms of moderately to severely active polyarticular JIA in patients 2 years of age and older.
3. Reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in adult patients with active PsA.
4. Reducing signs and symptoms in adult patients with active AS.
5. Reducing signs and symptoms and inducing and maintaining clinical remission in adult patients with moderately to severely active Crohn's disease who have had an inadequate response to conventional therapy. Reducing signs and symptoms and inducing clinical remission in these patients if they have also lost response to or are intolerant to infliximab.
6. Reducing signs and symptoms and inducing and maintaining clinical remission in pediatric patients 6 years of age and older with moderately to severely active Crohn's disease who have had an inadequate response to corticosteroids or immunomodulators such as azathioprine, 6-mercaptopurine (6-MP), or methotrexate.
7. Inducing and sustaining clinical remission in adult patients with moderately to severely active ulcerative colitis who have had an inadequate response to immunosuppressants such as corticosteroids, azathioprine or 6-mercaptopurine (6-MP).
8. The treatment of adult patients with moderate to severe chronic plaque psoriasis who are candidates for systemic therapy or phototherapy, and when other systemic therapies are medically less appropriate.
9. The treatment of moderate to severe hidradenitis suppurativa in patients 12 years of age and older.
10. The treatment of non-infectious intermediate, posterior, and panuveitis in adults and pediatric patients 2 years of age and older.

B. Compendial Uses

Axial spondyloarthritis
Behcet's disease
Pyoderma gangrenosum
Oligoarticular juvenile idiopathic arthritis

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Moderately to severely active rheumatoid arthritis (RA)

1. Authorization of 12 months may be granted for members who have previously received a biologic or targeted synthetic DMARD (e.g., Rinvoq, Xeljanz) indicated for treatment of moderately to severely active rheumatoid arthritis.
2. Authorization of 12 months may be granted for treatment of moderately to severely active RA when any of the following criteria is met:
 - a. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to 20 mg/week).
 - b. Member has an intolerance or contraindication to methotrexate (see Appendix A).

B. Moderately to severely active articular juvenile idiopathic arthritis

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for moderately to severely active articular juvenile idiopathic arthritis.
2. Authorization of 12 months may be granted for treatment of moderately to severely active articular juvenile idiopathic arthritis when any of the following criteria is met:
 - a. The member has had an inadequate response to methotrexate or another non-biologic DMARD administered at an adequate dose and duration.
 - b. The member has risk factors (See Appendix E) and the member also meets one of the following:
 - i. High-risk joints are involved (e.g., cervical spine, wrist, or hip).
 - ii. High disease activity.
 - iii. Are judged to be at high risk for disabling joint disease.

C. Active psoriatic arthritis (PsA)

Authorization of 12 months may be granted for treatment of active psoriatic arthritis (PsA).

D. Active ankylosing spondylitis (AS) and axial spondyloarthritis

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for treatment of active ankylosing spondylitis or axial spondyloarthritis.
2. Authorization of 12 months may be granted for treatment of active ankylosing spondylitis and axial spondyloarthritis when any of the following criteria is met:
 - a. Member has experienced an inadequate response to at least two non-steroidal anti-inflammatory drugs (NSAIDs).
 - b. Member has an intolerance or contraindication to two or more NSAIDs.

E. Moderately to severely active Crohn's disease (CD)

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for treatment of Crohn's disease.
2. Authorization of 12 months may be granted for treatment of moderately to severely active CD when the member has had an inadequate response, intolerance or contraindication to at least one conventional therapy option (see Appendix B).
3. Authorization of 12 months may be granted for treatment of fistulizing CD.

F. Moderately to severely active ulcerative colitis (UC)

1. Authorization of 12 months may be granted for members who have previously received a biologic or targeted synthetic disease modifying drug (e.g., Xeljanz) indicated for treatment of moderately to severely active ulcerative colitis.

2. Authorization of 12 months may be granted for treatment of moderately to severely active UC when the member has had an inadequate response, intolerance or contraindication to at least one conventional therapy option (see Appendix C).
3. Authorization of 12 months may be granted for members who have been hospitalized for acute severe UC (e.g., continuous bleeding, severe toxic symptoms, including fever and anorexia).

G. Moderate to severe chronic plaque psoriasis (PsO)

1. Authorization of 12 months may be granted for members who have previously received Otezla or a biologic indicated for the treatment of moderate to severe chronic plaque psoriasis.
2. Authorization of 12 months may be granted for treatment of moderate to severe chronic plaque psoriasis when all of the following criteria are met:
 - a. At least 3% of body surface area (BSA) is affected OR crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
 - b. Member meets any of the following criteria:
 - i. Member has had an inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) or a pharmacologic treatment with methotrexate, cyclosporine or acitretin.
 - ii. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine and acitretin (see Appendix D).
 - iii. Member has severe psoriasis that warrants a biologic DMARD as first-line therapy (i.e. at least 10% of the body surface area (BSA) or crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected).

H. Moderate to severe hidradenitis suppurativa

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for treatment of moderate to severe hidradenitis suppurativa.
2. Authorization of 12 months may be granted for treatment of moderate to severe hidradenitis suppurativa when either of the following is met:
 - a. Member has experienced an inadequate response to oral antibiotics for at least 90 days.
 - b. Member has an intolerance or contraindication to oral antibiotics.

I. Uveitis (non-infectious intermediate, posterior and panuveitis)

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for intermediate, posterior, and panuveitis.
2. Authorization of 12 months may be granted for treatment of non-infectious intermediate, posterior and panuveitis when either of the following is met:
 - a. Member has experienced an inadequate response with corticosteroids or immunosuppressive medications (e.g., azathioprine, cyclosporine, methotrexate).
 - b. Member has an intolerance or contraindication to corticosteroids and immunosuppressive therapy (e.g., azathioprine, cyclosporine, methotrexate).

J. Behcet's disease

1. Authorization of 12 months may be granted for members who have previously received Otezla or a biologic indicated for the treatment of Behcet's disease.
2. Authorization of 12 months may be granted for the treatment of Behcet's disease when the member has had an inadequate response to at least one nonbiologic medication for Behcet's disease (e.g., apremilast, colchicine, systemic glucocorticoids, azathioprine).

K. Pyoderma gangrenosum

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for treatment of pyoderma gangrenosum.
3. Authorization of 12 months may be granted for treatment of pyoderma gangrenosum when either of the following is met:
 - a. Member has experienced an inadequate response to corticosteroids or immunosuppressive therapy (e.g., cyclosporine or mycophenolate mofetil).
 - b. Member has an intolerance or contraindication to corticosteroids and immunosuppressive therapy (e.g. cyclosporine, mycophenolate mofetil).

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who are using Humira for an indication outlined in section II and who achieve or maintain a positive clinical response with Humira as evidenced by low disease activity or improvement in signs and symptoms of the condition.

OTHER

For all indications: Member has had a documented negative TB test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic DMARDs or targeted synthetic DMARDs (e.g., Xeljanz), and repeated yearly for members with risk factors** for TB that are continuing therapy with biologics.

*If the screening testing for TB is positive, there must be documentation of further testing to confirm there is no active disease. Do not administer adalimumab to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of adalimumab.

** Risk factors for TB include: Persons with close contact to people with infectious TB disease; persons who have recently immigrated from areas of the world with high rates of TB (e.g., Africa, Asia, Eastern Europe, Latin America, Russia); children less than 5 years of age who have a positive TB test; groups with high rates of TB transmission (e.g., homeless persons, injection drug users, persons with HIV infection); persons who work or reside with people who are at an increased risk for active TB (e.g., hospitals, long-term care facilities, correctional facilities, homeless shelters).

For all indications: Member cannot use Humira concomitantly with any other biologic DMARD or targeted synthetic DMARD.

IV. APPENDICES**Appendix A: Examples of Contraindications to Methotrexate**

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
4. Elevated liver transaminases
5. History of intolerance or adverse event
6. Hypersensitivity
7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
8. Myelodysplasia
9. Pregnancy or planning pregnancy

10. Renal impairment
11. Significant drug interaction

Appendix B: Examples of Conventional Therapy Options for CD

1. Mild to moderate disease – induction of remission:
 - a. Oral budesonide
 - b. Alternatives: metronidazole, ciprofloxacin, rifaximin
2. Mild to moderate disease – maintenance of remission:
 - a. Azathioprine, mercaptopurine
 - b. Alternatives: oral budesonide, methotrexate intramuscularly (IM) or subcutaneously (SC), sulfasalazine
3. Moderate to severe disease – induction of remission:
 - a. Prednisone, methylprednisolone intravenously (IV)
 - b. Alternatives: methotrexate IM or SC
4. Moderate to severe disease – maintenance of remission:
 - a. Azathioprine, mercaptopurine
 - b. Alternative: methotrexate IM or SC
5. Perianal and fistulizing disease – induction of remission
 - a. Metronidazole ± ciprofloxacin, tacrolimus
6. Perianal and fistulizing disease – maintenance of remission
 - a. Azathioprine, mercaptopurine
 - b. Alternative: methotrexate IM or SC

Appendix C: Examples of Conventional Therapy Options for UC

1. Mild to moderate disease – induction of remission:
 - a. Oral mesalamine (e.g., Asacol, Asacol HD, Lialda, Pentasa), balsalazide, olsalazine
 - b. Rectal mesalamine (e.g., Canasa, Rowasa)
 - c. Rectal hydrocortisone (e.g., Colocort, Cortifoam)
 - d. Alternatives: prednisone, azathioprine, mercaptopurine, sulfasalazine
2. Mild to moderate disease – maintenance of remission:
 - a. Oral mesalamine, balsalazide, olsalazine, rectal mesalamine
 - b. Alternatives: azathioprine, mercaptopurine, sulfasalazine
3. Severe disease – induction of remission:
 - a. Prednisone, hydrocortisone IV, methylprednisolone IV
 - b. Alternatives: cyclosporine IV, tacrolimus, sulfasalazine
4. Severe disease – maintenance of remission:
 - a. Azathioprine, mercaptopurine
 - b. Alternative: sulfasalazine
5. Pouchitis: Metronidazole, ciprofloxacin
 - a. Alternative: rectal mesalamine

Appendix D: Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine or Acitretin.

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Drug interaction
4. Cannot be used due to risk of treatment-related toxicity
5. Pregnancy or planning pregnancy
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

APPENDIX E: Risk factors for Articular Juvenile Idiopathic Arthritis

1. Positive rheumatoid factor
2. Positive anti-cyclic citrullinated peptide antibodies
3. Pre-existing joint damage

V. REFERENCES

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SPECIALTY GUIDELINE MANAGEMENT

DUROLANE (hyaluronic acid)
EUFLEXXA (1% sodium hyaluronate)
GEL-ONE (cross-linked hyaluronate)
GELSYN-3 (sodium hyaluronate 0.84%)
GENVISC 850 (sodium hyaluronate)
HYALGAN (sodium hyaluronate)
HYMOVIS (high molecular weight viscoelastic hyaluronan)
MONOVISC (high molecular weight hyaluronan)
ORTHOVISC (high molecular weight hyaluronan)
SUPARTZ (sodium hyaluronate)
SYNOJOYNT (1% sodium hyaluronate)
SYNVISC (hylan G-F 20)
SYNVISC ONE (hylan G-F 20)
TRILURON (sodium hyaluronate)
TRIVISC (sodium hyaluronate)
VISCO-3 (sodium hyaluronate)
1% sodium hyaluronate

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Treatment of pain in osteoarthritis of the knee in patients who have failed to respond adequately to conservative non-pharmacologic therapy and simple analgesics (e.g., acetaminophen)

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Osteoarthritis (OA) of the Knee

Authorization of 12 months may be granted for treatment of osteoarthritis (OA) in the knee when all of the following criteria are met:

- A. The diagnosis is supported by radiographic evidence of osteoarthritis of the knee (e.g., joint space narrowing, subchondral sclerosis, osteophytes and sub-chondral cysts) or the member has at least 5 of the following signs and symptoms:
 1. Bony enlargement

2. Bony tenderness
3. Crepitus (noisy, grating sound) on active motion
4. Erythrocyte sedimentation rate (ESR) less than 40 mm/hr
5. Less than 30 minutes of morning stiffness
6. No palpable warmth of synovium
7. Over 50 years of age
8. Rheumatoid factor less than 1:40 titer (agglutination method)
9. Synovial fluid signs (clear fluid of normal viscosity and WBC less than 2000/mm³)
- B. The member has knee pain which interferes with functional activities (e.g., ambulation, prolonged standing).
- C. The member has experienced an inadequate response or adverse effects with non-pharmacologic treatment options (e.g., physical therapy, regular exercise, insoles, knee bracing, weight reduction).
- D. The member has experienced an inadequate response or intolerance or has a contraindication to a trial of an analgesic (e.g., acetaminophen up to 3 to 4 grams per day, non-steroidal anti-inflammatory drugs [NSAIDs], topical capsaicin cream) for at least 3 months.
- E. The member has experienced an inadequate response or intolerance or has a contraindication to a trial of intraarticular steroid injections for at least 3 months.
- F. The member is not scheduled to undergo a total knee replacement within 6 months of starting treatment.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment of osteoarthritis in knee when all of the following criteria are met:

- A. Member meets all criteria for initial approval
- B. Member has experienced improvement in pain and functional capacity following the previous injections.

IV. REFERENCES

1. Durolane [package insert]. Durham, NC: Bioventus LLC; September 2017.
2. Euflexxa [package insert]. Parsippany, NJ: Ferring Pharmaceuticals, Inc.; July 2016.
3. Gel-One [package insert]. Warsaw, IN: Zimmer, Inc.; May 2011.
4. Gelsyn-3 [package insert]. Durham, NC: Bioventus LLC; February 2016.
5. GenVisc 850 [package insert]. Doylestown, PA: OrthogenRx, Inc.; September 2015.
6. Hyalgan [package insert]. Parsippany, NJ: Fidia Pharma USA Inc.; May 2014.
7. Hymovis [package insert]. Parsippany, NJ: Fidia Pharma USA Inc.; October 2015.
8. Monovisc [package insert]. Bedford, MA: Anika Therapeutics, Inc.; December 2013.
9. Orthovisc [package insert]. Raynham, MA: DePuy Mitek, Inc.; June 2005.
10. Supartz [package insert]. Durham, NC: Bioventus LLC; April 2015.
11. Synjoyn [package insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; March 2019.
12. Synvisc [package insert]. Ridgefield, NJ: Genzyme Biosurgery; September 2014.
13. Synvisc One [package insert]. Ridgefield, NJ: Genzyme Biosurgery; September 2014.
14. Triluron [package insert]. Florham Park, NJ: Fidia Pharma USA Inc.; March 2019.
15. Trivisc [package insert]. Doylestown, PA: OrthogenRX; September 2018.
16. Visco-3 [package insert]. Durham, NC: Bioventus LLC; December 2015.
17. 1% Sodium Hyaluronate [package insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; March 2019.
18. Jordan KM, Arden NK, Doherty M, et al. EULAR recommendations 2003: an evidence based approach to the management of knee osteoarthritis: report of a task force of the standing committee for international clinical studies including therapeutic trials (ESCISIT). *Ann Rheum Dis.* 2003;62:1145-1155.

Reference number
1765-A

19. Hochberg MC, Altman RD, April KT, et al. American College of Rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee. *Arthritis Care Res.* 2012;64(4):465-474.
20. Neustadt DH. Intra-articular injections for osteoarthritis of the knee. *Cleve Clin J Med.* 2006;73(10):897-911.
21. Zhang W, Moskowitz RW, Nuki G, et al. OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. *Osteoarthritis Cartilage.* 2008;16(2):137-162.
22. McAlindon TE, Bannuru RR, Sullivan MC, et al. OARSI guidelines for the non-surgical management of knee osteoarthritis. *Osteoarthritis Cartilage.* 2014;22(3):363-88.

SPECIALTY GUIDELINE MANAGEMENT

HYCAMTIN CAPSULES (topotecan)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Hycamtin capsules are indicated for the treatment of relapsed small cell lung cancer (SCLC) in patients with a prior complete or partial response and who are at least 45 days from the end of first-line chemotherapy.

B. Compendial Uses

1. SCLC
2. Merkel Cell Carcinoma, disseminated, distant metastatic (clinical M1), if contraindications to checkpoint immunotherapy

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Small cell lung cancer (SCLC)**

Authorization of 12 months may be granted for treatment of small cell lung cancer.

B. **Merkel Cell Carcinoma**

Authorization of 12 months may be granted for treatment of Merkel cell carcinoma when all of the following criteria are met:

1. Member has disseminated distant metastatic disease.
2. Member has contraindications to checkpoint immunotherapy [e.g., Bavencio (avelumab), Keytruda (pembrolizumab)].

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced disease progression or an unacceptable toxicity.

IV. REFERENCES

1. Hycamtin Capsules [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corp.; September 2018.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed March 17, 2019.

Reference number(s)
1659-A

3. The NCCN Clinical Practice Guidelines in Oncology® Small Cell Lung Cancer (Version 1.2019). © 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 17, 2019.
4. The NCCN Clinical Practice Guidelines in Oncology® Merkel Cell Carcinoma (Version 2.2019). © 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 17, 2019.

SPECIALTY GUIDELINE MANAGEMENT

MAKENA (hydroxyprogesterone caproate) hydroxyprogesterone caproate (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Makena is indicated to reduce the risk of preterm birth in women with a singleton pregnancy who have a history of singleton spontaneous preterm birth. The effectiveness of Makena is based on improvement in the proportion of women who delivered < 37 weeks of gestation. There are no controlled trials demonstrating a direct clinical benefit, such as improvement in neonatal mortality and morbidity.

Limitation of use: While there are many risk factors for preterm birth, safety and efficacy of Makena has been demonstrated only in women with a prior spontaneous singleton preterm birth. **It is not intended for use in women with multiple gestations or other risk factors for preterm birth.**

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

Coverage will not be provided for members with any of the following exclusions:

- A. Current or history of thrombosis or thromboembolic disorders
- B. Known or suspected breast cancer, other hormone-sensitive cancer, or a history of these conditions
- C. Undiagnosed abnormal vaginal bleeding unrelated to pregnancy
- D. Cholestatic jaundice of pregnancy
- E. Liver tumors, benign or malignant, or active liver disease
- F. Uncontrolled hypertension

III. CRITERIA FOR INITIAL APPROVAL

Prevention of preterm birth

Authorization of 21 weeks or through 36 weeks, 6 days of gestational age, whichever is less, may be granted for the prevention of preterm birth when all of the following criteria are met:

- A. The current pregnancy is a singleton pregnancy.
- B. The member has a history of singleton spontaneous preterm birth, defined as delivery at less than 37 weeks gestation following preterm labor, preterm rupture of membranes, and cervical insufficiency.
- C. Makena will be initiated between 16 weeks, 0 days and 24 weeks, 6 days of gestation.

Reference number(s)
1780-A

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. REFERENCES

1. Makena [package insert]. Waltham, MA: AMAG Pharmaceuticals; February 2018.
2. Hydroxyprogesterone caproate [package insert]. Shirley, NY. American Regent, Inc; July 2018.
3. American College of Obstetricians and Gynecologists Committee on Practice Bulletins—Obstetrics. ACOG practice bulletin no. 130: prediction and prevention of preterm birth. *Obstet Gynecol.* 2012;120(4):964-973.

SPECIALTY GUIDELINE MANAGEMENT

IBRANCE (palbociclib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Ibrance is indicated for the treatment of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer in combination with:

1. an aromatase inhibitor as initial endocrine based therapy in postmenopausal women or in men, or
2. fulvestrant in women with disease progression following endocrine therapy.

B. Compendial Uses

Soft tissue sarcoma: well-differentiated/dedifferentiated liposarcoma

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of hormone receptor (HR) and human epidermal growth factor receptor 2 (HER2) status is necessary to initiate the prior authorization review, where applicable.

III. CRITERIA FOR INITIAL APPROVAL

A. **Breast cancer**

Authorization of 12 months may be granted for the treatment of HR-positive, HER2-negative recurrent, advanced or metastatic breast cancer when one of the following criteria is met:

1. Ibrance is used in combination with an aromatase inhibitor (e.g., anastrozole, exemestane, letrozole).
2. Ibrance is used in combination with fulvestrant.

B. **Soft tissue sarcoma**

Authorization of 12 months may be granted for treatment of well-differentiated/dedifferentiated liposarcoma when used as a single agent.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy for an indication outlined in section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

Reference number(s)
1726-A

1. Ibrance [package insert]. New York, NY: Pfizer Inc.; April 2019.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed August 12, 2019.
3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Breast Cancer. Version 2.2019. http://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed August 12, 2019.

ENHANCED SPECIALTY GUIDELINE MANAGEMENT

FIRAZYR (icatibant) icatibant (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Treatment of acute attacks of hereditary angioedema in adults 18 years of age and older

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

- A. C4 levels and C1 inhibitor functional and antigenic protein levels
- B. F12, angiotensinogen-1 or plasminogen gene mutation testing, if applicable
- C. Chart notes confirming family history of angioedema, if applicable

III. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of acute hereditary angioedema attacks when the requested medication will not be used in combination with Berinert, Kalbitor, or Ruconest, and either of the following criteria is met:

- A. Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing:
 - 1. C1 inhibitor (C1-INH) antigenic level is below the lower limit of normal as defined by the laboratory performing the test, or
 - 2. Normal C1-INH antigenic level and a low C1-INH functional level (functional C1-INH less than 50% or C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test).
- B. Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
 - 1. Member has an F12, angiotensinogen-1, or plasminogen gene mutation as confirmed by genetic testing, or
 - 2. Member has a documented family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine (e.g., cetirizine) for at least one month.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy when all of the following criteria are met:

- A. Member meets the criteria for initial approval.

- B. Member has experienced reduction in severity and/or duration of attacks when they use the requested medication to treat an acute attack.

V. REFERENCES

1. Firazyr [package insert]. Lexington, MA: Shire Orphan Therapies, Inc.; December 2015.
2. icatibant [package insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; March 2019.
3. Bowen T, Cicardi M, Farkas H, et al. 2010 International consensus algorithm for the diagnosis, therapy, and management of hereditary angioedema. *Allergy Asthma Clin Immunol*. 2010;6(1):24.
4. Cicardi M, Bork K, Caballero T, et al. Hereditary Angioedema International Working Group. Evidence-based recommendations for the therapeutic management of angioedema owing to hereditary C1 inhibitor deficiency: consensus report of an International Working Group. *Allergy*. 2012;67:147-157.
5. Zuraw BL, Banerji A, Bernstein JA, et al. US Hereditary Angioedema Association Medical Advisory Board 2013 recommendations for the management of hereditary angioedema due to C1 inhibitor deficiency. *J Allergy Clin Immunol: In Practice*. 2013; 1(5): 458-467.
6. Zuraw BL, Bork K, Binkley KE, et al. Hereditary angioedema with normal C1 inhibitor function: consensus of an international expert panel. *Allergy Asthma Proc*. 2012; 33(6):S145-S156.
7. Maurer M, Magerl M, Ansotegui I, et al. The international WAO/EAACI guideline for the management of hereditary angioedema – the 2017 revision and update. *Allergy*. 2018;00:1-22.
8. Lang DM, Aberer W, Bernstein JA, et al. International consensus on hereditary and acquired angioedema. *Ann Allergy Asthma Immunol*. 2012; 109:395-202.
9. Cicardi M, Aberer W, Banerji A, et al. Classification, diagnosis, and approach to treatment for angioedema: consensus report from the Hereditary Angioedema International Working Group. *Allergy*. 2014;69: 602-616.
10. Bowen T. Hereditary angioedema: beyond international consensus – circa December 2010 – The Canadian Society of Allergy and Clinical Immunology Dr. David McCourtie Lecture. *Allergy Asthma Clin Immunol*. 2011;7(1):1.
11. Bernstein J. Update on angioedema: Evaluation, diagnosis, and treatment. *Allergy and Asthma Proceedings*. 2011;32(6):408-412.
12. Longhurst H, Cicardi M. Hereditary angio-edema. *Lancet*. 2012;379:474-481.
13. Farkas H, Martinez-Saguer I, Bork K, et al. International consensus on the diagnosis and management of pediatric patients with hereditary angioedema with C1 inhibitor deficiency. *Allergy*. 2017;72(2):300-313.
14. Henao MP, Kraschnewski J, Kelbel T, Craig T. Diagnosis and screening of patients with hereditary angioedema in primary care. *Therapeutics and Clin Risk Management*. 2016; 12: 701-711.

Reference number(s)
2173-A

SPECIALTY GUIDELINE MANAGEMENT

ICLUSIG (ponatinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Adult patients with chronic phase, accelerated phase, or blast phase chronic myeloid leukemia (CML) or Ph+ ALL for whom no other tyrosine kinase inhibitor (TKI) therapy is indicated
2. Adult patients with T315I-positive CML (chronic phase, accelerated phase, or blast phase) or T315I-positive Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL)

Limitation of use: Iclusig is not indicated and is not recommended for the treatment of patients with newly diagnosed chronic phase CML.

B. Compendial Uses

1. Primary treatment of advanced phase CML (accelerated phase or blast phase)
2. Follow-up therapy for after hematopoietic stem cell transplant (HSCT) for CML and ALL patients
3. Treatment of Ph+ ALL

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review:

- A. Prior to initiation of therapy for treatment of CML or Ph+ ALL: results of cytogenetic and/or molecular testing for detection of the Ph chromosome or the BCR-ABL gene
- B. For members requesting initiation of Iclusig therapy for treatment of T315I-positive CML: results of T315I mutation testing

III. CRITERIA FOR INITIAL APPROVAL

A. **Chronic Myeloid Leukemia (CML)**

Authorization of 6 months may be granted for treatment of CML that has been confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing when any of the following criteria are met:

1. Member has T315I-positive CML OR treatment with any other TKI is not indicated for the member (e.g., bosutinib, dasatinib, imatinib, nilotinib)
2. Member has accelerated phase (AP) or blast phase (BP) disease
3. Member has received HSCT for CML

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2173-A

B. Ph+ Acute Lymphoblastic Leukemia (ALL)/Lymphoblastic Lymphoma (LL)

Authorization of 12 months may be granted for treatment of Ph+ ALL or LL that has been confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing when the member has T315I-positive disease OR treatment with any other TKI is not indicated for the member (e.g., bosutinib, dasatinib, imatinib, nilotinib).

IV. CONTINUATION OF THERAPY

A. CML

Authorization of 12 months may be granted for continued treatment of CML that has been confirmed by detection of Ph chromosome or BCR-ABL gene by cytogenetic and/ or molecular testing when any of the following criteria are met:

1. BCR-ABL1 \leq 10% for members who have been receiving Iclusig for \leq 12 months
2. No evidence of disease progression for members who have been receiving Iclusig for $>$ 12 months
3. Member has received HSCT

B. Ph+ ALL/LL

Authorization of 12 months may be granted for continued treatment of Ph+ ALL or LL that has been confirmed by detection of Ph chromosome or BCR-ABL gene by cytogenetic and/ or molecular testing when either of the following criteria are met:

1. Member has not experienced disease progression or an unacceptable toxicity
2. Member has received HSCT

V. REFERENCES

1. Iclusig [package insert]. Cambridge, MA: Ariad Pharmaceuticals, Inc.; October 2018.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed April 19, 2019.
3. NCCN Clinical Practice Guidelines in Oncology® Chronic Myelogenous Leukemia (Version 1.2019). © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed April 16, 2019.
4. NCCN Clinical Practice Guidelines in Oncology® Acute Lymphoblastic Leukemia (Version 1.2019). © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed April 17, 2019.

SPECIALTY GUIDELINE MANAGEMENT

IDHIFA (enasidenib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Idhifa is indicated for the treatment of adult patients with relapsed or refractory acute myeloid leukemia (AML) with an isocitrate dehydrogenase-2 (IDH-2) mutation as detected by an FDA-approved test.

B. Compendial Uses

As a single agent in patients 60 years of age or older with IDH2-mutated AML in the following settings:

1. Treatment induction when not a candidate for intensive remission induction therapy or declines intensive therapy
2. Post-remission therapy following response to previous lower intensity therapy with the same regimen

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review (new starts only): medical record documentation of isocitrate dehydrogenase-2 (IDH2) mutation as detected by an FDA-approved test

III. CRITERIA FOR INITIAL APPROVAL

Acute Myeloid Leukemia (AML)

- A. Authorization of 12 months may be granted for treatment induction of newly diagnosed AML with a susceptible IDH2 mutation when all of the following criteria is met:

1. The requested medication will be used as a single-agent
2. Member is 60 years of age or older
3. Member has comorbidities that preclude the use of intensive induction chemotherapy or declines intensive induction chemotherapy

- B. Authorization of 12 months may be granted for post-remission therapy for AML with a susceptible IDH2 mutation when all of the following criteria is met:

1. The requested medication will be used as a single-agent
2. Member is 60 years of age or older
3. Member has experienced response to previous lower intensive therapy with the same requested regimen

- C. Authorization of 12 months may be granted for treatment of relapsed or refractory AML with a susceptible IDH2 mutation.

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2238-A

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced an unacceptable toxicity.

V. REFERENCES

1. Idhifa [package insert]. Summit, NJ: Celgene Corporation; August 2017.
2. National Comprehensive Cancer Network. The NCCN Drugs & Biologics Compendium. <http://www.nccn.org>. Accessed July 10, 2019.
3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Acute Myeloid Leukemia. Version 3.2019. https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf. Accessed July 10, 2019.

SPECIALTY GUIDELINE MANAGEMENT

ILARIS (canakinumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

A. Periodic Fever Syndromes:

- Cryopyrin-Associated Periodic Syndromes (CAPS):
Ilaris is indicated for the treatment of Cryopyrin-Associated Periodic Syndromes (CAPS), in adults and children 4 years of age and older including Familial Cold Autoinflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS).
- Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS)
Ilaris is indicated for the treatment of TRAPS in adult and pediatric patients.
- Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD)
Ilaris is indicated for the treatment of HIDS and MKD in adult and pediatric patients.
- Familial Mediterranean Fever (FMF)
Ilaris is indicated for the treatment of FMF in adult and pediatric patients.

B. Active Systemic Juvenile Idiopathic Arthritis (SJIA)

Ilaris is indicated for the treatment of active systemic juvenile idiopathic arthritis (SJIA) in patients aged 2 years and older.

Compendial Use

Gout and pseudogout

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Periodic Fever Syndromes

1. Authorization of 12 months may be granted for treatment of CAPS when all of the following criteria are met:
 - a. Member has a diagnosis of familial cold auto-inflammatory syndrome (FCAS) with classic signs and symptoms (i.e., recurrent, intermittent fever and rash that were often exacerbated by exposure to generalized cool ambient temperature) or Muckle-Wells syndrome (MWS) with classic signs and symptoms (i.e., chronic fever and rash of waxing and waning intensity, sometimes exacerbated by exposure to generalized cool ambient temperature).
 - b. Member has functional impairment limiting the activities of daily living

2. Authorization of 12 months may be granted for treatment of TRAPS when all of the following criteria are met:
 - a. Member has chronic or recurrent disease activity with active flares within the last 6 months
 - b. Physician's Global Assessment score greater than or equal to 2 or C-reactive protein (CRP) greater than 10 mg/L
3. Authorization of 12 months may be granted for treatment of HIDS/MKD when all of the following criteria are met:
 - a. Member has had active flares within the last 6 months
 - b. Physician's Global Assessment score greater than or equal to 2 or C-reactive protein (CRP) greater than 10 mg/L
4. Authorization of 12 months may be granted for treatment of FMF when all of the following criteria are met:
 - a. Member has active disease with flares within the last 6 months
 - b. C-reactive protein (CRP) greater than 10 mg/L
 - c. Member has had an inadequate response or intolerance to or has a contraindication to colchicine.

B. Active Systemic Juvenile Idiopathic Arthritis (sJIA)

1. Authorization of 12 months may be granted for members who have received Ilaris or another biologic indicated for systemic juvenile idiopathic arthritis.
2. Authorization of 12 months may be granted for the treatment of active sJIA when any of the following criteria is met:
 - a. Member has had an inadequate response to at least a 1-month trial of nonsteroidal anti-inflammatory drugs (NSAIDs)
 - b. Member has had an inadequate response to at least a 2-week trial of corticosteroids
 - c. Member has had an inadequate response to at least a 3-month trial of methotrexate or leflunomide

C. Management of gout and pseudogout flares

Authorization of 6 months may be granted for the management of flares for gout or pseudogout (also known as calcium pyrophosphate deposition disease) when any of the following criteria is met:

1. Member has had an inadequate response or intolerance to maximum tolerated doses of non-steroidal anti-inflammatory drugs (NSAIDs), colchicine and oral and injectable corticosteroid
2. Member has a contraindication to NSAIDs and colchicine, and has a clinical reason to avoid repeated courses of corticosteroids.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who are using Ilaris for an indication outlined in Section II and who achieve or maintain positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

- A. Member has had a documented negative TB test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who

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1801-A

are naïve to biologic DMARDs or targeted synthetic DMARDs (e.g., Xeljanz), and repeated yearly for members with risk factors** for TB that are continuing therapy with biologics.

* If the screening testing for TB is positive, there must be documentation of further testing to confirm there is no active disease. Do not administer canakinumab to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of treatment.

** Risk factors for TB include: Persons with close contact to people with infectious TB disease; persons who have recently immigrated from areas of the world with high rates of TB (e.g., Africa, Asia, Eastern Europe, Latin America, Russia); children less than 5 years of age who have a positive TB test; groups with high rates of TB transmission (e.g., homeless persons, injection drug users, persons with HIV infection); persons who work or reside with people who are at an increased risk for active TB (e.g., hospitals, long-term care facilities, correctional facilities, homeless shelters).

- B. The requested drug will not be used concomitantly with any other biologic DMARD (e.g., adalimumab, anakinra, rilonacept, etanercept, infliximab, tocilizumab) or targeted synthetic DMARD (e.g. tofacitinib).

V. REFERENCES

1. Ilaris [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; December 2016.
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SPECIALTY GUIDELINE MANAGEMENT

ILUMYA (tildrakizumab-asmn)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Treatment of adult patients with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Moderate to severe plaque psoriasis

- A. Authorization of 12 months may be granted for members who have previously received Otezla or a biologic indicated for the treatment of moderate to severe plaque psoriasis.
- B. Authorization of 12 months may be granted for treatment of moderate to severe plaque psoriasis when all of the following criteria are met:
 1. At least 3% of body surface area (BSA) is affected OR crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
 2. Member meets any of the following criteria:
 - i. Member has had an inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) or pharmacologic treatment with methotrexate, cyclosporine or acitretin.
 - ii. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine and acitretin (see Appendix).
 - iii. Member has severe psoriasis that warrants a biologic DMARD as first-line therapy (i.e. at least 10% of the body surface area (BSA) or crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected).

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who are using Ilumya for an indication outlined in section II and who achieve or maintain positive clinical response with Ilumya as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

For all indications: Member has had a documented negative TB test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons

Reference number
2538-A

who are naïve to biologic DMARDs or targeted synthetic DMARDs (e.g., Xeljanz), and repeated yearly for members with risk factors** for TB that are continuing therapy with biologics.

* If the screening testing for TB is positive, there must be documentation of further testing to confirm there is no active disease. Do not administer tildrakizumab-asmn to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of tildrakizumab-asmn.

** Risk factors for TB include: Persons with close contact to people with infectious TB disease; persons who have recently immigrated from areas of the world with high rates of TB (e.g., Africa, Asia, Eastern Europe, Latin America, Russia); children less than 5 years of age who have a positive TB test; groups with high rates of TB transmission (e.g., homeless persons, injection drug users, persons with HIV infection); persons who work or reside with people who are at an increased risk for active TB (e.g., hospitals, long-term care facilities, correctional facilities, homeless shelters).

For all indications: Member cannot use Ilumya concomitantly with any other biologic DMARD or targeted synthetic DMARD.

V. APPENDIX

Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine or Acitretin

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Cannot be used due to risk of treatment-related toxicity
4. Drug interaction
5. Pregnancy or planning pregnancy
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

VI. REFERENCES

1. Ilumya [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; August 2018.
2. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 4: Guidelines of care for the management and treatment of psoriasis with traditional systemic agents. *J Am Acad Dermatol*. 2009;61:451-485.
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4. Menter A, Strober BE, Kaplan DH, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. *J Am Acad Dermatol*. 2019;80(4):1029-1072.
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SPECIALTY GUIDELINE MANAGEMENT

GLEEVEC (imatinib mesylate) imatinib mesylate (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Newly diagnosed adult and pediatric patients with Philadelphia chromosome positive chronic myeloid leukemia (Ph+ CML) in chronic phase
2. Patients with Ph+ CML in blast crisis, accelerated phase, or in chronic phase after failure of interferon-alpha therapy
3. Adult patients with relapsed or refractory Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL)
4. Pediatric patients with newly diagnosed Ph+ ALL in combination with chemotherapy
5. Adult patients with myelodysplastic/myeloproliferative diseases (MDS/MPD) associated with PDGFR (platelet-derived growth factor receptor) gene re-arrangements as determined with an FDA-approved test
6. Adult patients with aggressive systemic mastocytosis without the D816V c-Kit mutation as determined with an FDA-approved test or with c-Kit mutational status unknown
7. Adult patients with hypereosinophilic syndrome (HES) and/or chronic eosinophilic leukemia (CEL) who have the FIP1L1-PDGFRα fusion kinase (mutational analysis or FISH demonstration of CHIC2 allele deletion) and for patients with HES and/or CEL who are FIP1L1-PDGFRα fusion kinase negative or unknown
8. Adult patients with unresectable, recurrent and/or metastatic dermatofibrosarcoma protuberans (DFSP)
9. Patients with Kit (CD117) positive unresectable and/or metastatic malignant gastrointestinal stromal tumors (GIST)
10. Adjuvant treatment of adult patients following complete gross resection of Kit (CD117) positive GIST

B. Compendial Uses

1. Primary treatment of advanced phase CML (accelerated phase or blast phase)
2. Follow-up therapy for CML patients after hematopoietic stem cell transplant (HSCT)
3. Induction/consolidation and maintenance therapy for Ph+ ALL
4. GIST (primary, postoperative and continued treatment)
5. Desmoid tumors
6. Pigmented villonodular synovitis/tenosynovial giant cell tumor
7. Recurrent chordoma
8. Metastatic or unresectable C-Kit mutated melanoma as second-line or subsequent therapy
9. AIDS-related Kaposi sarcoma that has progressed on or not responded to first-line systemic therapy
10. Chronic myelomonocytic leukemia

All other indications are considered experimental/investigational and not medically necessary.

Reference number(s)
2172-A

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review prior to initiation of therapy for treatment of CML or Ph+ ALL: results of cytogenetic and/or molecular testing for detection of the Ph chromosome or the BCR-ABL gene.

III. CRITERIA FOR INITIAL APPROVAL

A. Chronic Myeloid Leukemia (CML)

Authorization of 6 months may be granted for treatment of CML that has been confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing when the member did not fail (other than due to intolerance) prior therapy with a TKI (e.g., dasatinib, nilotinib, bosutinib, ponatinib).

B. Ph+ Acute Lymphoblastic Leukemia (ALL)/Lymphoblastic Lymphoma (LL)

Authorization of 12 months may be granted for treatment of Ph+ ALL or lymphoblastic lymphoma that has been confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing.

C. Gastrointestinal Stromal Tumor (GIST), Desmoid Tumors, Pigmented Villonodular Synovitis/Tenosynovial Giant Cell Tumor (PVNS/TGCT), Hypereosinophilic Syndrome/Chronic Eosinophilic Leukemia (HES/CEL), Dermatofibrosarcoma Protuberans (DFSP), Chordoma

Authorization of 12 months may be granted for treatment of GIST, desmoid tumors, PVNS/TGCT, HES/CEL, DFSP, or recurrent chordoma

D. Myelodysplastic Syndromes/Myeloproliferative Diseases (MDS/MPD) and Chronic Myelomonocytic Leukemia (CMML)

Authorization of 12 months may be granted for treatment of MDS/MPD or CMML when the member's disease is associated with PDGFR gene rearrangements

E. Aggressive Systemic Mastocytosis (ASM)

Authorization of 12 months may be granted for treatment of ASM without the D816V c-Kit mutation or with c-Kit mutational status unknown.

F. Melanoma

Authorization of 12 months may be granted for treatment of metastatic or unresectable c-Kit mutation-positive melanoma as second-line or subsequent therapy.

G. AIDS-related Kaposi Sarcoma

Authorization of 12 months may be granted for treatment of AIDS-related Kaposi sarcoma that has progressed on or not responded to first-line systemic therapy.

IV. CONTINUATION OF THERAPY

A. CML

Authorization of 12 months may be granted for continued treatment of CML that has been confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing when any of the following criteria are met:

Reference number(s)
2172-A

1. BCR-ABL1 \leq 10% for members who have been receiving imatinib/Gleevec for \leq 12 months
2. No evidence of disease progression for members who have been receiving imatinib/Gleevec for > 12 months
3. Member has received HSCT

B. Ph+ ALL/LL

Authorization of 12 months may be granted for continued treatment of Ph+ ALL or LL that has been confirmed by detection of Ph chromosome or BCR-ABL gene by cytogenetic and/ or molecular testing in members who have not experienced disease progression or an unacceptable toxicity.

C. GIST, Desmoid Tumors, PVNS/TGCT, HES/CEL, DFSP, Chordoma, MDS/MPD, CMML, ASM, Melanoma, AIDS-related Kaposi sarcoma

Authorization of 12 months may be granted for continued treatment of GIST, desmoid tumors, PVNS/TGCT, HES/CEL, DFSP, recurrent chordoma, MDS/MPD, CMML, ASM, metastatic or unresectable melanoma, or AIDS-related Kaposi sarcoma in members who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES

1. Gleevec [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2018.
2. imatinib [package insert]. Cranbury, NJ: Sun Pharmaceuticals Inc.; November 2018.
3. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed April 22, 2019.
4. NCCN Clinical Practice Guidelines in Oncology® Chronic Myeloid Leukemia (Version 1.2019). © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed April 16, 2019.
5. NCCN Clinical Practice Guidelines in Oncology® Acute Lymphoblastic Leukemia (Version 1.2019). © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed April 17, 2019.
6. NCCN Clinical Practice Guidelines in Oncology® Soft Tissue Sarcoma (Version 2.2019). © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed April 18, 2019.
7. NCCN Clinical Practice Guidelines in Oncology® Bone Cancer (Version 2.2019). © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed April 18, 2019.
8. NCCN Clinical Practice Guidelines in Oncology® Cutaneous Melanoma (Version 2.2019). © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed April 23, 2019.
9. NCCN Clinical Practice Guidelines in Oncology® AIDS-Related Kaposi Sarcoma (Version 2.2019). © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed April 23, 2019.

SPECIALTY GUIDELINE MANAGEMENT

IMBRUVICA (ibrutinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Mantle Cell Lymphoma (MCL)
Imbruvica is indicated for the treatment of adult patients with MCL who have received at least one prior therapy.
2. Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL)
 - i. Imbruvica is indicated for the treatment of adult patients with CLL/SLL.
 - ii. Imbruvica is indicated for the treatment of adult patients with CLL/SLL with 17p deletion.
3. Waldenström's Macroglobulinemia (WM)
Imbruvica is indicated for the treatment of adult patients with WM.
4. Marginal Zone Lymphoma (MZL)
Imbruvica is indicated for the treatment of adult patients with MZL who require systemic therapy and have received at least one prior anti-CD20-based therapy.
5. Chronic Graft versus Host Disease (cGVHD)
Imbruvica is indicated for the treatment of adult patients with cGVHD after failure of one or more lines of systemic therapy.

B. Compendial Use

1. Mantle cell lymphoma, in combination with rituximab as pretreatment in order to limit the number of cycles of less aggressive induction therapy with RHyperCVAD (rituximab, cyclophosphamide, vincristine, doxorubicin, and dexamethasone) regimen
2. Gastric MALT lymphoma, second-line or subsequent therapy for recurrent or progressive disease
3. Non-gastric MALT lymphoma, second-line or subsequent therapy for refractory or progressive disease
4. Hairy cell leukemia, for progression
5. Lymphoplasmacytic lymphoma (LPL)
6. Primary central nervous system lymphoma, for relapsed or refractory disease
7. Follicular lymphoma
8. Nodal marginal zone lymphoma, second-line or subsequent therapy for refractory or progressive disease
9. Splenic marginal zone lymphoma, second-line or subsequent therapy
10. Histologic transformation of marginal zone lymphoma to diffuse large B-cell lymphoma in members who have received prior chemoimmunotherapy

11. Diffuse large B-cell lymphoma, second-line or subsequent therapy for refractory or progressive disease
12. High-grade B-cell lymphoma, second-line or subsequent therapy for refractory or progressive disease
13. AIDS-related B-cell lymphoma, for second-line or subsequent therapy for relapsed disease
14. Post-transplant lymphoproliferative disorders, subsequent therapy for members with partial response, persistent, or progressive disease after receiving chemoimmunotherapy

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Mantle Cell Lymphoma (MCL)

Authorization of 12 months may be granted for the treatment of MCL when any of the following criteria is met:

1. The member has received at least one prior therapy when the requested medication is used as a single agent or in combination with rituximab.
2. The requested medication will be used in combination with rituximab as pretreatment to induction therapy with RHyperCVAD (rituximab, cyclophosphamide, vincristine, doxorubicin, and dexamethasone) regimen.

B. Chronic Lymphocytic Leukemia (CLL) and Small Lymphocytic Lymphoma (SLL)

Authorization of 12 months may be granted for the treatment of CLL/SLL.

C. Waldenström's Macroglobulinemia/lymphoplasmacytic lymphoma (WM/LPL)

Authorization of 12 months may be granted for the treatment of WM/LPL when the requested medication is used as a single agent or in combination with rituximab.

D. Marginal Zone Lymphoma (MZL)

Authorization of 12 months may be granted for the treatment of MZL, such as gastric or non-gastric MALT lymphoma, nodal marginal zone lymphoma, or splenic marginal zone lymphoma when the member has received at least one prior therapy.

E. Chronic Graft-Versus-Host Disease (cGVHD)

Authorization of 12 months may be granted for the treatment of cGVHD when the member has failed one or more lines of therapy.

F. Hairy Cell Leukemia

Authorization of 12 months may be granted for the treatment of hairy cell leukemia when the requested medication is used as a single agent for disease progression.

G. Primary central nervous system lymphoma

Authorization of 12 months may be granted for the treatment of relapsed or refractory primary central nervous system lymphoma when the requested medication is used as a single agent.

H. Follicular lymphoma (FL)

Authorization of 12 months may be granted for the treatment of follicular lymphoma when the requested medication is used as a single agent.

I. Histologic transformation of marginal zone lymphoma to diffuse large B-cell lymphoma

Reference number
1997-A

Authorization of 12 months may be granted to members with histologic transformation of marginal zone lymphoma to diffuse large B-cell lymphoma in members who have received prior chemoimmunotherapy.

J. Diffuse large B-cell lymphoma

Authorization of 12 months may be granted for the treatment of diffuse large B-cell lymphoma when the requested medication is used as second-line or subsequent therapy.

K. High-grade B-cell lymphoma

Authorization of 12 months may be granted for the treatment of high-grade B-cell lymphoma when the requested medication is used as second-line or subsequent therapy.

L. AIDS-related B-cell lymphoma

Authorization for 12 months may be granted for the treatment of relapsed AIDS-related B-cell lymphoma when the requested medication is used as a single agent and as second-line or subsequent therapy.

M. Post-transplant lymphoproliferative disorders

Authorization for 12 months may be granted for the treatment of partial response, persistent, progressive post-transplant lymphoproliferative disorders after receiving chemoimmunotherapy.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced disease progression or an unacceptable toxicity.

IV. REFERENCES

1. Imbruvica [package insert]. Sunnyvale, CA: Pharmacyclics LLC; July 2019.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network. The NCCN Drugs & Biologics Compendium. <http://www.nccn.org>. Accessed June 27, 2019.
3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: B-cell Lymphomas. Version 4.2019. https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed June 28, 2019.
4. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Hairy Cell Leukemia. Version 4.2018. https://www.nccn.org/professionals/physician_gls/pdf/hairy_cell.pdf. Accessed August 2, 2018.

SPECIALTY GUIDELINE MANAGEMENT

IMFINZI (durvalumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

- A. Locally advanced or metastatic urothelial carcinoma in patients with disease progression during or following platinum-containing chemotherapy or with disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.
- B. Unresectable, Stage III non-small cell lung cancer (NSCLC) whose disease has not progressed following concurrent platinum-based chemotherapy and radiation therapy.

Compendial Indications

- A. Bladder cancer as subsequent systemic therapy post-platinum as a single agent
- B. Metastatic upper GU tract tumors as a single agent for subsequent systemic therapy post platinum
- C. Metastatic carcinoma of the prostate as a single agent for subsequent therapy post platinum
- D. Recurrent or metastatic carcinoma of the urethra as a single agent for subsequent systemic therapy post platinum

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

Coverage will not be provided for members who have experienced disease progression while on PD-1 or PD-L1 inhibitor therapy.

III. CRITERIA FOR INITIAL APPROVAL

A. Urothelial Carcinoma – Bladder Cancer

Authorization of 6 months may be granted as a single agent for treatment of bladder cancer when any of the following criteria is met:

- 1. As subsequent therapy following platinum-containing chemotherapy for locally advanced or metastatic disease.
- 2. Member has metastatic or local recurrence post-cystectomy.

B. Urothelial Carcinoma – Primary Carcinoma of the Urethra

Authorization of 6 months may be granted as a single agent for treatment of primary carcinoma of the urethra as a single agent for subsequent therapy for recurrent, locally advanced, or metastatic disease following platinum-containing chemotherapy.

Reference number(s)
1820-A

C. Urothelial Carcinoma – Upper Genitourinary Tract Tumors or Urothelial Carcinoma of the Prostate
 Authorization of 6 months may be granted as a single agent for the treatment of upper genitourinary (GU) tract tumors or urothelial carcinoma of the prostate as subsequent therapy for locally advanced or metastatic disease as a single agent following platinum-containing chemotherapy.

D. Non-small cell lung cancer

Authorization of 6 months may be granted for treatment of unresectable, Stage III NSCLC that has not progressed following concurrent platinum-based chemotherapy and radiation therapy.

IV. CONTINUATION OF THERAPY

A. NSCLC

Authorization of 6 months may be granted (up to 12 months total) for continued treatment in members requesting reauthorization for an indication listed in Section IV who have not experienced disease progression or unacceptable toxicity.

B. All other indications

Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section IV who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES

1. Imfinzi [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; February 2018.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed July 19, 2019.
3. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Bladder Cancer (Version 4.2019) © 2019 National Comprehensive Cancer Network, Inc. Available at <http://www.nccn.org>. Accessed July 16, 2019.

Reference number(s)
1680-A

SPECIALTY GUIDELINE MANAGEMENT

IMLYGIC (talimogene laherparepvec)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Imlygic is indicated for the local treatment of unresectable cutaneous, subcutaneous, and nodal lesions in patients with melanoma recurrent after initial surgery.

Limitations of use: Imlygic has not been shown to improve overall survival or have an effect on visceral metastases.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Melanoma

Authorization of 12 months may be granted for treatment of unresectable cutaneous, subcutaneous, and nodal lesions in members with melanoma.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy for an indication outlined in section II when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Imlygic [package insert]. Thousand Oaks, CA: Amgen Inc.; December 2018.
2. The NCCN Drugs & Biologics Compendium® © 2018 National Comprehensive Cancer Network, Inc. Available at: <https://www.nccn.org> Accessed May 14, 2019.
3. The NCCN Clinical Practice Guidelines in Oncology™ Melanoma (Version 2.2019). ©2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org> Accessed May 14, 2019.

SPECIALTY GUIDELINE MANAGEMENT

INBRIJA (levodopa inhalation powder)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Inbrija is indicated for the intermittent treatment of OFF episodes in patients with Parkinson's disease treated with carbidopa/levodopa.

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

Coverage will not be provided for members with any of the following exclusions:

- A. Asthma
- B. Chronic obstructive pulmonary disease (COPD)
- C. Other chronic underlying lung disease
- D. Members who are receiving concomitant treatment with nonselective monoamine oxidase (MAO) inhibitors (e.g. phenelzine, tranylcypromine)

III. CRITERIA FOR INITIAL APPROVAL

Parkinson's disease

Authorization of 6 months may be granted for intermittent treatment of "off" episodes in members with Parkinson's disease when all of the following criteria are met:

- A. The member experiences at least 2 hours per day of off time
- B. The member is currently being treated with oral carbidopa/levodopa
- C. Attempts to manage off episodes by adjusting the dosing or formulation of carbidopa/levodopa were ineffective
- D. Treatment with carbidopa/levodopa plus one of the following therapies was ineffective at managing off episodes:
 - 1. Dopamine agonist (e.g., pramipexole, ropinirole)
 - 2. Monoamine oxidase B (MAO-B) inhibitor (e.g., selegiline, rasagiline)
 - 3. Catechol-O-methyl transferase (COMT) inhibitor (e.g., entacapone, tolcapone)

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for intermittent treatment of "off" episodes in members with Parkinson's disease when all of the following criteria are met:

- A. The member is currently being treated with oral carbidopa/levodopa

- B. The member is experiencing improvement on Inbrija therapy (e.g., reduction in daily off time, improvement in motor function post-administration)

V. REFERENCES

1. Inbrija [package insert]. Ardsley, NY: Acorda Therapeutics, Inc.; December 2018.
2. Miyasaki JM, Martin W, Suchowersky O, et al. Practice parameter: Initiation of treatment for Parkinson's disease: An evidence-based review. *Neurology* Jan 2002, 58 (1) 11-17.
3. National Institute for Clinical Excellence: Parkinson's disease in adults. July 2017. <https://www.nice.org.uk/guidance/ng71/resources/parkinsons-disease-in-adults-pdf-1837629189061>. Accessed August 15, 2019.
4. Fox SH, Katzenschlager R, Lim SY, et al. International Parkinson and movement disorder society evidence-based medicine review: update on treatments for the motor symptoms of Parkinson's disease. *Mov Disord*. 2018; 33(8):1248-1266.

SPECIALTY GUIDELINE MANAGEMENT

INCRELEX (mecasermin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no contraindications or exclusions to the prescribed therapy.

FDA-Approved Indications

Increlex is indicated for the treatment of growth failure in children with severe primary insulin-like growth factor-1 (IGF-1) deficiency or with growth hormone (GH) gene deletion who have developed neutralizing antibodies to GH.

Severe primary IGF-1 deficiency is defined by:

- Height standard deviation (SD) score ≤ -3.0 and
- Basal IGF-1 SD score ≤ -3.0 and
- Normal or elevated GH.

Severe primary IGF-1 deficiency includes classical and other forms of GH insensitivity. Patients with primary IGF-1 deficiency may have mutations in the GH receptor (GHR), post-GHR signaling pathway including the IGF-1 gene. They are not GH deficient, and therefore, they cannot be expected to respond adequately to exogenous GH treatment. Increlex is not intended for use in subjects with secondary forms of IGF-1 deficiency, such as GH deficiency, malnutrition, hypothyroidism, or chronic treatment with pharmacologic doses of anti-inflammatory steroids. Thyroid and nutritional deficiencies should be corrected before initiating Increlex treatment.

Limitations of use: Increlex is not a substitute to GH for approved GH indications.

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review for continuation of therapy requests:

- A. Total duration of treatment (approximate duration is acceptable)
- B. Date of last dose administered
- C. Approving health plan/pharmacy benefit manager
- D. Date of prior authorization/approval
- E. Prior authorization approval letter

III. CRITERIA FOR INITIAL APPROVAL

Severe Primary IGF-1 Deficiency

Reference number(s)
1740-A

Authorization of 12 months may be granted to members with severe primary IGF-1 deficiency or GH gene deletion with neutralizing antibodies to GH when ALL of the following criteria are met:

- A. Pretreatment height is ≥ 3 standard deviations (SD) below the mean for age and gender
- B. Pretreatment basal IGF-1 level is ≥ 3 SD below the mean for age and gender
- C. Pediatric GH deficiency has been ruled out with a provocative GH test (i.e., peak GH level ≥ 10 ng/mL)
- D. Epiphyses are open

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for the continuation of therapy of severe primary IGF-1 deficiency or GH gene deletion with neutralizing antibodies to GH when ALL of the following criteria are met:

- A. The member's growth rate is > 2 cm/year or there is a documented clinical reason for lack of efficacy (e.g., on treatment less than 1 year, nearing final adult height/late stages of puberty).
- B. Epiphyses are open (confirmed by X-ray or X-ray is not available).

V. REFERENCES

1. Increlex [package insert]. Basking Ridge, NJ: Ipsen Biopharmaceuticals, Inc.; January 2019.

SPECIALTY GUIDELINE MANAGEMENT

INGREZZA (valbenazine)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Treatment of adults with tardive dyskinesia

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Documentation of score of items 1 to 7 of the Abnormal Involuntary Movement Scale (AIMS).

III. CRITERIA FOR INITIAL APPROVAL

Tardive dyskinesia

Authorization of 6 months may be granted for treatment of tardive dyskinesia when the baseline AIMS score for items 1 to 7 is obtained.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for treatment of tardive dyskinesia when the member's tardive dyskinesia symptoms have improved as indicated by a decreased AIMS score (items 1 to 7) from baseline.

V. REFERENCES

1. Ingrezza [package insert]. San Diego, CA: Neurocrine Biosciences, Inc.; July 2019.
2. Hauser, Robert, et al. KINECT-3: A Phase 3 Randomized, Double-Blind, Placebo-Controlled Trial of Valbenazine for Tardive Dyskinesia. *American Journal of Psychiatry*. 2017 Mar 21: 1-9.

Reference number
2079-A

SPECIALTY GUIDELINE MANAGEMENT

INLYTA (axitinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Inlyta is indicated for the treatment of advanced renal cell carcinoma (RCC) after failure of one prior systemic therapy.

B. Compendial Uses

1. Relapsed or surgically unresectable stage IV renal cell carcinoma
2. Papillary, Hürthle cell, or follicular thyroid carcinoma

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Renal Cell Carcinoma**

Authorization of 12 months may be granted for treatment of relapsed, metastatic, or unresectable renal cell carcinoma as a single agent or in combination with pembrolizumab.

B. **Papillary, Hürthle cell, or Follicular Thyroid Carcinoma**

Authorization of 12 months may be granted for treatment of radioiodine refractory papillary, Hürthle cell, or follicular thyroid carcinoma.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy for an indication outlined in Section II when there is no evidence of unacceptable toxicity or disease progression on the current regimen.

IV. REFERENCES

1. Inlyta [package insert]. New York, NY: Pfizer Inc., August 2018.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed May 24, 2019.
3. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Kidney Cancer. Version 4.2019. Accessed May 24, 2019. https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf.
4. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Thyroid Carcinoma. Version 1.2019. Accessed May 24, 2019. https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf.

SPECIALTY GUIDELINE MANAGEMENT

INREBIC (fedratinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Inrebic is indicated for the treatment of adult patients with intermediate-2 or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis (MF).

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Myelofibrosis

Authorization of 12 months may be granted for the treatment of intermediate-2 or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis (MF).

III. CONTINUATION OF THERAPY

Myelofibrosis

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have improvement in symptoms and no unacceptable toxicity.

IV. REFERENCES

1. Inrebic [package insert]. Summit, NJ: Celgene Corporation; August 2019.

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS**INSOMNIA AGENTS****BRAND NAME***
(generic)**BELSOMRA**
(suvorexant)**Status: CVS Caremark Criteria****Type: Initial Prior Authorization****Ref # 1177-C**

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Belsomra (suvorexant) is indicated for the treatment of insomnia characterized by difficulties with sleep onset and/or sleep maintenance.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the treatment of insomnia characterized by difficulties with sleep onset and/or sleep maintenance
AND
- Potential causes of sleep disturbances have been addressed (e.g., inappropriate sleep hygiene and sleep environment issues or treatable medical/psychological causes of chronic insomnia)
AND
- If the patient is less than 65 years of age, the patient experienced an inadequate treatment response, intolerance or contraindication to a generic non-benzodiazepine sedative-hypnotic (e.g., eszopiclone, zaleplon, zolpidem) OR a short/intermediate-acting benzodiazepine (e.g., temazepam, triazolam)

Quantity Limits apply.

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Belsomra (suvorexant) is indicated for the treatment of insomnia characterized by difficulties with sleep onset and/or sleep maintenance.

Insomnia disorder is defined in the International Classification of Sleep Disorders, Third Edition as a complaint of trouble initiating or maintaining sleep which is associated with daytime consequences and is not attributable to environmental circumstances or inadequate opportunity to sleep. The disorder is identified as chronic when it has persisted for at least three months at a frequency of at least three times per week. When the disorder meets the symptom criteria but has persisted for less than three months, it is considered short-term insomnia.^{4,5} Chronic insomnia, also referred to as "chronic insomnia disorder" in the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5), is diagnosed according to the DSM-5 and the International Classification of Sleep Disorders, which have similar criteria for making the diagnosis. These criteria specify that symptoms must cause clinically significant functional distress or impairment; be present for at least three nights per week for at least three months; and not be linked to other sleep, medical, or mental disorders.⁶

Insomnia can occur independently or be caused by another disease.^{6,7} According to the American Academy of Sleep Medicine (AASM), general treatment measures for insomnia include the treatment of comorbid medical and psychiatric conditions, modifying sleep-interfering medications and substances, and optimizing the sleep environment.⁴ The goal of treatment for insomnia is to improve sleep and alleviate distress or dysfunction caused by the disorder.^{4,6-8} Insomnia can be managed with psychological therapy, pharmacologic therapy, or a combination of both. Psychological therapy options include cognitive behavioral therapy for insomnia (CBT-I); multicomponent behavioral therapy or brief behavioral therapy (BBT) for insomnia; and other interventions such as stimulus control, relaxation strategies, and sleep restriction. Cognitive behavioral therapy for insomnia consists of a combination of cognitive therapy, behavioral interventions (such as sleep restriction and stimulus control), and educational interventions (such as sleep hygiene). The cognitive component is aimed at changing patient's beliefs and attitudes about insomnia. Sleep hygiene education is often also included.⁶⁻⁸ The American College of Physicians (ACP) recommends that all adult patients receive CBT-I as the initial treatment for chronic insomnia disorder.¹⁵ Despite the clearly favorable benefit to risk ratio of CBT-I, not all patients with an insomnia disorder can and will derive benefit from this treatment alone.^{4,6}

The AASM Clinical Practice Guideline for the Pharmacological Treatment of Chronic Insomnia in Adults makes recommendations for treating sleep onset insomnia and sleep maintenance insomnia. Recommendations are not made for specific drugs over other drugs, rather the recommendations are made for treatment with a specific drug versus no treatment. The classes of drugs that received favorable recommendations include: orexin receptor agonists (suvorexant), non-benzodiazepine sedative hypnotics (eszopiclone, zaleplon, zolpidem), short/intermediate-acting benzodiazepines (triazolam and temazepam), melatonin agonists (ramelteon), and heterocyclics (Silenor [doxepin 3 mg, 6 mg]). Suvorexant is recommended for treating sleep maintenance insomnia as is Silenor. Triazolam, ramelteon, and zaleplon are recommended for the treatment of sleep onset insomnia. The guidelines recommend temazepam, eszopiclone, and zolpidem for the treatment of both sleep maintenance insomnia as well as sleep onset insomnia.⁴

Because non-benzodiazepine sedative hypnotics and short/intermediate-acting benzodiazepines are the only drug classes recommended by the AASM for both sleep onset and sleep maintenance insomnia, coverage will be provided for Belsomra (suvorexant) in patients less than 65 years of age for the treatment of insomnia when an inadequate treatment response, intolerance or contraindication to a generic non-benzodiazepine sedative hypnotic (e.g., eszopiclone, zaleplon, zolpidem) or a short/intermediate-acting benzodiazepine (e.g., temazepam, triazolam) has been demonstrated.

Inappropriate drug prescribing can be defined as the use of medications whose risks outweigh the benefits. One common approach to this issue has been development of explicit "drugs-to-avoid" criteria. These criteria were initially developed by Dr. Mark H. Beers and later updated. Drugs-to-avoid lists include medications that should be avoided in any circumstance, doses that should not be exceeded, and drugs to avoid in patients with specific disorders. The National Committee for Quality Assurance (NCQA) assessed the Beers criteria as a quality indicator for ambulatory care. In 2002, NCQA convened a Medication Management Technical Subgroup. The NCQA has provided medication measures included in the U.S. Health Plan Employer Data and Information Set (HEDIS) as part of the standard assessment of quality in ambulatory care.^{9,10} NCQA and the Pharmacy Quality Alliance (PQA) utilize the American Geriatrics Society (AGS) Beers Criteria to designate the quality measure Use of High-Risk Medications in the Elderly (HRM). The Centers for Medicare and Medicaid Services (CMS) utilize the HRM measure to monitor and evaluate the quality of care provided to Medicare beneficiaries. NCQA additionally uses the AGS Beers Criteria to designate the quality measure Potentially Harmful Drug–Disease Interactions in the Elderly.¹² In 2015, The American Geriatrics Society updated the Beers Criteria for Potentially Inappropriate Medications to Be Used with Caution with Older Adults. According to the 2015 update, and confirmed in the 2019 update, drug classes to avoid include short and intermediate acting benzodiazepines and benzodiazepine receptor agonists. Older adults have increased sensitivity to benzodiazepines; benzodiazepines increase risk of cognitive impairment, delirium, falls, fractures, and motor vehicle crashes. Benzodiazepine receptor agonists have adverse reactions similar to those of benzodiazepines in older adults (e.g., delirium, falls, fractures); increased emergency department visits and hospitalizations; motor vehicle crashes; minimal improvement in sleep latency and duration.¹¹ Therefore, a trial of a generic non-benzodiazepine sedative hypnotic (e.g., eszopiclone, zaleplon, zolpidem) or a short/intermediate-acting benzodiazepine (e.g., temazepam, triazolam) will not be required for patients 65 years of age or older.

The recommended dose for Belsomra (suvorexant) is 10 mg, taken no more than once per night and within 30 minutes of going to bed, with at least 7 hours remaining before the planned time of awakening. If the 10 mg dose is well-tolerated but not effective, the dose can be increased. The maximum recommended dose of Belsomra (suvorexant) is 20 mg once daily. It is recommended to use the lowest effective dose for the patient. Belsomra (suvorexant) is available as 5 mg, 10 mg, 15 mg, and 20 mg tablets.

Belsomra (suvorexant) is supplied in unit-of-use blisters of 30 tablets. Due to the possibility of the package not being split at the time of dispensing, Belsomra (suvorexant) is not included in the Insomnia Limit criteria.

REFERENCES

1. Belsomra [package insert]. Whitehouse Station, NY: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc.; July 2018.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed March 2019.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed March 2019.
4. Sateia MJ, Buysse DJ, Krystal AD, Neubauer DN, Heald JL. Clinical practice guideline for the pharmacologic treatment of chronic insomnia in adults: An American Academy of Sleep Medicine clinical practice guideline. *J Clin Sleep Med*. 2017;13(2):307-349.
5. Sateia MJ. International Classification of Sleep Disorders: highlights and modifications. *CHEST*. 2014; 146 (5): 1387-1394. doi: 10.1378/chest.14-0970
6. Qaseem A, Kansagara D, Forcica MA, Cooke M, Denberg TD, Management of chronic insomnia disorder in adults: A clinical practice guideline from the American College of Physicians. *Ann Intern Med*. Epub, 2016. 165(2):125-33. doi: 10.7326/M15-2175. Epub 2016 May 3.
7. Morgenthaler T; Kramer M; Alessi C et al. Practice parameters for the psychological and behavioral treatment of insomnia: An update. An American Academy of Sleep Medicine report. *SLEEP* 2006; 29(11):1415-1419.
8. Schutte-Rodin S, Broch L, Buysse D, Dorsey C, Sateia M. Clinical guideline for the evaluation and management of chronic insomnia in adults. *J Clin Sleep Med* 2008; 4(5):487-504.
9. NCQA. 2018. (on line) www.ncqa.org. Accessed March 2019.
10. Albert, S, Colombi, A, et al. Potentially Inappropriate Medications and Risk of Hospitalization in Retirees. *Drugs Aging* 2010 May; 27(5):407-415.
11. The American Geriatrics Society 2015 Beers Criteria Update Expert Panel. American Geriatrics Society 2015 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. American Geriatrics Society. 2015.
12. Hanlon, Joseph T, PharmD, MS, Semla, Todd P. MS, PharmD and Schmader, Kenneth E. MD. Alternative Medications for Medications in the Use of High-Risk Medications in the Elderly and Potentially Harmful Drug–Disease Interactions in the Elderly Quality Measures. *Journal of American Geriatrics Society*.2015.
13. The American Geriatrics Society 2019 Beers Criteria Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. American Geriatrics Society. 2019.

Written by: UM Development (CT)
Date Written: 08/2014
Last Revised: 03/2015, 05/2015, 05/2016; 05/2017; (KM) 05/2018 (no clinical changes); (DS) 03/2019
Reviewed: Medical Affairs (KC) 08/2014; (WF) 04/2015; (DNC) 05/2015; (LCB) 05/2016; (AN) 05/2017, 03/2019; (CHART) 08/22/19
External Review: 09/2014, 08/2015, 08/2016, 08/2017, 08/2018, 08/2019

CRITERIA FOR APPROVAL

- | | | | |
|---|---|-----|----|
| 1 | Is the requested drug being prescribed for the treatment of insomnia characterized by difficulties with sleep onset and/or sleep maintenance? | Yes | No |
| 2 | Have potential causes of sleep disturbances been addressed (e.g., inappropriate sleep hygiene and sleep environment issues or treatable medical/psychological causes of chronic insomnia)? | Yes | No |
| 3 | Is the patient 65 years of age or older?
[If yes, then skip to question 5.] | Yes | No |
| 4 | Has the patient experienced an inadequate treatment response, intolerance or contraindication to a generic non-benzodiazepine sedative-hypnotic (e.g., eszopiclone, zaleplon, zolpidem) OR a short/intermediate-acting benzodiazepine (e.g., temazepam, triazolam)? | Yes | No |
| 5 | Does the patient require use of MORE than the plan allowance of 30 tablets per month of Belsomra (suvorexant)? | Yes | No |

[RPh Note: If yes, then deny and enter a partial approval for 30 tablets per 25 days or 90 tablets per 75 days]

Mapping Instructions			
	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have insomnia. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
2.	Go to 3	Deny	You do not meet the requirements of your plan. Your plan covers this drug when reasons for insomnia have been addressed. Your request has been denied based on the information we have. [Short Description: No confirmation that causes of sleep disturbances have been addressed]
3.	Go to 5	Go to 4	
4.	Go to 5	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions: <ul style="list-style-type: none"> - You are 64 years of age or younger - You tried another drug for insomnia first (generic non-benzodiazepine sedative-hypnotic such as eszopiclone, zaleplon, zolpidem OR a short/intermediate-acting benzodiazepine such as temazepam, triazolam) - The other drugs did not work for you or you cannot use them Your request has been denied based on the information we have. [Short Description: Less than 65 years of age and no inadequate response, intolerance or contraindication a generic non-benzodiazepine sedative-hypnotic OR a short acting benzodiazepine]

5.	Deny	Approve, 36 months 30 tablets/25 days* or 90 tablets/75 days* to accumulate across all strengths	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 30 tablets/month of the requested drug and strength. You have been approved for the maximum quantity that your plan covers for a duration of 36 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity]
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**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS

INSOMNIA AGENTS

BRAND NAME* (generic)

**EDLUAR SUBLINGUAL TABLETS
(zolpidem)**

**INTERMEZZO SUBLINGUAL TABLETS
(zolpidem)**

**ZOLPIMIST ORAL SPRAY
(zolpidem)**

**Status: CVS Caremark Criteria
Type: Initial Prior Authorization**

Ref # 387-C

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Edluar

Edluar sublingual tablets are indicated for the short-term treatment of insomnia characterized by difficulties with sleep initiation. The clinical trials performed with Edluar in support of efficacy were 4-5 weeks in duration with the final formal assessments of sleep latency performed at the end of treatment.

Intermezzo

Intermezzo sublingual tablet is indicated for use as needed for the treatment of insomnia when a middle-of-the-night awakening is followed by difficulty returning to sleep.

Limitations of Use: Intermezzo is not indicated for the treatment of middle-of-the-night insomnia when the patient has fewer than 4 hours of bedtime remaining before the planned time of waking.

ZolpiMist

ZolpiMist oral spray is indicated for the short-term treatment of insomnia characterized by difficulties with sleep initiation. ZolpiMist has been shown to decrease sleep latency for up to 35 days in controlled clinical studies. The clinical trials performed in support of efficacy were 4-5 weeks in duration with the final formal assessment of sleep latency performed at the end of treatment.

COVERAGE CRITERIA

ZolpiMist (zolpidem) oral spray and Edluar (zolpidem) sublingual tablets

The requested drug will be covered with prior authorization when the following criteria are met:

- The drug is being prescribed for insomnia characterized by difficulties with sleep initiation

AND

- Potential causes of sleep disturbances have been addressed (e.g., inappropriate sleep hygiene and sleep environment issues or treatable medical/psychological causes of chronic insomnia)

AND

- The patient is unable to swallow tablets/capsules

OR

Intermezzo (zolpidem) sublingual tablets

The requested drug will be covered with prior authorization when the following criteria are met:

- The drug is being prescribed for insomnia when middle-of-the-night awakening is followed by difficulty returning to sleep

AND

- Potential causes of sleep disturbances have been addressed (e.g., inappropriate sleep hygiene and sleep environment issues or treatable medical/psychological causes of chronic insomnia)

AND

- The patient is one of the following: biological male or a person that self-identifies as a male, 65 years of age and under, or not taking the requested drug concomitantly with other CNS depressants (e.g., benzodiazepines, opioids, tricyclic antidepressants, alcohol)

OR

- The patient is one of the following: biological female or a person that self-identifies as a female, over 65 years old or taking the requested drug concomitantly with other CNS depressants (e.g., benzodiazepines, opioids, tricyclic antidepressants, alcohol)

AND

- The request is for the 1.75 mg strength

Quantity Limits apply.

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Edluar (zolpidem) and ZolpiMist (zolpidem) are indicated for the short-term treatment of insomnia characterized by difficulties with sleep initiation. ZolpiMist (zolpidem) oral spray and Edluar (zolpidem) sublingual tablets are an alternative treatment for patients who are unable to swallow tablets/capsules.

Intermezzo (zolpidem) is indicated for use as needed for the treatment of insomnia when a middle-of-the-night awakening is followed by difficulty returning to sleep. Intermezzo (zolpidem) is not indicated for the treatment of middle-of-the-night insomnia when the patient has fewer than 4 hours of bedtime remaining before the planned time of waking. Intermezzo (zolpidem) will be considered for coverage for patients who have middle-of-the-night awakening followed by difficulty returning to sleep and when other potential causes of sleep disturbances have been addressed.

Insomnia disorder is defined in the International Classification of Sleep Disorders, Third Edition as a complaint of trouble initiating or maintaining sleep which is associated with daytime consequences and is not attributable to environmental circumstances or inadequate opportunity to sleep. The disorder is identified as chronic when it has persisted for at least three months at a frequency of at least three times per week. When the disorder meets the symptom criteria but has persisted for less than three months, it is considered short-term insomnia.^{6,7} Chronic insomnia, also referred to as “chronic insomnia disorder” in the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5), is diagnosed according to the DSM-5 and the International Classification of Sleep Disorders, which have similar criteria for making the diagnosis. These criteria specify that symptoms must cause clinically significant functional distress or impairment; be present for at least three nights per week for at least three months; and not be linked to other sleep, medical, or mental disorders.⁸

Insomnia can occur independently or be caused by another disease.^{8,9} According to the American Academy of Sleep Medicine (AASM), general treatment measures for insomnia include the treatment of comorbid medical and psychiatric conditions, modifying sleep-interfering medications and substances, and optimizing the sleep environment.⁶ The goal of treatment for insomnia is to improve sleep and alleviate distress or dysfunction caused by the disorder.^{6,8-10} Insomnia can be managed with psychological therapy, pharmacologic therapy, or a combination of both. Psychological therapy options include cognitive behavioral therapy for insomnia (CBT-I); multicomponent behavioral therapy or brief behavioral therapy (BBT) for insomnia; and other interventions such as stimulus control, relaxation strategies, and sleep restriction. Cognitive

behavioral therapy for insomnia consists of a combination of cognitive therapy, behavioral interventions (such as sleep restriction and stimulus control), and educational interventions (such as sleep hygiene). The cognitive component is aimed at changing patient's beliefs and attitudes about insomnia. Sleep hygiene education is often also included.⁸⁻¹⁰ The American College of Physicians (ACP) recommends that all adult patients receive cognitive CBT-I as the initial treatment for chronic insomnia disorder.⁸ Despite the clearly favorable benefit to risk ratio of CBT-I, not all patients with an insomnia disorder can and will derive benefit from this treatment alone.^{6,8}

The recommended initial dose of Edluar (zolpidem) and ZolpiMist (zolpidem) is 5 mg for women and either 5 or 10 mg for men, taken only once per night immediately before bedtime with at least 7-8 hours remaining before the planned time of awakening. If the 5 mg dose is not effective, the dose can be increased to 10 mg. In some patients, the higher morning blood levels following use of the 10 mg dose increase the risk of next day impairment of driving and other activities that require full alertness. The total dose of Edluar (zolpidem) or ZolpiMist (zolpidem) should not exceed 10 mg once daily immediately before bedtime. The recommended doses for women and men are different because zolpidem clearance is lower in women. It is recommended to use the lowest effective dose for the patient.

The recommended and maximum dose of Intermezzo (zolpidem) is 1.75 mg for women and 3.5 mg for men, taken only once per night as needed if a middle-of-the-night awakening is following by difficulty returning to sleep. The recommended doses for women and men are different because women clear zolpidem from the body at a lower rate than men. The recommended dose of Intermezzo (zolpidem) in men and women over 65 years of age is 1.75 mg. The recommended dose for patients who are taking concomitant CNS depressants (e.g., benzodiazepines, opioids, tricyclic antidepressants, alcohol) is also 1.75 mg.

REFERENCES

1. Edluar [package insert]. Somerset, NJ: Meda Pharmaceuticals Inc.; December 2018.
2. Intermezzo [package insert]. Stamford, CT: Purdue Pharma L.P.; December 2018.
3. ZolpiMist [package insert]. Englewood, CO: Aytu BioScience, Inc.; February 2019.
4. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed March 2019.
5. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed March 2019.
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7. Sateia MJ. International Classification of Sleep Disorders: highlights and modifications. *CHEST*. 2014; 146 (5): 1387-1394. doi: 10.1378/chest.14-0970
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10. Schutte-Rodin S, Broch L, Buysse D, Dorsey C, Sateia M. Clinical guideline for the evaluation and management of chronic insomnia in adults. *J Clin Sleep Med* 2008; 4(5):487-504.

Written by: UM Development (CT)
Date Written: 01/2009
Last Revised: UM Development (CT) 03/2009, 04/2009 (Edluar added 01/2009(3)), 11/2009, 09/2010, 08/2011, 11/2011 (added Intermezzo), 06/2012, 10/2012 (extended duration); 11/2012 (removed renewal questions); 05/2013, (SE) 07/2013 (removed quantity limits); (CT) 05/2014, 05/2015, 05/2016, 05/2017; (KM) 05/2018 (no clinical changes); (DS) 03/2019 (no clinical changes)
Reviewed: Medical Affairs (WF) 01/2009, 03/2009, 04/2009, 11/2009, 09/2010; (KP) 08/2011, 12/2011, 06/2012, 10/2012; (LMS) 11/2012; (LCB) 05/2013, (LMS) 07/2013; (LMS) 05/2014; (KRU) 05/2015; (LCB) 05/2016; (AN) 05/2017, 03/2019
External P&T Review: 01/2009, 02/2009, 03/2010, 12/2010, 10/2011, 02/2012, 10/2012, 08/2013, 08/2014, 08/2015, 08/2016, 08/2017, 08/2018, 08/2019

CRITERIA FOR APPROVAL

1	Have potential causes of sleep disturbances been addressed (e.g., inappropriate sleep hygiene and sleep environment issues or treatable medical/psychological causes of chronic insomnia)?	Yes	No
2	Is the request for ZolpiMist (zolpidem) oral spray or Edluar (zolpidem) sublingual tablets? [If no, then skip to question 6.]	Yes	No
3	Is the requested drug being prescribed for insomnia characterized by difficulties with sleep initiation?	Yes	No
4	Is the patient unable to swallow tablets/capsules?	Yes	No
5	Does the patient require use of MORE than 30 tablets per month of Edluar (zolpidem) sublingual tablets or 1 container of ZolpiMist (zolpidem) oral spray? [No further questions.] [RPh Note: If yes, then deny and enter a partial approval for 30 tablets per 25 days or 90 tablets per 75 days of Edluar (zolpidem) sublingual tablets or 1 container per 25 days or 3 containers per 75 days of ZolpiMist (zolpidem) oral spray.]	Yes	No
6	Is the requested drug being prescribed for insomnia when middle-of-the-night awakening is followed by difficulty returning to sleep?	Yes	No
7	Is the patient one of the following: A) biological female or a person that self-identifies as a female, B) over 65 years old, C) taking the requested drug concomitantly with other CNS depressants (e.g., benzodiazepines, opioids, tricyclic antidepressants, alcohol)? [If yes, then go to question 9.]	Yes	No
8	Does the patient require use of MORE than 30 tablets per month of Intermezzo (zolpidem) sublingual tablets 1.75 mg or 3.5 mg? [No further questions.] [RPh Note: If yes, then deny and enter a partial approval for 30 tablets per 25 days or 90 tablets per 75 days of Intermezzo (zolpidem) sublingual tablets 1.75 mg or 3.5 mg.]	Yes	No
9	Is the request for the 1.75 mg strength for a dose not exceeding 1.75 mg per day?	Yes	No
10	Does the patient require use of MORE than 30 tablets per month of Intermezzo (zolpidem) sublingual tablets 1.75 mg? [RPh Note: If yes, then deny and enter a partial approval for 30 tablets per 25 days or 90 tablets per 75 days of Intermezzo (zolpidem) sublingual tablets 1.75 mg.]	Yes	No

Mapping Instructions

	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when reasons for insomnia have been addressed. Your request has been denied based on the information we have. [Short Description: No confirmation that causes of sleep disturbances have been addressed]
2.	Go to 3	Go to 6	
3.	Go to 4	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have difficulty falling asleep. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
4.	Go to 5	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you are unable to swallow tablets/capsules. Your request has been denied based on the information we have. [Short Description: No confirmation dosage form required]
5.	Deny	Approve, 36 months Edluar - 30 sublingual tabs/25* days or 90 sublingual tabs/75 days* or ZolpiMist - 1 container/25 days* or 3 containers/75 days*	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 30 tablets per month of Edluar (zolpidem sublingual tablets) or - 1 container per month of ZolpiMist (zolpidem oral spray) You have been approved for the maximum quantity that your plan covers for a duration of 36 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity]
6.	Go to 7	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have middle-of-the-night awakening. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
7.	Go to 9	Go to 8	
8.	Deny	Approve, 36 months Intermezzo 1.75 mg – 30 sublingual tabs/25 days* or 90 sublingual tabs/75 days* Intermezzo 3.5 mg – 30 sublingual tabs*/25 days or 90 sublingual tabs/75 days*	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 30 tablets per month of the requested drug and strength. You have been approved for the maximum quantity that your plan covers for a duration of 36 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity]
9.	Go to 10	Deny	You do not meet the requirements of your plan. Your plan covers this drug if you meet one of the following: - You are a biological female or a person that self-identifies as a female - You are over 65 years old - You are taking this drug at the same time as another CNS depressants (e.g., benzodiazepines, opioids, tricyclic antidepressants, alcohol) AND

			<p>- You are not taking more than 1.75 mg per day Your request has been denied based on the information we have.</p> <p>[Short Description: Over max approvable dose]</p>
10.	Deny	<p>Approve, 36 months Intermezzo 1.75 mg Only– 30 sublingual tabs/25 days* or 90 sublingual tabs/75 days*</p>	<p>You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 30 tablets/month of the requested drug and strength. You have been approved for the maximum quantity that your plan covers for a duration of 36 months. Your request for additional quantities of the requested drug and strength has been denied.</p> <p>[Short Description: Over max quantity]</p>

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

SPECIALTY GUIDELINE MANAGEMENT

INTRON A (interferon alfa-2b)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Malignant melanoma
2. Condylomata acuminata
3. Hairy cell leukemia
4. AIDS-related Kaposi sarcoma
5. Chronic hepatitis B virus infection
6. Chronic hepatitis C virus infection
7. Follicular non-Hodgkin's lymphoma

B. Compendial Uses

1. Non-Hodgkin's lymphoma
 - i. Adult T-cell leukemia/lymphoma (ATLL)
 - ii. Mycosis fungoides (MF)/Sezary syndrome (SS)
2. Myeloproliferative neoplasms
 - i. Essential thrombocythemia
 - ii. Myelofibrosis
 - iii. Polycythemia vera
3. Renal cell carcinoma
4. Chronic myelogenous leukemia (CML)
5. Giant cell tumor of the bone
6. Acute hepatitis C virus infection
7. Desmoid tumors (soft tissue sarcoma)
8. Systemic mastocytosis
9. Carcinoid syndrome
10. Hypereosinophilic syndrome
11. Kasabach-Merritt syndrome
12. Leptomeningeal metastases
13. Life threatening hemangioma of infancy
14. Meningeoma
15. Neuroendocrine tumors of the GI tract, lung, or thymus (carcinoid tumors)
16. Ocular surface neoplasia (conjunctival and corneal neoplasm)
17. Respiratory papillomatosis
18. Vulvar vestibulitis

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Malignant melanoma

Authorization of 12 months may be granted for treatment of malignant melanoma.

B. Non-Hodgkin's lymphoma (NHL)

Authorization of 12 months may be granted for treatment of NHL with any of the following subtypes:

1. Adult T-cell leukemia/lymphoma (ATLL) when used in combination with either of the following:
 - a. Zidovudine, or
 - b. Arsenic trioxide
2. Mycosis fungoides (MF)/Sezary syndrome (SS)
3. Hairy cell leukemia when used as a single agent
4. Follicular lymphoma (clinically aggressive)

C. Renal cell carcinoma

Authorization of 12 months may be granted for treatment of renal cell carcinoma when both of the following criteria are met:

1. Intron-A will be used in combination with bevacizumab.
2. The disease is of clear-cell histology.

D. Condylomata acuminata

Authorization of 12 months may be granted for treatment of condylomata acuminata.

E. AIDS-related Kaposi sarcoma

Authorization of 12 months may be granted for treatment of AIDS-related Kaposi sarcoma when both of the following are met:

1. Intron-A is used for subsequent therapy.
2. Intron-A will be given with antiretroviral therapy (ART).

F. Chronic myelogenous leukemia (CML)

Authorization of 6 months may be granted for treatment of CML.

G. Giant cell tumor of the bone

Authorization of 12 months may be granted for treatment of giant cell tumor of the bone when either of the following criteria are met:

1. Intron-A will be used as a single agent, or
2. Intron-A will be used in combination with denosumab.

H. Desmoid tumors (soft tissue sarcoma)

Authorization of 12 months may be granted for treatment of desmoid tumors when used as a single agent.

I. Acute and chronic hepatitis C virus infection

Authorization of up to 48 weeks may be granted for treatment of acute and chronic hepatitis C virus infection.

J. Chronic hepatitis B (including hepatitis D virus co-infection) virus infection

Authorization of 48 weeks may be granted for treatment of chronic hepatitis B (including hepatitis D virus co-infection) virus infection.

K. Myeloproliferative neoplasms

Authorization of 12 months may be granted for treatment of symptomatic low-risk myelofibrosis, essential thrombocythemia, and polycythemia vera.

L. Systemic mastocytosis

Authorization of 12 months may be granted for treatment of systemic mastocytosis when either of the following criteria are met:

1. Intron-A will be used as a single agent, or
2. Intron-A will be used in combination with prednisone.

M. Hypereosinophilic syndrome

Authorization of 12 months may be granted for treatment of hypereosinophilic syndrome when the patient has had an inadequate response or has contraindication to corticosteroids.

N. Kasabach-Merritt syndrome

Authorization of 12 months may be granted for treatment of Kasabach-Merritt syndrome.

O. Leptomeningeal metastases

Authorization of 12 months may be granted for treatment of leptomeningeal metastases.

P. Life threatening hemangioma of infancy

Authorization of 12 months may be granted for treatment of life threatening hemangioma in an infant patient who has had an inadequate response or contraindication to corticosteroids.

Q. Meningeoma

Authorization of 12 months may be granted for treatment of meningioma when either of the following criteria are met:

1. The disease is recurrent, or
2. The disease is surgically inaccessible.

R. Neuroendocrine tumors of the GI tract, lung, or thymus (carcinoid tumors)

Authorization of 12 months may be granted for treatment of neuroendocrine tumors of the GI tract, lung, or thymus.

S. Carcinoid syndrome

Authorization of 12 months may be granted for treatment of carcinoid syndrome.

T. Ocular surface neoplasia (conjunctival and corneal neoplasm)

Authorization of 12 months may be granted for treatment of ocular surface neoplasia (conjunctival and corneal neoplasm).

U. Respiratory papillomatosis

Authorization of 12 months may be granted for treatment of respiratory papillomatosis.

V. Vulvar vestibulitis

Authorization of 12 months may be granted for treatment of vulvar vestibulitis

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced disease progression or an unacceptable toxicity.

IV. REFERENCES

Reference number(s)
1703-A

1. Intron A [package insert]. Whitehouse Station, NJ: Schering Corporation; October 2017.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed April 28, 2019.
3. Micromedex Solutions [database online]. Truven Health Analytics, Greenwood Village, Colorado, USA. Available at: <http://www.micromedexsolutions.com/>. Accessed April 28, 2019.
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9. Leventhal BG, Kashima HK, Mounts P, et al. Long-term response of recurrent respiratory papillomatosis to treatment with lymphoblastoid interferon alfa-n-1. *N Engl J Med*. 1991;325:613-617.
10. Frieden IJ, Eichenfield LF, Esterly NB, et al. Guidelines of care of hemangiomas of infancy. American Academy of Dermatology/Outcome Committee. *J Am Acad Dermatol*. 1997;37(4):631-637.
11. Shah SU, Kaliki S, Kim HJ, Lally SE, Shields JA, Shields CL. Topical Interferon Alfa-2b for Management of Ocular Surface Squamous Neoplasia in 23 Cases: Outcomes Based on American Joint Committee on Cancer Classification. *Arch Ophthalmol*. 2012;130(2):159–164.
12. Chamberlain MC. A phase II trial of intra-cerebrospinal fluid alpha interferon in the treatment of neoplastic meningitis. *Cancer*. 2002; 94:2675-2680.
13. Kaba SE, De Monte F, Bruner JM et al. The treatment of recurrent unresectable and malignant meningiomas with interferon alpha2B. *Neurosurgery*. 1997;40:271-275.

SPECIALTY GUIDELINE MANAGEMENT

IRESSA (gefitinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication¹

Iressa is indicated for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test.

Limitation of Use: Safety and efficacy of Iressa have not been established in patients who have EGFR mutations other than exon 19 deletions or exon 21 (L858R) substitution mutations.

B. Compendial Use²⁻⁴

1. EGFR mutation-positive recurrent, advanced, or metastatic NSCLC
2. Brain metastases from sensitizing EGFR mutation-positive NSCLC

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: EGFR mutation testing results.

III. CRITERIA FOR INITIAL APPROVAL

Non-small cell lung cancer (NSCLC)¹⁻⁴

Authorization of 12 months may be granted for treatment of recurrent, advanced, or metastatic NSCLC (including brain metastases from NSCLC) in members with sensitizing EGFR mutation-positive disease.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced an unacceptable toxicity.

V. REFERENCES

1. Iressa [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; August 2018.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. Available at: <https://www.nccn.org>. Accessed March 5, 2019.
3. The NCCN Clinical Practice Guidelines in Oncology® Non-Small Cell Lung Cancer Version 3.2019. © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed March 5, 2019.

Reference number(s)
1660-A

4. The NCCN Clinical Practice Guidelines in Oncology® Central Nervous System Cancers Version 2.2018. ©2018 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed March 5, 2019.

SPECIALTY GUIDELINE MANAGEMENT

ISTODAX (romidepsin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Cutaneous T-cell lymphoma (CTCL) in patients who have received at least one prior systemic therapy
2. Peripheral T-cell lymphoma (PTCL) in patients who have received at least one prior therapy

1. Compendial Uses Mycosis fungoides (MF)
2. Sézary syndrome (SS)

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

Coverage will not be provided for members with the following exclusion: Concomitant use of romidepsin with vorinostat (Zolinza).

III. CRITERIA FOR INITIAL APPROVAL

A. Cutaneous T-cell lymphoma (CTCL)

Authorization of 12 months may be granted for treatment of CTCL (e.g., mycosis fungoides, Sézary syndrome, primary cutaneous anaplastic large cell lymphoma).

B. Peripheral T-cell lymphoma (PTCL) (see Appendix)

Authorization of 12 months may be granted for treatment of PTCL.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced disease progression or an unacceptable toxicity.

V. APPENDIX: PTCL subtypes

1. Peripheral T-cell lymphoma not otherwise specified (PTCL-NOS)
2. Angioimmunoblastic T-cell lymphoma (AITL)
3. Anaplastic large cell lymphoma (ALCL), anaplastic lymphoma kinase (ALK)+/ALK-
4. Enteropathy-associated T-cell lymphoma (EATL)

Reference number
1859-A

5. Monomorphic epitheliotropic intestinal T-cell lymphoma (MEITL)
6. Nodal peripheral T-cell lymphoma with TFH phenotype (PTCL, TFH)
7. Follicular T-cell lymphoma (FTCL)
8. Extranodal NK/T-cell lymphoma, nasal type (ENKL)
9. Hepatosplenic gamma-delta-T-cell lymphoma (HSGDTCL)

VI. REFERENCES

1. Istodax [package insert]. Summit, NJ: Celgene Corp.; November 2018.
2. The NCCN Drugs & Biologics Compendium™ © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org> Accessed September 11, 2019.
3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Primary Cutaneous Lymphomas (Version 2.2019). <https://www.nccn.org>. Accessed September 11, 2019.
4. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: T-Cell Lymphomas (Version 2.2019). <https://www.nccn.org>. Accessed September 11, 2019.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

ONMEL
(itraconazole tablets)

Status: CVS Caremark Criteria

Type: Initial Prior Authorization

MDC-1

Ref # 919-A

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Onmel is indicated for the treatment of onychomycosis of the toenail due to *Trichophyton rubrum* or *T. mentagrophytes* in non-immunocompromised patients. Prior to initiating treatment, appropriate nail specimens for laboratory testing (KOH preparation, fungal culture, or nail biopsy) should be obtained to confirm the diagnosis of onychomycosis.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the treatment of onychomycosis of the toenail due to *Trichophyton* that has been confirmed by a fungal diagnostic test

RATIONALE

These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Onmel is indicated for the treatment of onychomycosis of the toenail due to *Trichophyton rubrum* or *T. mentagrophytes* in non-immunocompromised patients. Prior to initiating treatment, appropriate nail specimens for laboratory testing potassium hydroxide (KOH preparation, fungal culture, or nail biopsy) should be obtained to confirm the diagnosis of onychomycosis. The recommended dose of Onmel is 200 mg once daily for 12 consecutive weeks.

REFERENCES

1. Onmel [package insert]. Greensboro, NC: Merz Pharmaceuticals, LLC; October 2012.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed February 2019.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed February 2019.

Written by: UM Development (CT)

Date Written: 01/2013

Revised: (PL) 08/2013, 08/2014; (MS) 05/2015, 05/2016 (no clinical changes), (SE) 06/2016 (created separate Med D); (MS) 04/2017; (DS) 04/2018 (no clinical changes), (ME) 02/2019 (no clinical changes)

Reviewed: Medical Affairs: (DNC) 01/2013; (DNC) 08/2013; (LCB) 08/2014; (LS) 05/2015; (AN) 04/2017; (DNC) 04/2018

External Review: 01/2013, 02/2013, 12/2013, 10/2014, 10/2015, 08/2016, 08/2017, 06/2018, 06/2019

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for the treatment of onychomycosis of the toenail due to <i>Trichophyton</i> that has been confirmed by a fungal diagnostic test?	Yes	No
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Guidelines for Approval	
Duration of Approval	3 Months
Set 1	
Yes to questions	No to questions
1	None

Mapping Instructions			
	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Approve, 3 months	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions:</p> <ul style="list-style-type: none"> - You have a specific fungal infection of the toenail - You had a test to confirm your toenail fungus <p>Your request has been denied based on the information we have. [Short Description: No approvable diagnosis, no confirmation of diagnosis]</p>

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

SPORANOX ORAL CAPSULES
(itraconazole)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

MDC-1
Ref # 280-A

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Sporanox (itraconazole) Capsules are indicated for the treatment of the following fungal infections in immunocompromised and non-immunocompromised patients:

1. Blastomycosis, pulmonary and extrapulmonary
2. Histoplasmosis, including chronic cavitary pulmonary disease and disseminated, non-meningeal histoplasmosis, and
3. Aspergillosis, pulmonary and extrapulmonary, in patients who are intolerant of or who are refractory to amphotericin B therapy.

Specimens for fungal cultures and other relevant laboratory studies (wet mount, histopathology, serology) should be obtained before therapy to isolate and identify causative organisms. Therapy may be instituted before the results of the cultures and other laboratory studies are known; however, once these results become available, anti-infective therapy should be adjusted accordingly.

Sporanox Capsules are also indicated for the treatment of the following fungal infections in non-immunocompromised patients:

1. Onychomycosis of the toenail, with or without fingernail involvement, due to dermatophytes (tinea unguium), and
2. Onychomycosis of the fingernail due to dermatophytes (tinea unguium).

Prior to initiating treatment, appropriate nail specimens for laboratory testing (KOH preparation, fungal culture, or nail biopsy) should be obtained to confirm the diagnosis of onychomycosis.

Compendial Uses

Coccidioidomycosis^{2,3}

Cryptococcosis^{2,3}

Microsporidiosis²

Penicilliosis²

Pityriasis versicolor/Tinea versicolor^{2,3}

Sporotrichosis^{2,3}

Tinea corporis, Tinea cruris, Tinea capitis, Tinea manuum, Tinea pedis³

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- Patient has one of the following diagnoses: A) Pityriasis versicolor, B) Tinea versicolor, C) Onychomycosis due to tinea that has been confirmed by a fungal diagnostic test

OR

- Patient has one of the following diagnoses: A) Blastomycosis, B) Histoplasmosis, C) Aspergillosis, D) Coccidioidomycosis, E) Cryptococcosis, F) Sporotrichosis, G) Penicilliosis, H) Microsporidiosis

OR

- Patient has one of the following diagnoses: A) Tinea corporis, B) Tinea cruris, C) Tinea capitis, D) Tinea manuum, E) Tinea pedis

AND

- Patient experienced an inadequate treatment response, adverse event, intolerance, or contraindication to griseofulvin

RATIONALE

These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. The criteria do not provide treatment for cosmetic purposes. Sporanox (itraconazole) capsules are indicated for the treatment of blastomycosis, pulmonary and extrapulmonary; histoplasmosis, including chronic cavitary pulmonary disease and disseminated, non-meningeal histoplasmosis, and; aspergillosis, pulmonary and extrapulmonary, in patients who are intolerant of or who are refractory to amphotericin B therapy. Specimens for fungal cultures and other relevant laboratory studies (wet mount, histopathology, serology) should be obtained before therapy to isolate and identify causative organisms. Therapy may be instituted before the results of the cultures and other laboratory studies are known; however, once these results become available, anti-infective therapy should be adjusted accordingly. Acceptable compendia also indicate that itraconazole is appropriate for the treatment of coccidioidomycosis, cryptococcosis, sporotrichosis, penicilliosis, and microsporidiosis.^{2,3,7,8} Sporanox capsules are also indicated in non-immunocompromised patients for the treatment of onychomycosis of the toenail, with or without fingernail involvement, due to dermatophytes (*tinea unguium*); and onychomycosis of the fingernail due to dermatophytes (*tinea unguium*). Prior to initiating treatment, appropriate nail specimens for laboratory testing potassium hydroxide (KOH) preparation, fungal culture, or nail biopsy should be obtained to confirm the diagnosis of onychomycosis. Per the compendia, itraconazole is suggested as an alternative therapy for the treatment of pityriasis versicolor, tinea versicolor, tinea corporis, tinea cruris, tinea capitis, tinea manuum or tinea pedis.^{2,3}

Itraconazole will be approved for the treatment of onychomycosis due to dermatophytes (*tinea unguium*) following confirmation with a fungal diagnostic test (e.g., KOH preparation, fungal culture, or nail biopsy). Itraconazole will be approved for the treatment of patients with either pityriasis versicolor or tinea versicolor. Itraconazole will be approved for the treatment of tinea corporis, tinea cruris, tinea capitis, tinea manuum or tinea pedis following a trial of griseofulvin as it is FDA approved as first line therapy. Itraconazole will be approved for the treatment of blastomycosis, histoplasmosis, aspergillosis, coccidioidomycosis, cryptococcosis, sporotrichosis, penicilliosis, and microsporidiosis.

The recommended treatment course for onychomycosis of the toenails, with or without fingernail involvement, is 200 mg once daily for 12 weeks.¹ The suggested dosing for superficial tinea infections is similar to that of onychomycosis of the toenails, 200 mg once daily, although for a shorter duration.³ Therefore, coverage for these conditions will be approved for up to 3 months. The recommended and suggested treatments for the remainder of the approvable indications vary depending on the type of infection and patient specific factors. It is noted, however, that treatment in life-threatening situations should be continued for a minimum of 3 months and until clinical parameters and laboratory tests indicate that the active fungal infection has subsided. An inadequate period of treatment may lead to recurrence of active infection.¹ Because of this, the duration of approval for these indications will be set at 6 months.

REFERENCES

1. Sporanox capsule [package insert]. Titusville, NJ: Janssen Pharmaceuticals, Inc.; May 2018.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed February 2019.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed February 2019.
4. Patterson TF, Thompson GR, Denning DW, et al. Practice Guidelines for the Diagnosis and Management of Aspergillosis: 2016 Update by the Infectious Diseases Society of America. *Clinical Infectious Diseases*. 2016;63:112–146.
5. Wheat L, Freifeld A, Kleiman M, et al. Clinical Practice Guidelines for the Management of Patients with Histoplasmosis: 2007 Update by the Infectious Diseases Society of America. *Clinical Infectious Diseases*. 2007;45:807–25.
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8. Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents. Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/adult_o.pdf. Accessed February 2019.

Written by: UM Development (SE)
 Date written: 12/2009
 Revised: (KD/SE) CAS Adapted 09/2010, (TM) 08/2011; (RP) 08/2012; (PL) 08/2013, 08/2014; (MS) 05/2015, 05/2016 (no clinical changes), (SE) 06/2016 (created separate Med D); (MS) 04/2017; (DS) 04/2018, (ME) 02/2019 (no clinical changes)
 Reviewed: Medical Affairs (KP) 12/2009, (KP) 07/2010, (KP) 08/2011; (DC) 08/2012; (DNC) 08/2013; (LCB) 08/2014; (LS) 05/2015; (AN) 04/2017; (DNC) 04/2018
 External Review: 02/2010, 12/2010, 10/2011, 12/2011, 12/2012, 12/2013, 10/2014, 10/2015, 08/2016, 08/2017, 06/2018, 06/2019

CRITERIA FOR APPROVAL

1	Does the patient have one of the following diagnoses: A) Pityriasis versicolor, B) Tinea versicolor, C) Onychomycosis due to tinea that has been confirmed by a fungal diagnostic test? [If yes, then no further questions.]	Yes	No
2	Does the patient have any of the following diagnoses: A) Tinea corporis, B) Tinea cruris, C) Tinea capitis, D) Tinea manuum, E) Tinea pedis? [If no, then skip to question 4.]	Yes	No
3	Has the patient experienced an inadequate treatment response, intolerance or contraindication to griseofulvin? [No further questions.]	Yes	No
4	Does the patient have one of the following diagnoses: A) Blastomycosis, B) Histoplasmosis, C) Aspergillosis, D) Coccidioidomycosis, E) Cryptococcosis, F) Sporotrichosis, G) Penicilliosis, H) Microsporidiosis?	Yes	No

Guidelines for Approval			
Duration of Approval		3 Months	
Set 1		Set 2	
Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)
1	None	2	1
		3	
Duration of Approval		6 Months	
Set 3			
Yes to question(s)	No to question(s)		
4		1	
		2	

Mapping Instructions			
	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Approve, 3 months	Go to 2	
2.	Go to 3	Go to 4	
3.	Approve, 3 months	Deny	<p>You do not meet the requirements of your plan.</p> <p>Your plan covers this drug when you have these conditions:</p> <ul style="list-style-type: none"> - You had a poor response to griseofulvin or cannot take it. <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No approvable diagnosis, no inadequate response, intolerance or contraindication to griseofulvin]</p>
4.	Approve, 6 months	Deny	<p>You do not meet the requirements of your plan.</p> <p>Your plan covers this drug when you have one of these conditions:</p> <ul style="list-style-type: none"> - You have ringworm, a fungal infection of the groin, scalp, or hand, or athlete's foot - You have a specific fungal infection of the skin that causes spots - You have a specific nail fungus and it has been tested - You have Blastomycosis, Histoplasmosis, Aspergillosis, Coccidioidomycosis, Cryptococcosis, Sporotrichosis, Penicilliosis or Microsporidiosis <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No approvable diagnosis, no confirmation of diagnosis]</p>

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

SPORANOX ORAL SOLUTION
(itraconazole)

Status: CVS Caremark Criteria

Type: Initial Prior Authorization

Ref # 1286-A

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Sporanox (itraconazole) Oral Solution is indicated for the treatment of oropharyngeal and esophageal candidiasis.

COMPENDIAL USES

Blastomycosis^{3,4}
Histoplasmosis^{3,4}
Aspergillosis^{3,4}
Coccidioidomycosis^{3,4}
Cryptococcosis^{3,4}
Microsporidiosis³
Penicilliosis³
Pityriasis versicolor/Tinea versicolor⁴
Sporotrichosis^{3,4}
Tinea corporis, Tinea cruris, Tinea capitis, Tinea manuum, Tinea pedis⁴

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- Patient has a diagnosis of oropharyngeal candidiasis or esophageal candidiasis.
OR
- Patient is unable to take itraconazole capsules due to one of the following: inability to swallow itraconazole capsules or inability to achieve therapeutic levels with itraconazole capsules.
AND
- Patient has one of the following diagnoses: A) Pityriasis versicolor, B) Tinea versicolor, C) Onychomycosis due to tinea that has been confirmed by a fungal diagnostic test
OR
- Patient has one of the following diagnoses: A) Blastomycosis, B) Histoplasmosis, C) Aspergillosis, D) Coccidioidomycosis, E) Cryptococcosis, F) Sporotrichosis, G) Penicilliosis, H) Microsporidiosis
OR
- Patient has one of the following diagnoses: A) Tinea corporis, B) Tinea cruris, C) Tinea capitis, D) Tinea manuum, E) Tinea pedis.
AND
 - Patient experienced an inadequate treatment response, adverse event, intolerance, or contraindication to griseofulvin

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Sporanox (itraconazole) Oral Solution is indicated for the treatment of oropharyngeal and esophageal candidiasis.

For oropharyngeal candidiasis, Sporanox (itraconazole) Oral Solution should be taken for 1 to 2 weeks. For patients with oropharyngeal candidiasis unresponsive/refractory to treatment with fluconazole tablets responding to Sporanox (itraconazole) Oral Solution therapy, clinical response will be seen in 2 to 4 weeks. Patients may be expected to relapse shortly after discontinuing therapy. There is limited data on the safety of long-term use, greater than 6 months, of Sporanox (itraconazole) Oral Solution. For esophageal candidiasis, Sporanox (itraconazole) Oral Solution should be taken for a minimum treatment of 3 weeks. Treatment should continue for 2 weeks following resolution of symptoms. Sporanox (itraconazole) Oral Solution and Sporanox (itraconazole) Capsules should not be used interchangeably as only Sporanox (itraconazole) Oral Solution has been demonstrated effective for oral and/or esophageal candidiasis.¹⁻⁴

Although it is not recommended to use Sporanox (itraconazole) capsules interchangeably with Sporanox (itraconazole) Oral Solution for the treatment of oral and/or esophageal candidiasis, it is reasonable to assume that the interchange can work in the opposite direction. That is to say, Sporanox (itraconazole) Oral Solution can be approved for the same indications/compendia uses as Sporanox (itraconazole) capsules. For these uses, the patient must be unable to take the capsules (due to an inability to swallow or achieve therapeutic levels with itraconazole capsules). The criteria do not provide treatment for cosmetic purposes. Itraconazole can be used for the treatment of blastomycosis, pulmonary and extrapulmonary; histoplasmosis, including chronic cavitary pulmonary disease and disseminated, non-meningeal histoplasmosis, and; aspergillosis, pulmonary and extrapulmonary, in patients who are intolerant of or who are refractory to amphotericin B therapy.²⁻⁴ Specimens for fungal cultures and other relevant laboratory studies (wet mount, histopathology, serology) should be obtained before therapy to isolate and identify causative organisms. Therapy may be instituted before the results of the cultures and other laboratory studies are known; however, once these results become available, anti-infective therapy should be adjusted accordingly. Acceptable compendia also show that itraconazole is appropriate for the treatment of coccidioidomycosis, cryptococcosis, sporotrichosis, penicilliosis, and microsporidiosis. Itraconazole can also be used in non-immunocompromised patients for the treatment of onychomycosis of the toenail, with or without fingernail involvement, due to dermatophytes (tinea unguium); and onychomycosis of the fingernail due to dermatophytes (tinea unguium).^{3,4,9,10} Prior to initiating treatment, appropriate nail specimens for laboratory testing potassium hydroxide (KOH) preparation, fungal culture, or nail biopsy should be obtained to confirm the diagnosis of onychomycosis. Per the compendia, itraconazole is suggested as an alternative therapy for the treatment of pityriasis versicolor or tinea versicolor, tinea corporis, tinea cruris, tinea capitis, tinea manuum or tinea pedis.^{3,4}

Itraconazole will be approved for the treatment of onychomycosis due to dermatophytes (tinea unguium) following confirmation with a fungal diagnostic test (e.g., KOH preparation, fungal culture, or nail biopsy). Itraconazole will be approved for the treatment of patients with either pityriasis versicolor or tinea versicolor. Itraconazole will be approved for the treatment of tinea corporis, tinea cruris, tinea capitis, tinea manuum or tinea pedis following a trial of griseofulvin as it is FDA approved as first line therapy. Itraconazole will be approved for the treatment of blastomycosis, histoplasmosis, aspergillosis, coccidioidomycosis, cryptococcosis, sporotrichosis, penicilliosis, and microsporidiosis.

The recommended treatment course for onychomycosis of the toenails, with or without fingernail involvement, is 200 mg once daily for 12 weeks.² The suggested dosing for superficial tinea infections is similar to that of onychomycosis of the toenails, 200 mg once daily, although for a shorter duration.⁴ Therefore, coverage for these conditions will be approved for up to 3 months. The recommended and suggested treatments for the remainder of the approvable indications vary depending on the type of infection and patient specific factors. It is noted, however, that treatment in life-threatening situations should be continued for a minimum of 3 months and until clinical parameters and laboratory tests indicate that the active fungal infection has subsided. An inadequate period of treatment may lead to recurrence of active infection.² Because of this, the duration of approval for these indications will be set at 6 months.

REFERENCES

1. Sporanox Oral Solution [package insert]. Titusville, NJ: Janssen Pharmaceuticals, Inc.; April 2018.
2. Sporanox Capsule [package insert]. Titusville, NJ: Janssen Pharmaceuticals, Inc.; May 2018.
3. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed February 2019.
4. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed February 2019.
5. Pappas P, Kauffman C, Andes D, et al. Clinical Practice Guidelines for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America. *Clinical Infectious Diseases*. 2016;62:1-50.

6. Patterson TF, Thompson GR, Denning DW, et al. Practice Guidelines for the Diagnosis and Management of Aspergillosis: 2016 Update by the Infectious Diseases Society of America. *Clinical Infectious Diseases*. 2016;63:112–146.
7. Wheat L, Freifeld A, Kleiman M, et al. Clinical Practice Guidelines for the Management of Patients with Histoplasmosis: 2007 Update by the Infectious Diseases Society of America. *Clinical Infectious Diseases*. 2007;45:807–25.
8. Chapman S, Dismukes W, Proia L, et al. Clinical Practice Guidelines for the Management of Blastomycosis: 2008 Update by the Infectious Diseases Society of America. *Clinical Infectious Diseases*. 2008;46:1801–12.
9. Perfect J, Dismukes W, Dromer F, et al. Clinical Practice Guidelines for the Management of Cryptococcal Disease: 2010 Update by the Infectious Diseases Society of America. *Clinical Infectious Diseases*. 2010;50:291–322.
10. Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents. Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/adult_o.pdf. Accessed February 2019.

Written by: UM Development (CT)
 Date Written: 12/2005
 Revised: (NB) 08/2006, 07/2007, (MS) 07/2008, (SE) 07/2009, (TM) 07/2010, 08/2011; (RP) 08/2012; (PL) 08/2013, 08/2014; (MS) 05/2015, 08/2015 (Added itraconazole oral capsule indications), 05/2016 (no clinical changes), 04/2017; (DS) 04/2018, (ME) 02/2019 (no clinical changes)
 Reviewed: Medical Affairs (MM) 12/2005, 08/2006, (WF) 07/2007, (WF) 07/2008, 07/2009, (KP) 07/2010, (KP) 08/2011, (DC) 08/2012; (DNC) 08/2013; (LCB) 08/2014; (LS) 05/2015; (LB) 08/2015; (AN) 04/2017; (DNC) 04/2018
 External Review: 04/2006; 12/2006; 02/2008; 10/2008, 10/2009, 12/2010, 12/2011, 12/2012, 12/2013, 10/2014, 10/2015, 08/2016, 08/2017, 06/2018, 06/2019

CRITERIA FOR APPROVAL

1	Does the patient have any of the following diagnoses: A) Oropharyngeal candidiasis, B) Esophageal candidiasis? [If yes, then no further questions.]	Yes	No
2	Is the patient unable to take itraconazole capsules due to one of the following: A) inability to swallow itraconazole capsules, B) inability to achieve therapeutic levels with itraconazole capsules?	Yes	No
3	Does the patient have one of the following diagnoses: A) Pityriasis versicolor, B) Tinea versicolor, C) onychomycosis due to tinea that has been confirmed by a fungal diagnostic test? [If yes, then no further questions.]	Yes	No
4	Does the patient have one of the following diagnoses: A) Tinea corporis, B) Tinea cruris, C) Tinea capitis, D) Tinea manuum, E) Tinea pedis? [If no, then skip to question 6.]	Yes	No
5	Has the patient experienced an inadequate treatment response, intolerance or contraindication to griseofulvin? [No further questions.]	Yes	No
6	Does the patient have one of the following diagnoses: A) Blastomycosis, B) Histoplasmosis, C) Aspergillosis, D) Coccidioidomycosis, E) Cryptococcosis, F) Sporotrichosis, G) Penicilliosis, H) Microsporidiosis?	Yes	No

Mapping Instructions			
	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Approve, 6 months	Go to 2	
2.	Go to 3	Deny	<p>You do not meet the requirements of your plan.</p> <p>Your plan covers this drug when you meet one of these conditions:</p> <ul style="list-style-type: none"> - You have a fungal infection of the mouth or throat (Oropharyngeal candidiasis or Esophageal candidiasis) - You are unable to swallow capsules - You are unable to get a strong enough dose with capsules <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No approvable diagnosis, no justification for solution over capsules]</p>
3.	Approve, 3 months	Go to 4	
4.	Go to 5	Go to 6	
5.	Approve, 3 months	Deny	<p>You do not meet the requirements of your plan.</p> <p>Your plan covers this drug when you have these conditions:</p> <ul style="list-style-type: none"> - You had a poor response to griseofulvin or cannot take it <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No approvable diagnosis, no inadequate response, intolerance or contraindication to griseofulvin]</p>
6.	Approve, 6 months	Deny	<p>You do not meet the requirements of your plan.</p> <p>Your plan covers this drug when you have one of these conditions:</p> <ul style="list-style-type: none"> - You have ringworm, a fungal infection of the groin, scalp or hand, or athlete's foot - You have a specific fungal infection of the skin that causes spots - You have a specific nail fungus and it has been tested - You have Blastomycosis, Histoplasmosis, Aspergillosis, Coccidioidomycosis, Cryptococcosis, Sporotrichosis, Penicilliosis or Microsporidiosis <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No approvable diagnosis, no confirmation of diagnosis]</p>

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

TOLSURA
(itraconazole)

Status: CVS Caremark Criteria

Type: Initial Prior Authorization

Ref # 2845-A

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

TOLSURA is an azole antifungal indicated for the treatment of the following fungal infections in immunocompromised and non-immunocompromised adult patients:

1. Blastomycosis, pulmonary and extrapulmonary
2. Histoplasmosis, including chronic cavitary pulmonary disease and disseminated, non-meningeal histoplasmosis, and
3. Aspergillosis, pulmonary and extrapulmonary, in patients who are intolerant of or who are refractory to amphotericin B therapy.

Specimens for fungal cultures and other relevant laboratory studies (wet mount, histopathology, serology) should be obtained before therapy to isolate and identify causative organisms. Therapy may be instituted before the results of the cultures and other laboratory studies are known; however, once these results become available, anti-fungal therapy should be adjusted accordingly

Limitations of Use:

TOLSURA is not indicated for the treatment of onychomycosis

TOLSURA is NOT interchangeable or substitutable with other itraconazole products

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has one of the following diagnoses: A) Blastomycosis, B) Histoplasmosis, C) Aspergillosis

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. The criteria do not provide treatment for cosmetic purposes. Tolsura is indicated for the treatment of blastomycosis, pulmonary and extrapulmonary; histoplasmosis, including chronic cavitary pulmonary disease and disseminated, non-meningeal histoplasmosis, and aspergillosis, pulmonary and extrapulmonary, in patients who are intolerant of or who are refractory to amphotericin B therapy. Specimens for fungal cultures and other relevant laboratory studies (wet mount, histopathology, serology) should be obtained before therapy to isolate and identify causative organisms. Therapy may be instituted before the results of the cultures and other laboratory studies are known; however, once these results become available, anti-infective therapy should be adjusted accordingly.

Tolsura will be approved for the treatment of blastomycosis, histoplasmosis, aspergillosis. Treatment in life-threatening situations should be continued for a minimum of 3 months and until clinical parameters and laboratory tests indicate that the active fungal infection has subsided. An inadequate period of treatment may lead to recurrence of active infection.¹ Therefore, the duration of approval for these indications will be set at 6 months.

REFERENCES

1. Tolsura capsule [package insert]. Greenville, NC: Mayne Pharma, December 2018.
2. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed January 2019.

Written by: UM Development (ME)
 Date written: 01/2019
 Revised:
 Reviewed: Medical Affairs (AN) 01/2019
 External Review: 04/2019

CRITERIA FOR APPROVAL

1	Does the patient have one of the following diagnoses: A) Blastomycosis, B) Histoplasmosis, C) Aspergillosis?	Yes	No
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Mapping Instructions

	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Approve, 6 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have Blastomycosis, Histoplasmosis or Aspergillosis. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]

SPECIALTY GUIDELINE MANAGEMENT

Intravenous Immune Globulin (IVIG):

Asceniv™, Bivigam®, Carimune® NF, Flebogamma® DIF, Gammagard® Liquid, Gammagard® S/D, Gammaked™, Gammaplex®, Gamunex®-C, Octagam®, Panzyga®, and Privigen®

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Primary immunodeficiency
2. Idiopathic thrombocytopenic purpura (ITP)
3. Chronic inflammatory demyelinating polyneuropathy
4. Multifocal motor neuropathy
5. Kawasaki syndrome
6. B-cell chronic lymphocytic leukemia (CLL)

B. Compendial Uses

1. Prophylaxis of bacterial infections in pediatric human immunodeficiency virus (HIV) infection
2. Prophylaxis of bacterial infections in bone marrow transplant (BMT)/hematopoietic stem cell transplant (HSCT) recipients
3. Dermatomyositis
4. Polymyositis
5. Myasthenia gravis
6. Guillain-Barré syndrome
7. Lambert-Eaton myasthenic syndrome
8. Fetal/neonatal alloimmune thrombocytopenia
9. Parvovirus B19-induced pure red cell aplasia
10. Stiff-person syndrome
11. Management of immune checkpoint inhibitor-related nervous system adverse events
12. Acquired red cell aplasia
13. Acute disseminated encephalomyelitis
14. Autoimmune mucocutaneous blistering diseases
15. Autoimmune hemolytic anemia
16. Autoimmune neutropenia
17. Birdshot retinochoroidopathy
18. BK virus associated nephropathy
19. Churg-Strauss Syndrome
20. Enteroviral meningoencephalitis
21. Hematophagocytic lymphohistiocytosis (HLH) or macrophage activation syndrome (MAS)
22. Hemolytic disease of newborn
23. HIV-associated thrombocytopenia
24. Hyperimmunoglobulinemia E Syndrome
25. Hypogammaglobulinemia from chimeric antigen receptor T (CAR-T) therapy

Reference number(s)
2042-A

26. Multiple myeloma
27. Neonatal hemochromatosis, prophylaxis
28. Opsoclonus-myoclonus
29. Paraneoplastic opsonus-myoclonus ataxia associated with neuroblastoma
30. Post-transfusion purpura
31. Rasmussen encephalitis
32. Renal transplantation from a live donor with ABO incompatibility or positive cross match
33. Secondary immunosuppression associated with major surgery, hematological malignancy, major burns, and collagen-vascular diseases
34. Solid organ transplantation, for allosensitized members
35. Toxic epidermal necrolysis and Stevens-Johnson syndrome
36. Toxic shock syndrome
37. Systemic lupus erythematosus (SLE)
38. Toxic necrotizing fasciitis due to group A streptococcus

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

The following information is necessary to initiate the prior authorization review:

- A. Primary immunodeficiency
 1. Diagnostic test results (when applicable)
 - a. Copy of laboratory report with serum immunoglobulin levels: IgG, IgA, IgM, and IgG subclasses
 - b. Vaccine response to pneumococcal polysaccharide vaccine (post-vaccination *Streptococcus pneumoniae* antibody titers)
 - c. Pertinent genetic or molecular testing in members with a known genetic disorder
 - d. Copy of laboratory report with lymphocyte subset enumeration by flow cytometry
 2. IgG trough level for those continuing with IG therapy
- B. Myasthenia gravis
 1. Clinical records describing standard treatments tried and failed
- C. Secondary hypogammaglobulinemia (CLL, HIV, BMT/HSCT recipients, surgery, malignancy, burns, collagen-vascular disease)
 1. Copy of laboratory report with pre-treatment serum IgG level (when applicable)
- D. Chronic inflammatory demyelinating polyneuropathy (CIDP) and multifocal motor neuropathy (MMN)
 1. Pre-treatment electrodiagnostic studies (electromyography [EMG] or nerve conduction studies [NCS])
 2. For CIDP, pre-treatment cerebrospinal fluid (CSF) analysis (when available)
- E. Dermatomyositis and polymyositis
 1. Pre-treatment electrodiagnostic studies (EMG/NCS)
 2. Pre-treatment muscle biopsy report (when available)
 3. Clinical records describing standard treatments tried and failed
- F. Lambert-Eaton Myasthenic Syndrome (LEMS)
 1. Neurophysiology studies (e.g., electromyography) (when applicable)
 2. A positive anti- P/Q type voltage-gated calcium channel antibody test (when applicable)
- G. Idiopathic thrombocytopenic purpura
 1. Laboratory report with pre-treatment/current platelet count
 2. Chronic/persistent ITP: copy of medical records supporting trial and failure with corticosteroid or anti-D therapy (unless contraindicated)
- H. Parvovirus B19-indicated Pure Red Cell Aplasia (PRCA)
 1. Copy of test result confirming presence of parvovirus B19
- I. Stiff-person syndrome
 1. Anti-glutamic acid decarboxylase (GAD) antibody testing results

Reference number(s)
2042-A

2. Clinical records describing standard treatments tried and failed
- J. Toxic shock syndrome or toxic necrotizing fasciitis due to group A streptococcus
 1. Documented presence of fasciitis (when applicable)
 2. Microbiological data (culture or Gram stain)

III. CRITERIA FOR INITIAL APPROVAL

A. Primary Immunodeficiency

Initial authorization of 6 months may be granted for members with any of the following diagnoses:

1. Severe combined immunodeficiency (SCID) or congenital agammaglobulinemia (eg, X-linked or autosomal recessive agammaglobulinemia):
 - a. Diagnosis confirmed by genetic or molecular testing, or
 - b. Pretreatment IgG level < 200 mg/dL, or
 - c. Absence or very low number of T cells (CD3 T cells < 300/microliter) or the presence of maternal T cells in the circulation (SCID only)
2. Wiskott-Aldrich syndrome, DiGeorge syndrome, or ataxia-telangiectasia (or other non-SCID combined immunodeficiency):
 - a. Diagnosis confirmed by genetic or molecular testing (if applicable), and
 - b. History of recurrent bacterial infections (eg, pneumonia, otitis media, sinusitis, sepsis, gastrointestinal), and
 - c. Impaired antibody response to pneumococcal polysaccharide vaccine (see Appendix A)
3. Common variable immunodeficiency (CVID):
 - a. Age 4 years or older, and
 - b. Other causes of immune deficiency have been excluded (eg, drug induced, genetic disorders, infectious diseases such as HIV, malignancy), and
 - c. Pretreatment IgG level < 500 mg/dL or ≥ 2 SD below the mean for age, and
 - d. History of recurrent bacterial infections, and
 - e. Impaired antibody response to pneumococcal polysaccharide vaccine (see Appendix A)
4. Hypogammaglobulinemia (unspecified), IgG subclass deficiency, selective IgA deficiency, selective IgM deficiency, or specific antibody deficiency:
 - a. History of recurrent bacterial infections
 - b. Impaired antibody response to pneumococcal polysaccharide vaccine (see Appendix A)
 - c. Any of the following pre-treatment laboratory findings:
 - i. Hypogammaglobulinemia: IgG < 500 mg/dL or ≥ 2 SD below the mean for age
 - ii. Selective IgA deficiency: IgA level < 7 mg/dL with normal IgG and IgM levels
 - iii. Selective IgM deficiency: IgM level < 30 mg/dL with normal IgG and IgA levels
 - iv. IgG subclass deficiency: IgG1, IgG2, or IgG3 ≥ 2 SD below mean for age assessed on at least 2 occasions; normal IgG (total) and IgM levels, normal/low IgA levels
 - v. Specific antibody deficiency: normal IgG, IgA and IgM levels
5. Other predominant antibody deficiency disorders must meet a., b., and c.i. in section 4. above.
6. Other combined immunodeficiency must meet criteria in section 2. above.

Re-authorization of 6 months may be granted when the following criteria are met:

1. A reduction in the frequency of bacterial infections has been demonstrated since initiation of IG therapy, AND
2. IgG trough levels are monitored at least yearly and maintained at or above the lower range of normal for age (when applicable for indication), OR
3. The prescriber will re-evaluate the dose of IG and consider a dose adjustment (when appropriate).

B. Myasthenia Gravis

1. Authorization of 1 month may be granted to members who are prescribed IG for worsening weakness, acute exacerbation, or in preparation for surgery.
 - a. Worsening weakness includes an increase in any of the following symptoms: diplopia, ptosis, blurred vision, difficulty speaking (dysarthria), difficulty swallowing (dysphagia), difficulty chewing, impaired respiratory status, fatigue, and limb weakness. Acute exacerbations include more severe swallowing difficulties and/or respiratory failure
 - b. Pre-operative management (eg, prior to thymectomy)
2. Authorization of 6 months may be granted to members with refractory myasthenia gravis who have tried and failed 2 or more of standard therapies (eg, corticosteroids, azathioprine, cyclosporine, mycophenolate mofetil, rituximab).

C. Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

1. Initial authorization of 3 months may be granted when the following criteria are met:
 - a. Disease course is progressive or relapsing/remitting for 2 months or longer
 - b. Moderate to severe functional disability
 - c. The diagnosis was confirmed by electrodiagnostic studies and the evaluation of cerebrospinal fluid (CSF)
2. Re-authorization of 6 months may be granted when the following criteria are met:
 - a. Significant improvement in disability and maintenance of improvement since initiation of IG therapy
 - b. IG is being used at the lowest effective dose and frequency

D. Dermatomyositis or Polymyositis

1. Initial authorization of 3 months may be granted when the following criteria are met:
 - a. Member has at least 4 of the following:
 - i. Proximal muscle weakness (upper or lower extremity and trunk)
 - ii. Elevated serum creatine kinase (CK) or aldolase level
 - iii. Muscle pain on grasping or spontaneous pain
 - iv. Myogenic changes on EMG (short-duration, polyphasic motor unit potentials with spontaneous fibrillation potentials)
 - v. Positive anti-Jo-1 (histidyl tRNA synthetase) antibody
 - vi. Non-destructive arthritis or arthralgias
 - vii. Systemic inflammatory signs (fever: more than 37°C at axilla, elevated serum CRP level or accelerated ESR of more than 20 mm/h by the Westergren method,
 - viii. Pathological findings compatible with inflammatory myositis (inflammatory infiltration of skeletal evidence of active regeneration may be seen), and
 - b. Standard first-line treatments (corticosteroids) and second-line treatments (immunosuppressants) have been tried but were unsuccessful or not tolerated, or
 - c. Member is unable to receive standard first-line and second-line therapy because of a contraindication or other clinical reason.
2. Re-authorization of 6 months may be granted when the following criterion is met:
 - a. Significant improvement in disability and maintenance of improvement since initiation of IG therapy

E. Idiopathic Thrombocytopenic Purpura (Immune Thrombocytopenia)

1. Newly diagnosed ITP (diagnosed within the past 3 months) or initial therapy: authorization of 1 month may be granted when the following criteria are met:
 - a. Children (< 18 years of age)
 - i. Significant bleeding symptoms (mucosal bleeding or other moderate/severe bleeding) or
 - ii. High risk for bleeding* (see Appendix B), or
 - iii. Rapid increase in platelets is required* (eg, surgery or procedure)

- b. Adults (≥ 18 years of age)
 - i. Platelet count $< 30,000/\text{mcL}$, or
 - ii. Platelet count $< 50,000/\text{mcL}$ and significant bleeding symptoms, high risk for bleeding or rapid increase in platelets is required*, and
 - iii. Corticosteroid therapy is contraindicated and IG will be used alone or IG will be used in combination with corticosteroid therapy
 2. Chronic/persistent ITP (≥ 3 months from diagnosis) or ITP unresponsive to first-line therapy: authorization of 6 months may be granted when the following criteria are met:
 - a. Platelet count $< 30,000/\text{mcL}$, or
 - b. Platelet count $< 50,000/\text{mcL}$ and significant bleeding symptoms, high risk for bleeding* or rapid increase in platelets is required*, and
 - c. Relapse after previous response to IG or inadequate response/intolerance/contraindication to corticosteroid or anti-D therapy
 3. Adults with refractory ITP after splenectomy: authorization of 6 months may be granted when either of the following criteria is met:
 - a. Platelet count $< 30,000/\text{mcL}$, or
 - b. Significant bleeding symptoms
 4. ITP in pregnant women: authorization through delivery may be granted to pregnant women with ITP.

* The member's risk factor(s) for bleeding (see Appendix B) or reason requiring a rapid increase in platelets must be provided.

F. B-cell Chronic Lymphocytic Leukemia (CLL)

1. Initial authorization of 6 months may be granted when all of the following criteria are met:
 - a. IG is prescribed for prophylaxis of bacterial infections.
 - b. Member has a history of recurrent sinopulmonary infections requiring intravenous antibiotics or hospitalization.
 - c. Member has a pretreatment serum IgG level $< 500 \text{ mg/dL}$.
2. Re-authorization of 6 months may be granted when a reduction in the frequency of bacterial infections has been demonstrated since initiation of IG therapy.

G. Prophylaxis of Bacterial Infections in HIV-Infected Pediatric Patients

1. Initial authorization of up to 6 months may be granted to pediatric members with HIV infection when any of the following criteria are met:
 - a. IG is prescribed for primary prophylaxis of bacterial infections and pretreatment serum IgG $< 400 \text{ mg/dL}$, or
 - b. IG is prescribed for secondary prophylaxis of bacterial infections for members with a history of recurrent bacterial infections (> 2 serious bacterial infections in a 1-year period), or
 - c. Member has failed to form antibodies to common antigens, such as measles, pneumococcal, and/or Haemophilus influenzae type b vaccine, or
 - d. Member lives in an area where measles is highly prevalent and who have not developed an antibody response after two doses of measles, mumps, and rubella virus vaccine live, or
 - e. Member has been exposed to measles and request is for a single dose, or
 - f. Member has chronic bronchiectasis that is suboptimally responsive to antimicrobial and pulmonary therapy
2. Re-authorization of 6 months may be granted when a reduction in the frequency of bacterial infections has been demonstrated since initiation of IG therapy.

H. Prophylaxis of Bacterial Infections in BMT/HSCT Recipients

1. Initial authorization of 6 months may be granted to members who are BMT/HSCT recipients when the following criteria are met:

- a. IG is prescribed for prophylaxis of bacterial infections.
- b. Either of the following:
 - i. IG is requested within the first 100 days post-transplant.
 - ii. Member has a pretreatment serum IgG < 400 mg/dL.
2. Re-authorization of 6 months may be granted when a reduction in the frequency of bacterial infections has been demonstrated since initiation of IG therapy.

I. Multifocal Motor Neuropathy (MMN)

1. Initial authorization of 3 months may be granted when the following criteria are met:
 - a. Member experienced progressive, multifocal, asymmetrical weakness without objective sensory loss in 2 or more nerves for at least 1 month
 - b. The diagnosis was confirmed by electrodiagnostic studies
2. Re-authorization of 6 months may be granted when significant improvement in disability and maintenance of improvement have occurred since initiation of IG therapy

J. Guillain-Barre Syndrome (GBS)

Authorization of 2 months total may be granted for GBS when the following criteria are met:

1. Member has severe disease with significant weakness (eg inability to stand or walk without aid, respiratory weakness)
2. Onset of neurologic symptoms occurred less than 4 weeks from the anticipated start of therapy

K. Lambert-Eaton Myasthenic Syndrome (LEMS)

1. Initial authorization of 6 months may be granted for LEMS when the following criteria are met:
 - a. Diagnosis has been confirmed by either of the following:
 - i. Neurophysiology studies (e.g., electromyography)
 - ii. A positive anti- P/Q type voltage-gated calcium channel antibody test
 - b. Anticholinesterases (eg pyridostigmine) and amifampridine (eg 3,4-diaminopyridine phosphate, Firdapse) have been tried but were unsuccessful or not tolerated
 - c. Weakness is severe or there is difficulty with venous access for plasmapheresis
2. Re-authorization of 6 months may be granted when member is responding to therapy (i.e., there is stability or improvement in symptoms relative to the natural course of LEMS).

L. Kawasaki Syndrome

Authorization of 1 month may be granted for pediatric members with Kawasaki syndrome.

M. Fetal/Neonatal Alloimmune Thrombocytopenia (F/NAIT)

Authorization of 6 months may be granted for treatment of F/NAIT.

N. Parvovirus B19-induced Pure Red Cell Aplasia (PRCA)

Authorization of 6 months may be granted for severe, refractory anemia associated with bone marrow suppression, with parvovirus B19 viremia.

O. Stiff-person Syndrome

Authorization of 6 months may be granted for stiff-person syndrome when the following criteria are met:

1. Diagnosis has been confirmed by anti-glutamic acid decarboxylase (GAD) antibody testing
2. Member had an inadequate response to first-line treatment (benzodiazepines and/or baclofen)

P. Management of immune checkpoint inhibitor-related nervous system adverse events

Authorization of 1 month may be granted for management of immune checkpoint-inhibitor toxicities when all of the following criteria are met:

1. Member has experienced a moderate or severe adverse event to a PD-1 or PD-L1 inhibitor (eg, pembrolizumab, nivolumab, atezolizumab, avelumab, durvalumab)

2. The offending medication has been held or discontinued
3. Member experienced one or more of the following nervous system adverse events: pneumonitis, myasthenia gravis, peripheral neuropathy, encephalitis, transverse myelitis, or severe inflammatory arthritis

Q. Acquired Red Cell Aplasia

Authorization of 6 months may be granted for acquired red cell aplasia.

R. Acute Disseminated Encephalomyelitis

Authorization of 6 months may be granted for acute disseminated encephalomyelitis in members who have had an insufficient response to intravenous corticosteroid treatment.

S. Autoimmune Mucocutaneous Blistering Disease

Authorization of 6 months may be granted for autoimmune mucocutaneous blistering disease (includes pemphigus vulgaris, pemphigus foliaceus, bullous pemphigoid, mucous membrane pemphigoid, and epidermolysis bullosa acquisita) when the following criteria are met:

1. Diagnosis has been proven by biopsy and confirmed by pathology report, and
2. Condition is rapidly progressing, extensive or debilitating, and
3. Member has failed or experienced significant complications (eg diabetes, steroid-induced osteoporosis) from standard treatment (corticosteroids, immunosuppressive agents).

T. Autoimmune Hemolytic Anemia

Authorization of 6 months may be granted for warm-type autoimmune hemolytic anemia in members who do not respond or have a contraindication to corticosteroids or splenectomy.

U. Autoimmune Neutropenia

Authorization of 6 months may be granted for autoimmune neutropenia where treatment with G-CSF (granulocyte colony stimulating factor) is not appropriate.

V. Birdshot Retinochoroidopathy

Authorization of 6 months may be granted for birdshot (vitiliginous) retinochoroidopathy that is not responsive to immunosuppressives (eg corticosteroids, cyclosporine).

W. BK Virus Associated Nephropathy

Authorization of 6 months may be granted for BK virus associated nephropathy.

X. Churg-Strauss Syndrome

Authorization of 6 months may be granted for severe, active Churg-Strauss syndrome as adjunctive therapy for members who have experienced failure, intolerance, or are contraindicated to other interventions.

Y. Enteroviral Meningoencephalitis

Authorization of 6 months may be granted for severe cases of enteroviral meningoencephalitis.

Z. Hematophagocytic Lymphohistiocytosis (HLH) or Macrophage Activation Syndrome (MAS)

Authorization of 6 months may be granted for treatment of hypogammaglobulinemia in HLH or MAS when total IgG is less than 400 mg/dL or two standard deviations below the mean for age.

AA. Hemolytic Disease of Newborn

Authorization of 6 months may be granted for isoimmune hemolytic disease in neonates.

BB. HIV-associated Thrombocytopenia

Authorization of 6 months may be granted for HIV-associated thrombocytopenia when the following criteria are met:

1. Pediatric members with IgG < 400 mg/dL and one of the following:
 - a. 2 or more bacterial infections in a 1-year period despite antibiotic chemoprophylaxis with TMP-SMZ or another active agent, or
 - b. Received 2 doses of measles vaccine and lives in a region with a high prevalence of measles, or
 - c. HIV-associated thrombocytopenia despite anti-retroviral therapy, or
 - d. Chronic bronchiectasis that is suboptimally responsive to antimicrobial and pulmonary therapy, or
 - e. T4 cell count $\geq 200/\text{mm}^3$
2. Adult members with significant bleeding, platelet count < 20,000/mcL, and failure of RhIG in Rh-positive patients

CC. Hyperimmunoglobulinemia E Syndrome

Authorization of 6 months may be granted to treat severe eczema in hyperimmunoglobulinemia E syndrome.

DD. Hypogammaglobulinemia from CAR-T therapy

Authorization of 6 months may be granted for members with IgG < 400 mg/dL receiving treatment with CAR-T therapy (tisagenlecleucel [Kymriah] or axicabtagene ciloleucel [Yescarta]).

EE. Multiple Myeloma

Authorization of 6 months may be granted for multiple myeloma in members who have recurrent, serious infections despite the use of prophylactic antibiotics.

FF. Neonatal Hemochromatosis

Authorization of 6 months may be granted for prophylaxis in members who are pregnant with a history of pregnancy ending in documented neonatal hemochromatosis.

GG. Opsoclonus-myoelonus

Authorization of 6 months may be granted for treatment of either of the following:

1. Paraneoplastic opsoclonus-myoelonus-ataxia associated with neuroblastoma
2. Refractory opsoclonus-myoelonus, as last-resort treatment

HH. Post-transfusion Purpura

Authorization of 1 month may be granted for post-transfusion purpura.

II. Rasmussen Encephalitis

Authorization of 6 months may be granted for Rasmussen encephalitis in members whose symptoms do not improve with anti-epileptic drugs and corticosteroids.

JJ. Renal Transplantation

Authorization of 6 months may be granted for a member undergoing renal transplantation from a live donor with ABO incompatibility or positive cross match.

KK. Secondary Immunosuppression Associated with Major Surgery, Hematological Malignancy, Major Burns, and Collagen-Vascular Diseases

Authorization of 6 months may be granted to prevent or modify recurrent bacterial or viral infections in members with secondary immunosuppression (IgG < 400 mg/dL) associated with major surgery, hematological malignancy, extensive burns, or collagen-vascular disease.

LL. Solid Organ Transplantation

Authorization of 6 months may be granted for solid organ transplantation for allosensitized members.

MM. Toxic Epidermal Necrolysis and Stevens-Johnson Syndrome

Authorization of 1 month may be granted for severe cases of toxic epidermal necrolysis or Stevens-Johnson syndrome.

NN. Toxic Shock Syndrome

Authorization of 1 month may be granted for staphylococcal or streptococcal toxic shock syndrome when the infection is refractory to several hours of aggressive therapy, an undrainable focus is present, or the member has persistent oliguria with pulmonary edema.

OO. Systemic Lupus Erythematosus

Authorization of 6 months may be granted for severe, active SLE in members who have experienced inadequate response, intolerance or have a contraindication to first and second line therapies.

PP. Toxic Necrotizing Fasciitis Due To Group A Streptococcus

Authorization of 1 month may be granted for members with fasciitis due to invasive streptococcal infection.

IV. CONTINUATION OF THERAPY

Authorization may be granted for continuation of therapy when either the following criteria is met:

- A. For conditions with reauthorization criteria listed under section III: Members who are currently receiving IG therapy must meet the applicable reauthorization criteria for the member's condition.
- B. For all other conditions, all members (including new members) must meet initial authorization criteria.

V. APPENDICES

Appendix A: Impaired Antibody Response to Pneumococcal Polysaccharide Vaccine

- Age 2 years and older: impaired antibody response demonstrated to vaccination with a pneumococcal polysaccharide vaccine
- Not established for children less than 2 years of age
- Excludes the therapy initiated in the hospital setting

Appendix B: Examples of Risk Factors for Bleeding (not all inclusive)

- Undergoing a medical or dental procedure where blood loss is anticipated
- Comorbidity (eg, peptic ulcer disease, hypertension)
- Mandated anticoagulation therapy
- Profession or lifestyle predisposes patient to trauma (eg, construction worker, fireman, professional athlete)

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SPECIALTY GUIDELINE MANAGEMENT

IXEMPRA (ixabepilone)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. In combination with capecitabine for the treatment of metastatic or locally advanced breast cancer resistant to treatment with an anthracycline and a taxane, or whose cancer is taxane resistant and for whom further anthracycline therapy is contraindicated
2. Monotherapy for the treatment of metastatic or locally advanced breast cancer in patients whose tumors are resistant or refractory to anthracyclines, taxanes, and capecitabine

B. Compendial Uses

1. Human epidermal growth factor receptor 2 (HER2)-negative recurrent or stage IV (M1) breast cancer
2. HER2-positive recurrent or stage IV (M1) breast cancer in combination with trastuzumab

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: HER2 status testing results

III. CRITERIA FOR INITIAL APPROVAL

Breast Cancer

Authorization of 12 months may be granted for treatment of breast cancer when any of the following criteria are met:

1. Member has human epidermal growth factor receptor 2 (HER2)-negative recurrent or metastatic disease, as a single agent; or
2. Member has human epidermal growth factor receptor 2 (HER2)-positive recurrent or metastatic disease, in combination with trastuzumab; or
3. Ixemptra will be used in combination with capecitabine for the treatment of metastatic or locally advanced disease when the following criteria are met:
 - a. Member has failed an anthracycline and a taxane, or whose cancer is taxane resistant and for whom further anthracycline therapy is contraindicated; and
 - b. Member does not have aspartate aminotransferase (AST) or alanine aminotransferase (ALT) level greater than 2.5 times the upper limit of normal (ULN) or bilirubin greater than 1 time the ULN.

IV. CONTINUATION OF THERAPY

Reference number(s)
1897-A

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for breast cancer who have not experienced disease progression or an unacceptable toxicity.

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SPECIALTY GUIDELINE MANAGEMENT

JAKAFI (ruxolitinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Jakafi is indicated for treatment of intermediate or high-risk myelofibrosis (MF), including primary MF, post-polycythemia vera MF and post-essential thrombocythemia MF in adults.
2. Jakafi is indicated for treatment of polycythemia vera (PV) in adults who have had an inadequate response to or are intolerant of hydroxyurea.
3. Jakafi is indicated for treatment of steroid-refractory acute graft-versus-host disease (GVHD) in adult and pediatric patients 12 years and older.

B. Compendial Uses

1. Symptomatic low-risk or intermediate-risk 1 myelofibrosis
2. Accelerated phase or blast phase myelofibrosis/acute myeloid leukemia
3. Polycythemia vera in patients with inadequate response or loss of response to interferon therapy
4. Pediatric Acute Lymphoblastic Leukemia (ALL)

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
For pediatric acute lymphoblastic leukemia, medical record documentation confirming either a cytokine receptor-like factor 2 (CRLF2) mutation or a mutation associated with activation of the Janus kinase/signal transducers and activators of transcription (JAK/STAT) pathway.

III. CRITERIA FOR INITIAL APPROVAL

A. **Myelofibrosis/Acute Myeloid Leukemia**

Authorization of 12 months may be granted for the treatment of myelofibrosis/acute myeloid leukemia.

B. **Polycythemia Vera**

Authorization of 12 months may be granted for the treatment of polycythemia vera to members who have had an inadequate response or intolerance to hydroxyurea or interferon therapy (such as interferon alfa-2b, peginterferon alfa-2a, or peginterferon alfa-2b).

C. **Steroid-refractory acute or chronic graft versus host-disease (GVHD)**

Authorization of 12 months may be granted for the treatment of steroid-refractory acute or chronic graft versus host-disease (GVHD).

Reference number
1999-A

D. Pediatric Acute Lymphoblastic (Lymphocytic) Leukemia (ALL)

Authorization of 12 months may be granted for the treatment of pediatric acute lymphoblastic (lymphocytic) leukemia for members with either a cytokine receptor-like factor 2 (CRLF2) mutation or a mutation associated with activation of the Janus kinase/signal transducers and activators of transcription (JAK/STAT) pathway.

IV. CONTINUATION OF THERAPY

A. Myelofibrosis/Acute Myeloid Leukemia, Polycythemia Vera, and Steroid-Refractory Acute or Chronic Graft Versus Host-Disease

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have improvement in symptoms and no unacceptable toxicity

B. Pediatric Acute Lymphoblastic (Lymphocytic) Leukemia (ALL)

Authorization of 12 months may be granted for continued treatment in pediatric members requesting reauthorization for ALL who have not experienced disease progression or an unacceptable toxicity.

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10. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Pediatric Acute Lymphoblastic Leukemia. Version 1.2020. https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf. Accessed July 11, 2019.

SPECIALTY GUIDELINE MANAGEMENT

JETREA (ocriplasmin intravitreal injection)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Jetrea is indicated for the treatment of symptomatic vitreomacular adhesion.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Vitromacular adhesion

Authorization of 90 days for a single dose (for each eye) may be granted for treatment of symptomatic vitromacular adhesion.

III. REFERENCES

1. Jetrea [package insert]. Iselin, NJ: Thrombogenics, Inc; May 2017.

SPECIALTY GUIDELINE MANAGEMENT

JEVTANA (cabazitaxel)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Jevtana is indicated in combination with prednisone for the treatment of patients with hormone-refractory metastatic prostate cancer previously treated with a docetaxel-containing treatment regimen.

Compendial Use

Second-line or subsequent treatment with concurrent steroid for castration-resistant distant metastatic disease previously treated with a docetaxel-based regimen or in patients who are not candidates for, or are intolerant of docetaxel.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 6 months may be granted for the treatment of castration resistant metastatic prostate cancer previously treated with a docetaxel-containing regimen or in patients who are not candidates for or who are intolerant to docetaxel.

III. CONTINUATION OF THERAPY

Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced disease progression or an unacceptable toxicity.

IV. REFERENCES

1. Jevtana [package insert]. Bridgewater, NJ: sanofi-aventis; January 2018.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed July 22, 2019.
3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology® Prostate Cancer (Version 2.2019). <http://www.nccn.org>. Accessed July 20, 2019.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

JUBLIA
(efinaconazole topical solution)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

MDC-1
Ref # 1160-A

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Jublia (efinaconazole) topical solution, 10% is an azole antifungal indicated for the topical treatment of onychomycosis of the toenail(s) due to *Trichophyton rubrum* and *Trichophyton mentagrophytes*.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for onychomycosis of the toenail(s) due to *Trichophyton rubrum* or *Trichophyton mentagrophytes*, which has been confirmed with a fungal diagnostic test (e.g., potassium hydroxide [KOH] preparation, fungal culture, or nail biopsy)
- AND**
- The patient has experienced an inadequate treatment response, intolerance, or contraindication to an oral antifungal therapy (e.g., terbinafine, itraconazole)

RATIONALE

These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Jublia (efinaconazole) topical solution, 10% is an azole antifungal indicated for the topical treatment of onychomycosis of the toenail(s) due to *Trichophyton rubrum* and *Trichophyton mentagrophytes*. Jublia is to be applied to affected toenails once daily for 48 weeks, using the integrated flow-through brush applicator. When applying Jublia, the toenail, the toenail folds, toenail bed, hyponychium, and the undersurface of the toenail plate are to be completely covered.

Accurate diagnosis of onychomycosis involves physical and microscopic examination and culture. Only 50% of nail problems are caused by onychomycosis, and clinical diagnosis by physical examination alone can be inaccurate. When onychomycosis is suspected, samples should be taken to conduct diagnostic tests. Samples are then prepared with potassium hydroxide (KOH) solution to be viewed under a microscope to look for the presence of a fungal infection. Once infection is confirmed, cultures should then be performed to identify the organism causing the infection to help select the appropriate treatment regimen.⁵

Systemic antifungals are the most effective treatment for onychomycosis. Antifungals from the azole and allylamine classes are the most widely used oral medications for the treatment of onychomycosis. Terbinafine (Lamisil) is the most effective systemic agent available.⁵ Oral treatment of onychomycosis is the standard of care, however, drug interactions and risk of acute liver injury can limit their use.⁴ Difficulties in formulating topical treatment to penetrate the nail and reach the site of infection in the nail bed has hampered the development and the use of topical agents.⁴ Jublia is the first triazole antifungal for the treatment of onychomycosis. In 2 randomized trials, complete cure rate, defined as no evidence of fungal infection at week 52, was demonstrated in 15.2% to 17.8% of patients receiving efinaconazole (N=1236) compared with 3.3% to 5.5% receiving placebo (N=415) for the treatment of onychomycosis of the toenail. Jublia provided

an effective and well-tolerated treatment and may be the first topical treatment that can be considered a viable alternative to oral treatments.⁴

REFERENCES

1. Jublia [package insert]. Bridgewater, NJ: Valeant Pharmaceuticals; September 2016.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed February 2019.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed February 2019.
4. Elewski BE, Rich P, Pollak R, et al. Efinaconazole 10% solution in the treatment of toenail onychomycosis: Two phase III multicenter randomized, double-blind studies. *J Am Acad Dermatol* 2013;68:600-8.
5. Westerberg, DP, Voyack MJ. Onychomycosis: Current Trends in Diagnosis and Treatment. *American Family Physician* 2013;88(11):762-70.

Written by: UM Development (CT)
 Date Written: 06/2014
 Revised: (MS) 05/2015; (KM) 05/2016; (JH) 04/2017 (no clinical changes); (KC) 04/2018 (no clinical changes), (ME) 02/2019 (no clinical changes)
 Reviewed: Medical Affairs (LMS) 06/2014; (KU) 05/2015; (ME) 05/2016
 External Review: 07/2014, 10/2015, 08/2016, 08/2017, 06/2018, 06/2019

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for onychomycosis of the toenail(s) due to <i>Trichophyton rubrum</i> or <i>Trichophyton mentagrophytes</i> , which has been confirmed with a fungal diagnostic test (e.g., potassium hydroxide [KOH] preparation, fungal culture, or nail biopsy)?	Yes	No
2	Has the patient experienced an inadequate treatment response, intolerance, or contraindication to an oral antifungal therapy (e.g., terbinafine, itraconazole)?	Yes	No

Guidelines for Approval	
Duration of Approval	12 Months
Set 1	
Yes to question(s)	No to question(s)
1	None
2	

Mapping Instructions			
	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions: - You have a specific fungal infection of the toenail(s) - You had a test to confirm your toenail fungus Your request has been denied based on the information we have. [Short Description: No approvable diagnosis, no confirmation of diagnosis]
2.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have tried at least one oral medicine first and it did not work for you or you cannot use it. Your request has been denied based on the information we have. [Short Description: No inadequate response, intolerance, or contraindication to oral antifungals]

SPECIALTY GUIDELINE MANAGEMENT

JUXTAPID (lomitapide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Juxtapid is indicated as an adjunct to a low-fat diet and other lipid-lowering treatments, including LDL apheresis where available, to reduce low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC), apolipoprotein B (apo B), and non-high-density lipoprotein cholesterol (non-HDL-C) in patients with homozygous familial hypercholesterolemia (HoFH).

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of documentation supporting the diagnosis of homozygous familial hypercholesterolemia per Appendix A or B is necessary to initiate the prior authorization review.

III. CRITERIA FOR INITIAL APPROVAL

Homozygous familial hypercholesterolemia (HoFH)

Authorization for 6 months may be granted for members who meet all of the criteria listed below:

- A. Member has a documented diagnosis of HoFH confirmed by genetic analysis or clinical criteria (See Appendices).
- B. Prior to initiation of treatment with Juxtapid, patient is/was receiving a combination lipid-lowering regimen consisting of a high-intensity statin, ezetimibe, and evolocumab (Repatha), unless the member has known LDL-receptor negative mutations in both alleles.
- C. Prior to initiation of treatment with Juxtapid, patient is/was experiencing an inadequate response to such a combination regimen, as demonstrated a treated LDL-C of greater than or equal to 100 mg/dL (or greater than or equal to 70 mg/dL with clinical atherosclerotic cardiovascular disease [ASCVD]), unless the member has known LDL-receptor negative mutations in both alleles.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members (including new members) who meet all initial authorization criteria and have achieved or maintained a LDL-C reduction greater than 20% from the levels immediately prior to initiation of treatment with Juxtapid.

V. APPENDICES

APPENDIX A. Diagnosis of Homozygous Familial Hypercholesterolemia

- Genetic confirmation
 - Mutations in both alleles at LDL receptor, ApoB, PCSK9 or LDL receptor adaptor protein gene locus
- Clinical diagnosis
 - Untreated LDL-C > 500 mg/dL OR unknown untreated LDL-C with treated LDL-C > 300 mg/dL **plus**
 - One of the following:
 - Tendon or cutaneous xanthomas at age 10 or younger
 - Diagnosis of familial hypercholesterolemia (FH) by Simon-Broome Diagnostic Criteria or Dutch Lipid Clinic Network Criteria (See Appendix B) in both parents
 - Evidence of FH in both parents with a history including any of the following:
 - Total cholesterol \geq 310 mg/dL
 - Premature ASCVD (before 55 years in men and 60 years in women)
 - Tendon xanthoma
 - Sudden premature cardiac death

APPENDIX B: Diagnosis of familial hypercholesterolemia (FH)

A diagnosis of FH is made when one of the following diagnostic criteria is met:

- Genetic confirmation
 - An LDL-receptor mutation, familial defective apo B-100, or a PCSK9 gain-of-function mutation
- Simon-Broome Diagnostic Criteria for FH
 - Total cholesterol > 290 mg/dL or LDL-C > 190 mg/dL in patients over 16 years of age or total cholesterol > 260 mg/dL or LDL-C > 155 mg/dL in patients less than 16 years of age and one of the following
 - Tendon xanthomas in the patient, first (parent, sibling or child) or second degree relative (grandparent, uncle or aunt)
 - Family history of myocardial infarction in a first degree relative before the age of 60 or in a second degree relative before the age of 50
 - Total cholesterol greater than 290 mg/dL in an adult first or second degree relative
 - Total cholesterol greater than 260 mg/dL in a child, brother, or sister aged younger than 16 years
- Dutch Lipid Clinic Network Criteria for FH
 - Total score > 5 points

VI. REFERENCES

1. Juxtapid [package insert]. Cambridge, MA: Aegerion Pharmaceuticals, Inc.; August 2017.
2. Nordestgaard BG, Chapman MJ, Humphries SE, et al. Familial hypercholesterolaemia is underdiagnosed and undertreated in the general population: guidance for clinicians to prevent coronary heart disease. Consensus Statement of the European Atherosclerosis Society. *Eur Heart J*. 2013; 34:3478–3490.
3. Cuchel M, Bruckert E, Ginsberg HN, et al. Homozygous familial hypercholesterolaemia: new insights and guidance for clinicians to improve detection and clinical management. A position paper from the Consensus Panel on Familial Hypercholesterolaemia of the European Atherosclerosis Society. *Eur Heart J*. 2014; 35:2146-2157.
4. National Institute for Health and Clinical Excellence (2008). Identification and management of familial hypercholesterolaemia. NICE clinical guideline 71.
5. Cuchel M, Meagher EA, du Toit Theron H, et al. Efficacy and safety of a microsomal triglyceride transfer protein inhibitor in patients with homozygous familial hypercholesterolaemia: a single-arm, open-label, phase 3 study. *Lancet*. 2013; 381:40-46.
6. Goldberg AC, Hopkins PN, Toth PP, et al. Familial hypercholesterolemia: screening, diagnosis and management of pediatric and adult patients. Clinical guidance from the National Lipid Association Expert Panel on Familial Hypercholesterolemia. *J Clin Lipidol*. 2011; 5:S1–S8.

7. Raal JF, Santos RD. Homozygous familial hypercholesterolemia: current perspectives on diagnosis and treatment. *Atherosclerosis*. 2012; 223:262-268.
8. Liposorber System [package insert]. New York, NY: Kaneka Pharma America, LLC. Available at <http://www.liposorber.com/physician/prescribe/prescribe.htm>. Accessed: December 21, 2015.
9. Moriarty PM. LDL-apheresis therapy: current therapeutic practice and potential future use. *Future Lipidol*. 2006; 3:299-308.
10. Bays HE, Jones PH, Orringer CE, et al. National Lipid Annual Summary of Clinical Lipidology 2016. *J Clin Lipidol* 2016; 10:S1-S43.
11. Lloyd-Jones DM, Morris PB, Ballantyne CM, Birtcher KK, Daly DD Jr., DePalma SM, Minissian MB, Orringer CE, Smith SC Jr. 2017 focused update of the 2016 ACC expert consensus decision pathway on the role of non-statin therapies for LDL-cholesterol lowering in the management of atherosclerotic cardiovascular disease risk: a report of the American College of Cardiology Task Force on Clinical Expert Consensus Documents. *J Am Coll Cardiol* 2017;70:1785–822.

SPECIALTY GUIDELINE MANAGEMENT

JYNARQUE (tolvaptan)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Jynarque is indicated to slow kidney function decline in adults at risk of rapidly progressing autosomal dominant polycystic kidney disease (ADPKD).

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of autosomal dominant polycystic kidney disease (ADPKD) when all of the following criteria are met:

- A. Diagnosis of autosomal dominant polycystic kidney disease has been confirmed by ultrasonography, computed tomography (CT), magnetic resonance imaging (MRI) or genetic testing.
- B. The member has or is at risk for rapidly progressing disease as confirmed by any of the following:
 1. An annual estimated glomerular filtration rate (eGFR) decline of at least 5 mL/min/1.73 m² in 1 year and/or eGFR decline of at least 2.5 mL/min/1.73 m² per year over a period of 5 years
 2. A total kidney volume (TKV) increase of greater than 5% per year confirmed by at least 3 repeated ultrasound or MRI measurements taken at least 6 months apart
 3. Presence of truncating PKD1 mutation accompanied by early onset of clinical symptoms (e.g., hypertension before 35 years of age, first urological event [macroscopic hematuria, flank pain or cyst infection] before 35 years of age)
 4. Height-adjusted total kidney volume compatible with Mayo class 1C, 1D, or 1E disease
 5. Patient is less than 45 years of age with a kidney length of greater than 16.5 cm as assessed by ultrasound
- C. The member's estimated glomerular filtration rate (eGFR) is greater than or equal to 25 mL/min/1.73m².

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when the member has demonstrated a beneficial response to Jynarque therapy (e.g., slowed kidney function decline, decreased kidney pain) and the member's estimated glomerular filtration rate (eGFR) is greater than or equal to 25 mL/min/1.73m².

IV. REFERENCES

1. Jynarque [package insert]. Rockville, MD: Otsuka America Pharmaceutical, Inc.; February 2019.

Reference number
2572-A

2. Torres VE, Devuyst O, Chapman AB, et al; for the REPRISE Trial Investigators. Rationale and design of a clinical trial investigating tolvaptan safety and efficacy in autosomal dominant polycystic kidney disease. *Am J Nephrol*. 2017;45(3):257-266.
3. Chapman AB, Devuyst O, Eckardt KU, et al. Autosomal-dominant polycystic kidney disease (ADPKD): executive summary from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. *Kidney Int*. 2015;88(1):17-27.
4. Srivastava A, Patel N. Autosomal dominant polycystic kidney disease. *Am Fam Physician*. 2014 Sep 1;90(5):303-307.
5. Gansevoort RT, Arici M, Benzing T, et al. Recommendations for the use of tolvaptan in autosomal dominant polycystic kidney disease: a position statement on behalf of the ERA-EDTA Working Groups on Inherited Kidney Disorders and European Renal Best Practice. *Nephrol Dial Transplant*. 2016;31(3):337-348.

SPECIALTY GUIDELINE MANAGEMENT

KADCYLA (ado-trastuzumab emtansine)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Metastatic Breast Cancer (MBC)

Kadcyla, as a single agent, is indicated for the treatment of patients with human epidermal growth factor receptor 2 (HER2)-positive, metastatic breast cancer who previously received trastuzumab and a taxane, separately or in combination. Patients should have either received prior therapy for metastatic disease, or developed disease recurrence during or within six months of completing adjuvant therapy.

2. Early Breast Cancer (EBC)

Kadcyla, as a single agent, is indicated for the adjuvant treatment of patients with HER2-positive early breast cancer who have residual invasive disease after neoadjuvant taxane and trastuzumab-based treatment.

B. Compendial Uses

1. Single-agent therapy for recurrent or stage IV (M1) HER2-positive breast cancer
2. Non-small cell lung cancer with HER2 mutations

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of human epidermal growth factor receptor 2 (HER2) status is necessary to initiate the prior authorization review.

III. CRITERIA FOR INITIAL APPROVAL

A. **Breast cancer**

1. Authorization of 12 months may be granted for treatment of HER2-positive metastatic or recurrent breast cancer.
2. Authorization of 12 months may be granted for adjuvant treatment of HER2-positive early breast cancer who have residual invasive disease after neoadjuvant taxane and trastuzumab-based treatment.

B. **Non-small cell lung cancer**

Authorization of 12 months may be granted for treatment of lung cancer with HER2 mutations.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy for an indication outlined in section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen. Adjuvant treatment of breast cancer will be approved for a total of 12 months of therapy.

V. REFERENCES

1. Kadcyla [package insert]. South San Francisco, CA: Genentech, Inc.; May 2019.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed August 20, 2019.
3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Breast Cancer. Version 3.2018. https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed January 26, 2019.
4. National Comprehensive Cancer Network. NCCN Clinical practice Guidelines in Oncology: Non-Small Cell Lung Cancer. Version 3.2019 https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed January 28, 2019.

ENHANCED SPECIALTY GUIDELINE MANAGEMENT

KALBITOR (ecallantide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Treatment of acute attacks of hereditary angioedema (HAE) in patients 12 years of age and older

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

- A. C4 levels and C1 inhibitor functional and antigenic protein levels
- B. F12, angiopoietin-1 or plasminogen gene mutation testing, if applicable
- C. Chart notes confirming family history of angioedema, if applicable

III. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of acute hereditary angioedema attacks when the requested medication will not be used in combination with Berinert, Firazyr, or Ruconest and either of the following criteria is met:

- A. Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing:
 - 1. C1 inhibitor (C1-INH) antigenic level is below the lower limit of normal as defined by the laboratory performing the test, or
 - 2. Normal C1-INH antigenic level and a low C1-INH functional level (functional C1-INH less than 50% or C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test).
- B. Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
 - 1. Member has an F12, angiopoietin-1, or plasminogen gene mutation as confirmed by genetic testing, or
 - 2. Member has a documented family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine (e.g., cetirizine) for at least one month.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy when all of the following criteria are met:

- A. Member meets the criteria for initial approval.
- B. Member has experienced reduction in severity and/or duration of attacks when they use the requested medication to treat an acute attack.

V. REFERENCES

1. Kalbitor [package insert]. Burlington, MA: Dyax Corp.; March 2015.
2. Bowen T, Cicardi M, Farkas H, et al. 2010 International consensus algorithm for the diagnosis, therapy, and management of hereditary angioedema. *Allergy Asthma Clin Immunol*. 2010;6(1):24.
3. Cicardi M, Bork K, Caballero T, et al. Hereditary Angioedema International Working Group. Evidence-based recommendations for the therapeutic management of angioedema owing to hereditary C1 inhibitor deficiency: consensus report of an International Working Group. *Allergy*. 2012;67:147-157.
4. Zuraw BL, Banerji A, Bernstein JA, et al. US Hereditary Angioedema Association Medical Advisory Board 2013 recommendations for the management of hereditary angioedema due to C1 inhibitor deficiency. *J Allergy Clin Immunol: In Practice*. 2013; 1(5): 458-467.
5. Zuraw BL, Bork K, Binkley KE, et al. Hereditary angioedema with normal C1 inhibitor function: consensus of an international expert panel. *Allergy Asthma Proc*. 2012; 33(6):S145-S156.
6. Maurer M, Magerl M, Ansotegui I, et al. The international WAO/EAACI guideline for the management of hereditary angioedema – the 2017 revision and update. *Allergy*. 2018;00:1-22.
7. Lang DM, Aberer W, Bernstein JA, et al. International consensus on hereditary and acquired angioedema. *Ann Allergy Asthma Immunol*. 2012; 109:395-202.
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QUANTITY LIMIT PRIOR AUTHORIZATION CRITERIA

BRAND NAME KALETRA
(generic) (lopinavir/ritonavir)

Status: CVS Caremark Criteria
Type: Quantity Limit; Post Limit Prior Authorization

COVID19
Ref # 3695-M

FDA APPROVED INDICATION¹

Kaletra is indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and pediatric patients (14 days and older).

Compendial Use²

Coronavirus disease 2019 (COVID-19)

INITIAL STEP THERAPY

- If the patient has an ICD diagnosis code for human immunodeficiency virus (HIV), then the requested drug will be paid under that prescription benefit and quantity limits will not apply.
- If the patient has filled a prescription for at least a 30 day supply of Kaletra within the past 180 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit and quantity limits will not apply.

If the patient does not meet the above initial step therapy criteria, then initial quantity limits will apply (see initial quantity limit chart below).

INITIAL QUANTITY LIMIT**

LIMIT CRITERIA

Drug	2 Month Limit*	3 Month Limit*
Kaletra 200-50 mg	56 tablets / 50 days	Does Not Apply
Kaletra 100-25 mg	112 tablets / 50 days	Does Not Apply
Kaletra 400-100 mg / 5 mL oral solution	160 mL / 50 days	Does Not Apply

*The duration of 50 days is used for a 60-day fill period.

****If the patient is requesting more than the initial quantity limit supply, then the claim will reject with a message indicating that the patient can receive a quantity sufficient to treat COVID-19 and then prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.**

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the treatment of human immunodeficiency virus
[Note: Initial quantity limits allow for a sufficient quantity of the requested drug to treat coronavirus disease 2019 (COVID-19). A maximum of 112 tablets of 100-25mg, 56 tablets of 200-50mg, or 160 mL of 400-100mg/5mL oral solution is available without prior authorization.]

RATIONALE

If the patient does not meet the above initial step therapy criteria, then initial quantity limits will apply. Kaletra is available as 100-25 mg tablets, 200-50 mg tablets, and 400-100 mg/5mL oral solution. The dosing used for coronavirus disease 2019 (COVID-19) is 400 mg/100 mg twice daily.² Therefore, the quantity limit is set at 112 tablets of the 100-25 mg strength, 56 tablets of the 200-50 mg strength, and 160 mL of the 400-100 mg/5mL oral solution.

If initial quantity limits are exceeded, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

Since the initial quantity limits are sufficient to treat COVID-19, the post limit criteria will not approve additional quantities for this indication.

REFERENCES

1. Kaletra [package insert]. North Chicago, IL: AbbVie, Inc.; December 2019.
2. Clinical Pharmacology [database online]. Tampa, FL: Elsevier Inc. Copyright 2020.
<https://www.clinicalkey.com/pharmacology/>. Accessed March 2020

Written: Specialty Clinical Development (CN) 03/2020
Revised:
Reviewed: CDPR / CHART 03/19/2020
External Review: 03/2020

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for the treatment of human immunodeficiency virus (HIV)? [Note: Initial quantity limits allow for a sufficient quantity of the requested drug to treat coronavirus disease 2019 (COVID-19). A maximum of 112 tablets of 100-25mg, 56 tablets of 200-50mg, or 160 mL of 400-100mg/5mL solution is available without prior authorization.]	Yes	No
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Mapping Instructions

	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Approve, 12 months	Deny	<p>You do not meet the requirements of your plan. Your plan covers a sufficient quantity of the requested drug to treat coronavirus disease 2019 (COVID-19) up to a maximum of:</p> <ul style="list-style-type: none">- 112 tablets of Kaletra 100-25mg- 56 tablets of Kaletra 200-50mg- 160 mL of Kaletra 400-100mg/5mL <p>Your plan covers additional quantities of this drug when it is being used to treat human immunodeficiency virus.</p> <p>Your request has been denied based on the information we have.</p> <p>[Short Description: COVID-19]</p>

SPECIALTY GUIDELINE MANAGEMENT

KALYDECO (ivacaftor)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Kalydeco is a cystic fibrosis transmembrane conductance regulator (CFTR) potentiator indicated for the treatment of cystic fibrosis (CF) in patients age 6 months and older who have one mutation in the *CFTR* gene that is responsive to ivacaftor potentiation based on clinical and/or in vitro assay data.

If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of CFTR mutation followed by verification with bi-directional sequencing when recommended by the mutation test instructions for use.

All other indications are considered experimental/investigational and are not medically necessary.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review: genetic testing report confirming the presence of the appropriate *CFTR* gene mutation.

III. CRITERIA FOR INITIAL APPROVAL

Cystic Fibrosis

Authorization of 12 months may be granted for treatment of cystic fibrosis when all of the following criteria are met:

- A. Genetic testing was conducted to detect a mutation in the *CFTR* gene.
- B. The member has one of the following mutations in the *CFTR* gene: A455E, A1067T, D110E, D110H, D579G, D1152H, D1270N, E56K, E193K, F1052V, F1074L, G178R, G551D, G551S, G1069R, G1244E, G1349D, K1060T, L206W, P67L, R74W, R117C, R117H, R347H, R352Q, R1070Q, R1070W, S549N, S549R, S945L, S977F, S1251N, S1255P, 711+3A→G, E831X, 2789+5G→A, 3272-26A→G, 3849+10kbC→T.
- C. The member is at least 6 months of age.
- D. Kalydeco will not be used in combination with Orkambi or Symdeko.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who are experiencing benefit from therapy as evidenced by disease stability or disease improvement (e.g., improvement in FEV1 from baseline).

Reference number(s)
1884-A

V. REFERENCES

1. Kalydeco [package insert]. Boston, MA: Vertex Pharmaceuticals Inc.; April 2019.
2. Mogayzel PJ, Naureckas ET, Robinson KA, et al. Cystic fibrosis pulmonary guidelines. Chronic medications for maintenance of lung health. *Am J Respir Crit Care Med*. 2013;187:680-689.

SPECIALTY GUIDELINE MANAGEMENT

KANUMA (sebelipase alfa)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Kanuma is indicated for the treatment of patients with a diagnosis of Lysosomal Acid Lipase (LAL) deficiency.

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: lysosomal acid lipase enzyme assay or genetic testing results supporting diagnosis.

III. CRITERIA FOR INITIAL APPROVAL

Lysosomal acid lipase (LAL) deficiency

Authorization of 12 months may be granted for treatment of LAL deficiency when both of the following criteria are met:

- A. Diagnosis of LAL deficiency was confirmed by enzyme assay demonstrating a deficiency of lysosomal acid lipase enzyme activity or by genetic testing; AND
- B. Member has alanine aminotransferase level (ALT) ≥ 1.5 times the upper limit of normal (based on the age- and gender-specific normal ranges) on two consecutive ALT measurements obtained at least one week apart.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for lysosomal acid lipase (LAL) deficiency who are responding to therapy (e.g., improvement, stabilization, or slowing of disease progression for weight-for-age z-score if exhibiting growth failure, low-density lipoprotein [LDL], high-density lipoprotein [HDL], triglycerides, or alanine aminotransferase [ALT]).

V. REFERENCES

1. Kanuma [package insert]. Cheshire, CT: Alexion Pharmaceuticals Inc.; December 2015.
2. Burton BK, Balwani, M, Feillet F, et al. A Phase 3 Trial of Sebelipase Alfa in Lysosomal Acid Lipase Deficiency. N Engl J Med.2015;373:1010-20.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

KERYDIN
(tavaborole topical solution)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

MDC-1
Ref # 1169-A

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Kerydin (tavaborole) topical solution, 5% is an oxaborole antifungal indicated for the treatment of onychomycosis of the toenails due to *Trichophyton rubrum* or *Trichophyton mentagrophytes*.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for onychomycosis of the toenail(s) due to *Trichophyton rubrum* or *Trichophyton mentagrophytes*, which has been confirmed with a fungal diagnostic test (e.g., potassium hydroxide [KOH] preparation, fungal culture, or nail biopsy)
- AND**
- The patient has experienced an inadequate treatment response, intolerance, or contraindication to an oral antifungal therapy (e.g., terbinafine, itraconazole)

RATIONALE

These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Kerydin (tavaborole) topical solution, 5% is an oxaborole antifungal indicated for the treatment of onychomycosis of the toenails due to *Trichophyton rubrum* or *Trichophyton mentagrophytes*. Kerydin is to be applied to affected toenails once daily for 48 weeks. Kerydin should be applied to the entire toenail surface and under the tip of each toenail being treated. Kerydin is for topical use only and not for oral, ophthalmic, or intravaginal use.¹

Accurate diagnosis of onychomycosis involves physical and microscopic examination and culture. Only 50% of nail problems are caused by onychomycosis, and clinical diagnosis by physical examination alone can be inaccurate. When onychomycosis is suspected, samples should be taken to conduct diagnostic tests. Samples are then prepared with potassium hydroxide (KOH) solution to be viewed under a microscope to look for the presence of a fungal infection. Once infection is confirmed, cultures should then be performed to identify the organism causing the infection to help select the appropriate treatment regimen.⁵

Systemic antifungals are the most effective treatment for onychomycosis. Antifungals from the azole and allylamine classes are the most widely used oral medications for the treatment of onychomycosis. Terbinafine (Lamisil) is the most effective systemic agent available.⁵ Oral treatment of onychomycosis is the standard of care, however, drug interactions and risk of acute liver injury can limit their use.⁴ Difficulties in formulating topical treatment to penetrate the nail and reach the site of infection in the nail bed has hampered the development and the use of topical agents.⁴ In 2 randomized trials, complete cure rate, defined as no evidence of fungal infection at week 52, was demonstrated in 6.5% and 9.1% of patients receiving tavaborole compared with 0.5% and 1.5% receiving placebo for the treatment of onychomycosis of the toenail.¹

REFERENCES

1. Kerydin [package insert]. Palo Alto, CA. Anacor Pharmaceuticals; August 2018.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed February 2019.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed February 2019.
4. Elewski BE, Rich P, Pollak R, et al. Efinaconazole 10% solution in the treatment of toenail onychomycosis: Two phase III multicenter randomized, double-blind studies. *J Am Acad Dermatol* 2013;68:600-8.
5. Westerberg, DP, Voyack MJ. Onychomycosis: Current Trends in Diagnosis and Treatment. *American Family Physician* 2013;88(11):762-70.

Written by: UM Development (PL/WW)
 Date Written: 07/2014
 Revised: (MS) 05/2015; (KM) 05/2016; (JH) 04/2017 (no clinical changes); (KC) 04/2018; (ME) 02/2019 (no clinical changes)
 Reviewed: Medical Affairs (LMS) 07/2014; (KU) 05/2015; (ME) 05/2016
 External Review: 07/2014, 10/2015, 08/2016, 08/2017, 06/2018, 06/2019

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for onychomycosis of the toenail(s) due to <i>Trichophyton rubrum</i> or <i>Trichophyton mentagrophytes</i> , which has been confirmed with a fungal diagnostic test (e.g., potassium hydroxide [KOH] preparation, fungal culture, or nail biopsy)?	Yes	No
2	Has the patient experienced an inadequate treatment response, intolerance, or contraindication to an oral antifungal therapy (e.g., terbinafine, itraconazole)?	Yes	No

Guidelines for Approval	
Duration of Approval	12 Months
Set 1	
Yes to question(s)	No to question(s)
1	None
2	

Mapping Instructions			
	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions: - You have a specific fungal infection of the toenail(s) - You had a test to confirm your toenail fungus Your request has been denied based on the information we have. [Short Description: No approvable diagnosis, no confirmation of diagnosis]
2.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have tried at least one oral medicine first and it did not work for you or you cannot use it. Your request has been denied based on the information we have. [Short Description: No inadequate response, intolerance, or contraindication to an oral antifungal]

SPECIALTY GUIDELINE MANAGEMENT

KEVEYIS (dichlorphenamide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Treatment of primary hyperkalemic periodic paralysis, primary hypokalemic periodic paralysis, and related variants.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Primary Hypokalemic Periodic Paralysis

Authorization of 60 days may be granted to members who are initiating Keveyis therapy when the following criteria is met:

1. The diagnosis was supported by at least one of the following:
 - a. Genetic test results or
 - b. Patient has a family history of primary hypokalemic periodic paralysis, or
 - c. Patient's attacks are associated with hypokalemia AND both Andersen-Tawil syndrome and thyrotoxic periodic paralysis have been ruled out.
2. Trial with suboptimal response to treatment with acetazolamide

B. Primary Hyperkalemic Periodic Paralysis

Authorization of 60 days may be granted to members who are initiating Keveyis therapy when the following criteria is met:

1. The diagnosis was supported by at least one of the following:
 - a. Genetic test results, or
 - b. Patient has a family history of primary hyperkalemic periodic paralysis, or
 - c. Patient's attacks are associated with hyperkalemia AND Andersen-Tawil syndrome has been ruled out.
2. Trial with suboptimal response to treatment with acetazolamide

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted to members who have demonstrated a response to Keveyis therapy as demonstrated by an improvement in their condition (e.g. decrease in the number or severity of attacks).

IV. REFERENCE

1. Keveyis [package insert]. Feasterville-Trevose, PA: Strongbridge Biopharma; January 2017.
2. Micromedex Solutions [electronic version]. Truven Health Analytics, Greenwood Village, Colorado, USA. Available at: <http://www.micromedexsolutions.com/>. Accessed December 14, 2018.
3. Lexicomp Online®, Lexi-Drugs®, Hudson, Ohio: Wolters Kluwer Clinical Drug Information, Inc.; <http://online.lexi.com> Accessed December 14, 2018.
4. Clinical Pharmacology [database online]. Atlanta, GA: Elsevier, Inc.; 2018. <https://www.clinicalkey.com/pharmacology/> Accessed December 14, 2018
5. Lexicomp Online®, AHFS® Drug Information, Hudson, Ohio: Wolters Kluwer Clinical Drug Information, Inc.; <http://online.lexi.com> Accessed December 14, 2018.
6. Levitt JO. Practical aspects in the management of hypokalemic periodic paralysis. *Journal of Translational Medicine* 2008; 6:18.
7. Charles G, Zheng C, Lehmann-Horn F, et al. Characterization of hyperkalemic periodic paralysis: a survey of genetically diagnosed individuals. *JNeurol* 2013; 260:2606-2613.
8. Statland, Jeffrey & Fontaine, Bertrand & G. Hanna, Michael & Johnson, Nicholas & T. Kissel, John & A. Sansone, Valeria & Shieh, Perry & N. Tawil, Rabi & Trivedi, Jaya & Cannon, Stephen & C. Griggs, Robert. (2017). A Review of the Diagnosis and Treatment of Periodic Paralysis. *Muscle & Nerve* 10.1002/mus.26009.

SPECIALTY GUIDELINE MANAGEMENT

KEVZARA (sarilumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Kevzara is indicated for treatment of adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response or intolerance to one or more disease-modifying antirheumatic drugs (DMARDs)

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Moderately to severely active rheumatoid arthritis (RA)

- A. Authorization of 12 months may be granted for members who have previously received a biologic or targeted synthetic DMARD (e.g., Rinvoq, Xeljanz) indicated for moderately to severely active rheumatoid arthritis.
- B. Authorization of 12 months may be granted for treatment of moderately to severely active RA when any of the following criteria is met:
 1. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to 20 mg/week).
 2. Member has an intolerance or contraindication to methotrexate (see Appendix).

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who are using Kevzara for an indication outlined in section II and who achieve or maintain positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

For all indications: Member has had a documented negative TB test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic DMARDs or targeted synthetic DMARDs (e.g., Xeljanz), and repeated yearly for members with risk factors** for TB that are continuing therapy with biologics.

* If the screening testing for TB is positive, there must be documentation of further testing to confirm there is no active disease. Do not administer sarilumab to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of sarilumab.

Reference number
1957-A

** Risk factors for TB include: Persons with close contact to people with infectious TB disease; persons who have recently immigrated from areas of the world with high rates of TB (e.g., Africa, Asia, Eastern Europe, Latin America, Russia); children less than 5 years of age who have a positive TB test; groups with high rates of TB transmission (e.g., homeless persons, injection drug users, persons with HIV infection); persons who work or reside with people who are at an increased risk for active TB (e.g., hospitals, long-term care facilities, correctional facilities, homeless shelters).

For all indications: Members cannot use Kevzara concomitantly with any other biologic DMARD or targeted synthetic DMARD.

V. APPENDIX: Examples of Contraindications to Methotrexate

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
4. Elevated liver transaminases
5. History of intolerance or adverse event
6. Hypersensitivity
7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
8. Myelodysplasia
9. Pregnancy or planning pregnancy
10. Renal impairment
11. Significant drug interaction

VI. REFERENCES

1. Kevzara [package insert]. Bridgewater, NJ: Sanofi-aventis, U.S. LLC /Regeneron Pharmaceuticals, Inc.; April 2018.
2. Genovese MC, Fleischmann R, Kivitz AJ, et al. Sarilumab plus methotrexate in patients with active rheumatoid arthritis and inadequate response to methotrexate: results of a phase III study. *Arthritis Rheumatol*. June 2015;67(6):1424-37.
3. Strand V, Reaney M, Chen C, et al. Sarilumab improves patient-reported outcomes in rheumatoid arthritis patients with inadequate response/intolerance to tumour necrosis factor inhibitors. *RMD Open*. 2017; 3:e000416. doi: 10.1136/rmdopen-2016-000416.
4. Tuberculosis (TB). TB risk factors. Centers for Disease Control and Prevention. Retrieved on 21 June 2019 from: <https://www.cdc.gov/tb/topic/basics/risk.htm>.

SPECIALTY GUIDELINE MANAGEMENT

KEYTRUDA (pembrolizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Melanoma
 - i. Keytruda (pembrolizumab) is indicated for the treatment of patients with unresectable or metastatic melanoma.
 - ii. Keytruda is indicated for the adjuvant treatment of patients with melanoma with involvement of lymph node(s) following complete resection.
2. Non-Small Cell Lung Cancer
 - i. Keytruda, in combination with pemetrexed and platinum chemotherapy, is indicated for the first-line treatment of patients with metastatic nonsquamous non-small cell lung cancer (NSCLC), with no EGFR or ALK genomic tumor aberrations.
 - ii. Keytruda, in combination with carboplatin and either paclitaxel or paclitaxel protein-bound, is indicated for the first-line treatment of patients with metastatic squamous NSCLC.
 - iii. Keytruda, as a single agent, is indicated for the first-line treatment of patients with NSCLC expressing PD-L1 [Tumor Proportion Score (TPS) $\geq 1\%$] as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations, and is:
 - a. stage III where patients are not candidates for surgical resection or definitive chemoradiation, or
 - b. metastatic.
 - iv. Keytruda, as a single agent, is indicated for the treatment of patients with metastatic NSCLC whose tumors express PD-L1 (TPS $\geq 1\%$) as determined by an FDA approved test, with disease progression on or after platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Keytruda.
3. Small Cell Lung Cancer

Keytruda is indicated for the treatment of patients with metastatic small cell lung cancer (SCLC) with disease progression on or after platinum-based chemotherapy and at least one other prior line of therapy.
4. Head and Neck Squamous Cell Cancer
 - i. Keytruda, in combination with platinum and fluorouracil (FU), is indicated for the first-line treatment of patients with metastatic or with unresectable, recurrent head and neck squamous cell carcinoma (HNSCC).
 - ii. Keytruda, as a single agent, is indicated for the first line treatment of patients with metastatic or with unresectable, recurrent HNSCC whose tumors express PD-L1 [Combined Positive Score (CPS) ≥ 1] as determined by an FDA-approved test.

- iii. Keytruda, as a single agent, is indicated for the treatment of patients with recurrent or metastatic HNSCC with disease progression on or after platinum-containing chemotherapy.
- 5. Classical Hodgkin Lymphoma
Keytruda is indicated for the treatment of adult and pediatric patients with refractory classical Hodgkin lymphoma (cHL), or who have relapsed after 3 or more prior lines of therapy.
- 6. Primary Mediastinal Large B-cell Lymphoma
Keytruda is indicated for the treatment of adult and pediatric patients with refractory primary mediastinal large B-cell lymphoma (PMBCL), or who have relapsed after 2 or more prior lines of therapy.

Limitations of Use: Keytruda is not recommended for treatment of patients with PMBCL who require urgent cytoreductive therapy.

- 7. Urothelial Carcinoma
 - i. Keytruda is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma who are not eligible for cisplatin-containing chemotherapy and whose tumors express PD-L1 (CPS ≥ 10) as determined by an FDA-approved test, or in patients who are not eligible for any platinum-containing chemotherapy regardless of PD-L1 status.
 - ii. Keytruda is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.
 - iii. Keytruda is indicated for the treatment of patients with Bacillus Calmette-Guerin (BCG)-unresponsive, high-risk, non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with or without papillary tumors who are ineligible for or have elected not to undergo cystectomy.
- 8. Microsatellite Instability-High Cancer
Keytruda is indicated for the treatment of adult and pediatric patients with unresectable or metastatic, microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR)
 - i. Solid tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options, or
 - ii. Colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan.

Limitations of Use: The safety and effectiveness of Keytruda in pediatric patients with MSI-H central nervous system cancers have not been established.

- 9. Gastric Cancer
Keytruda is indicated for the treatment of patients with recurrent locally advanced or metastatic gastric or gastroesophageal junction adenocarcinoma whose tumors express PD-L1 (CPS ≥ 1) as determined by an FDA-approved test, with disease progression on or after two or more prior lines of therapy including fluoropyrimidine- and platinum-containing chemotherapy and if appropriate, HER2/neu-targeted therapy.
- 10. Esophageal Cancer
Keytruda is indicated for the treatment of patients with recurrent locally advanced or metastatic squamous cell carcinoma of the esophagus whose tumors express PD-L1 (CPS ≥ 10) as determined by an FDA-approved test, with disease progression after one or more prior lines of systemic therapy.
- 11. Cervical Cancer

Keytruda is indicated for the treatment of patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy whose tumor express PD-L1 (CPS ≥ 1) as determined by an FDA-approved test.

12. Hepatocellular Carcinoma

Keytruda is indicated for the treatment of patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib.

13. Merkel Cell Carcinoma

Keytruda is indicated for the treatment of adult and pediatric patients with recurrent locally advanced or metastatic Merkel cell carcinoma (MCC).

14. Renal Cell Carcinoma

Keytruda, in combination with axitinib, is indicated for the first-line treatment of patients with advanced renal cell carcinoma (RCC).

15. Endometrial Carcinoma

Keytruda, in combination with lenvatinib, is indicated for the treatment of patients with advanced endometrial carcinoma that is not MSI-H or dMMR, who have disease progression following prior systemic therapy and are not candidates for curative surgery or radiation.

B. Compendial Uses

1. Cutaneous melanoma
2. Non-small cell lung cancer
3. Head and neck squamous cell cancer
4. Classical Hodgkin Lymphoma
5. Urothelial carcinoma
 - i. Bladder cancer
 - ii. Primary carcinoma of the urethra
 - iii. Upper genitourinary tract tumors
 - iv. Urothelial carcinoma of the prostate
6. Solid tumors
7. Colorectal cancer
8. Malignant pleural mesothelioma
9. Gastric cancer and esophagogastric junction cancer
10. Esophageal cancer
11. Cervical cancer
12. Epithelial ovarian cancer/fallopian tube cancer/primary peritoneal cancer
13. Uveal melanoma
14. Testicular cancer
15. Endometrial carcinoma
16. Anal carcinoma
17. Central Nervous System (CNS) brain metastases
18. Primary mediastinal large B-cell lymphoma
19. Pancreatic adenocarcinoma
20. Hepatobiliary cancers
21. Vulvar cancer
22. Kidney cancer
23. Thymic carcinoma
24. Mycosis Fungoides/Sézary syndrome
25. T-cell lymphomas
26. Gestational trophoblastic neoplasia

27. Small cell lung cancer
28. Poorly differentiated neuroendocrine carcinoma/large or small cell carcinoma

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

- A. Documentation of programmed death ligand 1 (PD-L1) tumor expression, where applicable.
- B. Documentation of laboratory report confirming MSI-H or mismatch repair deficient (dMMR) tumor status, where applicable.

III. EXCLUSIONS

Coverage will not be provided for members with any of the following exclusions:

- A. Pediatric members with MSI-H central nervous system cancers.
- B. Members who have experienced disease progression while on programmed death receptor-1 (PD-1) or PD-L1 inhibitor therapy.

IV. CRITERIA FOR INITIAL APPROVAL

A. Cutaneous Melanoma

Authorization of 6 months may be granted as a single agent for treatment of cutaneous melanoma in either of the following settings:

1. For unresectable or metastatic disease.
2. Keytruda will be used as adjuvant treatment following complete lymph node resection or complete resection of metastatic disease.

B. Non-small Cell Lung Cancer (NSCLC)

Authorization of 6 months may be granted for treatment of NSCLC in any of the following settings:

1. Treatment of recurrent, advanced or metastatic nonsquamous NSCLC:
 - i. Keytruda will be used following EGFR or ALK therapy if EGFR or ALK positive, AND
 - ii. Keytruda will be used in combination with both of the following:
 - a. Pemetrexed
 - b. Carboplatin or cisplatin.
2. Treatment of recurrent, advanced or metastatic squamous NSCLC:

Keytruda will be used in combination with carboplatin or cisplatin and paclitaxel or paclitaxel protein-bound.
3. Treatment of recurrent, advanced or metastatic NSCLC expressing PD-L1 (TPS $\geq 1\%$):
 - i. Keytruda will be used as a single agent, AND
 - ii. Keytruda will be used following EGFR or ALK therapy if EGFR or ALK positive.
4. Continuation maintenance therapy may be granted in the following settings when tumor response or stable disease is achieved:
 - i. Keytruda will be used in combination with pemetrexed if given first-line as part of a Keytruda/pemetrexed and either cisplatin or carboplatin regimen for recurrent, advanced or metastatic disease for nonsquamous cell histology.
 - ii. Keytruda will be used as a single agent if:
 - a. Keytruda monotherapy was given for first-line recurrent, advanced or metastatic disease for nonsquamous cell histology.

- b. Keytruda was given as monotherapy or as part of a regimen with cisplatin or carboplatin and either paclitaxel or albumin bound paclitaxel for recurrent, advanced or metastatic squamous cell histology.

C. Head and Neck Squamous Cell Cancer

Authorization of 6 months may be granted for treatment of members with head and neck squamous cell carcinoma (HNSCC) when any of the following criteria is met:

1. Keytruda will be used as a single agent for first-line treatment of unresectable, metastatic, or second primary HNSCC in members whose tumors express PD-L1 (CPS ≥ 1).
2. Keytruda will be used as a single agent for subsequent therapy for unresectable, metastatic, or second primary HNSCC (regardless of PD-L1 status).
3. Keytruda will be used in combination with fluorouracil and either carboplatin or cisplatin for the treatment of members with unresectable, metastatic, or second primary HNSCC (regardless of PD-L1 status).

D. Classical Hodgkin Lymphoma

Authorization of 6 months may be granted as a single agent for treatment of classical Hodgkin lymphoma when any of the following criteria is met:

1. Member has refractory disease.
2. Member has relapsed after 2 or more prior lines of therapy or following hematopoietic stem cell transplant.
3. Member has relapsed disease and is transplant-ineligible.

E. Urothelial Carcinoma – Bladder Cancer

Authorization of 6 months may be granted as a single agent for treatment of bladder cancer when any of the following criteria is met:

1. Keytruda will be used as first-line therapy in cisplatin ineligible members whose tumors express PD-L1 (CPS ≥ 10), or in members who are not eligible for any platinum-containing chemotherapy regardless of PD-L1 expression for any of the following:
 - i. Stage II or Stage IIIA disease, if tumor is present following reassessment of tumor status 2-3 months after primary treatment with concurrent chemoradiotherapy.
 - ii. Locally advanced or metastatic disease.
 - iii. Metastatic or local recurrence post-cystectomy.
2. Keytruda will be used as subsequent therapy following platinum-containing chemotherapy for either of the following:
 - i. Locally advanced or metastatic disease.
 - ii. Metastatic or local recurrence post-cystectomy.
3. Keytruda will be used as subsequent therapy for the treatment of members with high-risk, non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) when both of the following criteria are met:
 - i. Disease is Bacillus Calmette-Guerin (BCG)-unresponsive.
 - ii. Member is ineligible for or has elected not to undergo cystectomy.

F. Urothelial Carcinoma – Primary Carcinoma of the Urethra

Authorization of 6 months may be granted as a single agent for treatment of primary carcinoma of the urethra when either of the following criteria is met:

1. Keytruda will be used as first-line therapy for recurrent, locally advanced, or metastatic disease in cisplatin ineligible members whose tumors express PD-L1 (CPS ≥ 10), or in members who are not eligible for any platinum-containing chemotherapy regardless of PD-L1 expression.
2. Keytruda will be used as subsequent therapy for recurrent, locally advanced or metastatic disease following platinum-containing chemotherapy.

G. Urothelial Carcinoma – Upper Genitourinary Tract Tumors or Urothelial Carcinoma of the Prostate

Authorization of 6 months may be granted as a single agent for treatment of upper genitourinary (GU) tract tumors or urothelial carcinoma of the prostate when either of the following criteria is met:

1. Keytruda will be used as first-line therapy for locally advanced or metastatic disease in cisplatin ineligible members whose tumors express PD-L1 (CPS \geq 10), or in members who are not eligible for any platinum-containing chemotherapy regardless of PD-L1 expression.
2. Keytruda will be used as subsequent therapy for locally advanced or metastatic disease following platinum-containing chemotherapy.

H. Solid Tumors

Authorization of 6 months may be granted for treatment of solid tumors in members with unresectable or metastatic, microsatellite instability-high or mismatch repair deficient solid tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options.

I. Colorectal Cancer

Authorization of 6 months may be granted as a single agent for the treatment of colorectal cancer, including small bowel adenocarcinoma, appendiceal carcinoma, and anal adenocarcinoma for microsatellite instability-high or mismatch repair deficient tumors when any of the following criteria is met:

1. Keytruda will be used as primary treatment for unresectable metachronous metastases and previous adjuvant FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin) within the past 12 months.
2. Keytruda will be used as initial therapy for unresectable advanced or metastatic disease who are not appropriate for intensive therapy.
3. Keytruda will be used as subsequent therapy for unresectable advanced or metastatic disease following previous oxaliplatin- irinotecan- and/or fluoropyrimidine-based therapy.

J. Malignant Pleural Mesothelioma

Authorization 6 months may be granted as a single agent for subsequent treatment of malignant pleural mesothelioma.

K. Merkel Cell Carcinoma

Authorization of 6 months may be granted for treatment of Merkel cell carcinoma in members with recurrent locally advanced or metastatic disease.

L. Gastric Cancer and Esophagogastric Junction Cancer

Authorization of 6 months may be granted for treatment of gastric cancer, including esophagogastric junction (EGJ) cancer, in members who are not surgical candidates or have locally advanced, recurrent, or metastatic disease when either of the following criteria is met:

1. Keytruda will be used as second-line or subsequent therapy as a single agent for a tumor with microsatellite instability-high or deficient mismatch repair.
2. Keytruda will be used as third-line or subsequent therapy as a single agent for a PD-L1 positive tumor (CPS \geq 1).

M. Esophageal Cancer

Authorization of 6 months may be granted for treatment of esophageal cancer in members who are not surgical candidates or have for locally advanced, recurrent, or metastatic disease when any of the following conditions are met:

1. Keytruda will be used as second-line or subsequent therapy as a single agent for a tumor with microsatellite instability-high or deficient mismatch repair.
2. Keytruda will be used as second-line therapy for a PD-L1 positive tumor (CPS \geq 10) for squamous cell carcinoma.

3. Keytruda will be used as third-line or subsequent therapy as a single agent for a PD-L1 positive tumor (CPS ≥ 1).

N. Cervical Cancer

Authorization of 6 months may be granted as a single agent for second-line therapy for the treatment of recurrent or metastatic cervical cancer when either of the following criteria is met:

1. Microsatellite instability-high or mismatch repair deficient tumors.
2. Member has experienced disease progression on or after chemotherapy for tumors that express PD-L1 (CPS ≥ 1).

O. Epithelial Ovarian Cancer, Fallopian Tube Cancer, Primary Peritoneal Cancer

Authorization of 6 months may be granted as a single agent for treatment of epithelial ovarian cancer, fallopian tube cancer, and primary peritoneal cancer for recurrent or persistent microsatellite instability-high or mismatch repair deficient tumors.

P. Uveal Melanoma

Authorization of 6 months may be granted as a single agent for treatment of uveal melanoma for distant metastatic disease.

Q. Testicular Cancer

Authorization of 6 months may be granted as a single agent for third-line therapy for treatment of testicular cancer in members with microsatellite instability-high or mismatch repair deficient tumors.

R. Endometrial Carcinoma

Authorization of 6 months may be granted for treatment of endometrial carcinoma when the member meets either of the following criteria:

1. Keytruda will be used for recurrent, metastatic, or high-risk microsatellite instability-high or mismatch repair deficient tumors that have progressed following prior cytotoxic chemotherapy.
2. Keytruda will be used in combination with lenvatinib for advanced endometrial carcinoma that is not microsatellite instability-high or mismatch repair deficient when the member has disease progression following prior systemic therapy and is not a candidate for curative surgery or radiation.

S. Anal Carcinoma

Authorization of 6 months may be granted as a single agent for treatment of anal carcinoma for metastatic disease as second-line or subsequent therapy.

T. CNS Brain Metastases

Authorization of 6 months may be granted as a single agent for treatment of CNS brain metastases in members with melanoma or PD-L1 positive non-small cell lung cancer.

U. Primary Mediastinal Large B-Cell Lymphoma

Authorization of 6 months may be granted for treatment of primary mediastinal large B-cell lymphoma in members with relapsed or refractory disease.

V. Pancreatic Adenocarcinoma

Authorization of 6 months may be granted as a single agent for treatment of pancreatic adenocarcinoma in members with microsatellite instability-high or mismatch repair deficient tumors in either of the following settings:

1. Keytruda will be used as subsequent therapy for locally advanced or metastatic disease.
2. For local recurrence in the pancreatic operative bed after resection.

W. Hepatobiliary Cancers

Authorization of 6 months may be granted as a single agent for treatment of hepatobiliary cancers, including intrahepatic and extrahepatic cholangiocarcinoma and gallbladder cancer when either of the following criteria is met:

1. Keytruda will be used as primary treatment for unresectable or metastatic disease that is microsatellite instability-high or mismatch repair deficient.
2. Keytruda will be used as adjuvant treatment for resected gross residual disease that is microsatellite instability-high or mismatch repair deficient.

X. Hepatocellular Carcinoma

Authorization of 6 months may be granted for treatment of members with hepatocellular carcinoma who have been previously treated with sorafenib.

Y. Vulvar Cancer

Authorization of 6 months may be granted as a single agent for second-line treatment of advanced, recurrent or metastatic disease in members with squamous cell vulvar cancer when either of the following criteria is met:

1. Member has microsatellite instability-high or mismatch repair deficient tumor.
2. Member has experienced disease progression on or after chemotherapy and whose tumor expresses PD-L1 (CPS \geq 1).

Z. Kidney Cancer

Authorization of 6 months may be granted for treatment of members with kidney cancer, including renal cell carcinoma, when either of the following criteria is met:

1. Keytruda will be used as first-line treatment in combination with axitinib for advanced, relapsed or stage IV disease.
2. Keytruda will be used as subsequent therapy in combination with axitinib for relapsed or stage IV disease with clear cell histology.

AA. Thymic Carcinoma

Authorization of 6 months may be granted as a single agent for treatment of thymic carcinoma as a second-line agent for unresectable, locally advanced, or metastatic disease.

BB. Mycosis Fungoides/Sezary Syndrome

Authorization of 6 months may be granted for treatment of stage III Mycosis Fungoides or Stage IV Sezary syndrome.

CC. T-Cell Lymphomas

Authorization of 6 months may be granted for treatment of extranodal NK/T-cell lymphoma, nasal type, in members with relapsed or refractory disease.

DD. Gestational Trophoblastic Neoplasia

Authorization of 6 months may be granted as a single agent for treatment of gestational trophoblastic neoplasia when either of the following criteria is met:

1. Member has recurrent or progressive intermediate trophoblastic tumor (placental site trophoblastic tumor or epithelioid trophoblastic tumor) following treatment with a platinum/etoposide-containing regimen.
2. Member has methotrexate-resistant high-risk disease.

EE. Small Cell Lung Cancer

Authorization of 6 months may be granted as a single agent for treatment of small cell lung cancer when any of the following criteria is met:

1. Disease has relapsed within 6 months following complete or partial response or stable disease with initial treatment.
2. Member has primary progressive disease.
3. Disease is metastatic and has progressed on or after platinum-based chemotherapy and at least one other prior line of therapy.

FF. Poorly Differentiated Neuroendocrine Carcinoma/Large or Small Cell Carcinoma

Authorization of 6 months may be granted for treatment of poorly differentiated neuroendocrine carcinoma/large or small cell carcinoma in members with microsatellite instability-high or mismatch repair deficient tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options.

V. CONTINUATION OF THERAPY

A. Adjuvant treatment of melanoma

Authorization of 6 months may be granted (up to 12 months total) for continued treatment in members requesting reauthorization for cutaneous melanoma who have not experienced disease recurrence or an unacceptable toxicity.

B. NSCLC, SCLC, HNSCC, cHL, PMBCL, MSI-H Cancers, Gastric Cancer, Esophageal Cancer, Cervical Cancer, HCC, MCC, RCC, Endometrial carcinoma

Authorization of 6 months may be granted (up to 24 months of continuous use) for continued treatment in members requesting reauthorization for NSCLC, SCLC, HNSCC, cHL, PMBCL, MSI-H cancers, gastric cancer, esophageal cancer, cervical cancer, HCC, MCC, RCC, and endometrial carcinoma who have not experienced disease progression or unacceptable toxicity.

C. Urothelial Carcinoma

Authorization of 6 months may be granted (up to 24 months of continuous use) for continued treatment in members requesting reauthorization for urothelial carcinoma when both of the following criteria are met:

1. Member has not experienced disease progression or unacceptable toxicity.
2. For high-risk BCG-unresponsive non-muscle invasive bladder cancer only: disease is not persistent or recurrent.

D. All other indications

Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section IV who have not experienced disease progression or an unacceptable toxicity.

VI. REFERENCES

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3. The NCCN Clinical Practice Guidelines in Oncology® Neuroendocrine and Adrenal Tumors 1.2019. ©2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed July 26, 2019.

SPECIALTY GUIDELINE MANAGEMENT

KINERET (anakinra)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Moderately to severely active rheumatoid arthritis (RA)
2. Cryopyrin-Associated Periodic Syndromes (CAPS), including Neonatal-Onset Multisystem Inflammatory Disease (NOMID)

B. Compendial Uses

1. Systemic juvenile idiopathic arthritis (sJIA)
2. Adult-onset Still's disease
3. Multicentric Castleman's disease
4. Recurrent pericarditis
5. Hyperimmunoglobulin D syndrome (HIDS) [Mevalonate Kinase Deficiency (MKD)]
6. Schnitzler's syndrome
7. Gout and pseudogout (calcium pyrophosphate deposition)

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Medical record documentation of prerequisite therapy listed in section III.E, if applicable.

III. CRITERIA FOR INITIAL APPROVAL

A. **Moderately to Severely Active Rheumatoid Arthritis (RA)**

1. Authorization of 12 months may be granted for the treatment of RA for members who have previously received Kineret or any other biologic DMARD or targeted synthetic DMARD (e.g., Olumiant, Rinvoq, Xeljanz) indicated for moderately to severely active rheumatoid arthritis.
2. Authorization of 12 months may be granted for the treatment of active RA when all of the following criteria are met:
 - a. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to 20 mg/week), or the member has an intolerance or contraindication to methotrexate.

- b. Member has experienced an inadequate response to at least a 3-month trial of a biologic DMARD or a targeted synthetic DMARD (e.g., Olumiant, Rinvoq, Xeljanz) or has intolerance to a biologic or targeted synthetic DMARD.

B. Adult-onset Still's disease

Authorization of 12 months may be granted for the treatment of adult-onset Still's disease when all of the following criteria are met:

1. Member has had an inadequate response to a 3-month trial of methotrexate or corticosteroids or has intolerance or contraindication to methotrexate and low dose corticosteroids.
2. Member will receive Kineret concurrently with methotrexate or corticosteroids or has intolerance or contraindication to methotrexate and low dose corticosteroids.

C. Active systemic juvenile idiopathic arthritis (sJIA)

1. Authorization of 12 months may be granted for the treatment of sJIA for members who have previously received Kineret or another biologic indicated for sJIA.
2. Authorization of 12 months may be granted for the treatment of active sJIA when any of the following criteria is met:
 - a. Member has had an inadequate response to a 1-month trial of nonsteroidal anti-inflammatory drugs (NSAIDs)
 - b. Member has had an inadequate response to a 2-week trial of corticosteroids
 - c. Member has had an inadequate response to a 3-month trial of methotrexate or leflunomide

D. Neonatal-onset multisystem inflammatory disease (NOMID)

Authorization of 12 months may be granted for the treatment of cryopyrin-associated periodic syndromes (CAPS), including NOMID (also known as chronic infantile neurologic cutaneous and articular syndrome [CINCA]).

E. Recurrent pericarditis

Authorization of 12 months may be granted for the treatment of recurrent pericarditis for members who have failed a first-line therapy agent (i.e., colchicine).

F. Multicentric Castleman's disease

Authorization of 12 months may be granted for the treatment of multicentric Castleman's disease when both of the following criteria are met:

1. The requested drug will be used as a single-agent.
2. The disease has progressed following treatment of relapsed/refractory or progressive disease.

G. Hyperimmunoglobulin D syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD)

Authorization of 12 months may be granted for the treatment of HIDS/MKD when all of the following criteria are met:

1. Member has had active flares within the last 6 months
2. Physician's Global Assessment greater than or equal to 2 or C-reactive protein (CRP) greater than 10 mg/L

H. Schnitzler's syndrome

Authorization of 12 months may be granted for the treatment of Schnitzler's syndrome when all of the following criteria are met:

1. Member has an urticarial rash, monoclonal IgM (or IgG) gammopathy and at least two of the following signs and symptoms: fever, joint pain or inflammation, bone pain, palpable lymph nodes, enlargement of the liver or spleen, elevated numbers of white blood cells (leukocytosis), elevated red blood cell

(erythrocyte) sedimentation rate or abnormalities on bone morphological study (e.g., increased bone density)

2. Other possible causes of the signs and symptoms have been ruled out, including but not limited to: hyperimmunoglobulin D syndrome, adult-onset Still disease, urticarial hypocomplementemic vasculitis, acquired C1 inhibitor deficiency and cryoglobulinemia.

I. Management of gout and pseudogout flares

Authorization of 6 months may be granted for the management of flares for gout or pseudogout (also known as calcium pyrophosphate deposition disease) when any of the following criteria is met:

1. Member has had an inadequate response or intolerance to maximum tolerated doses of non-steroidal anti-inflammatory drugs (NSAIDs), colchicine and oral and injectable corticosteroid
2. Member has a contraindication to NSAIDs and colchicine, and has a clinical reason to avoid repeated courses of corticosteroids.

IV. CONTINUATION OF THERAPY

A. Multicentric Castleman's disease

Authorization of 12 months may be granted for continued treatment of multicentric Castleman's disease in members requesting reauthorization who have not experienced disease progression or an unacceptable toxicity.

B. All other indications

Authorization of 12 months may be granted for all members (including new members) who are using Kineret for an indication outlined in Section III and who achieve or maintain positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition.

V. OTHER

- A. Member has had a documented negative TB test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic DMARDs or targeted synthetic DMARDs (e.g., Xeljanz), and repeated yearly for members with risk factors** for TB that are continuing therapy with biologics.

* If the screening testing for TB is positive, there must be documentation of further testing to confirm there is no active disease. Do not administer anakinra to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of treatment.

** Risk factors for TB include: Persons with close contact to people with infectious TB disease; persons who have recently immigrated from areas of the world with high rates of TB (e.g., Africa, Asia, Eastern Europe, Latin America, Russia); children less than 5 years of age who have a positive TB test; groups with high rates of TB transmission (e.g., homeless persons, injection drug users, persons with HIV infection); persons who work or reside with people who are at an increased risk for active TB (e.g., hospitals, long-term care facilities, correctional facilities, homeless shelters).

- B. The requested drug will not be used concomitantly with any other biologic DMARD (e.g., adalimumab, canakinumab, rilonacept, rituximab, etanercept, infliximab) or targeted synthetic DMARD (e.g. tofacitinib).

Reference number
1802-A

VI. APPENDIX: Examples of contraindications to methotrexate

1. History of intolerance or adverse event
2. Alcoholic liver disease or other chronic liver disease
3. Elevated liver transaminases
4. Interstitial pneumonitis or clinically significant pulmonary fibrosis
5. Renal impairment
6. Current pregnancy or planning pregnancy
7. Breastfeeding
8. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
9. Myelodysplasia
10. Hypersensitivity
11. Significant drug interaction

VII. REFERENCES

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SPECIALTY GUIDELINE MANAGEMENT

KISQALI (ribociclib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Kisqali is indicated in combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of pre/perimenopausal or postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer.
2. Kisqali is indicated in combination with fulvestrant for the treatment of postmenopausal women with (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer, as initial endocrine based therapy or following disease progression on endocrine therapy.

B. Compendial Uses

Kisqali is indicated in combination with tamoxifen for the treatment of HR-positive, HER2-negative advanced or metastatic breast cancer.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of hormone receptor (HR) and human epidermal growth factor receptor 2 (HER2) status is necessary to initiate the prior authorization review.

III. CRITERIA FOR INITIAL APPROVAL

Breast cancer

Authorization of 12 months may be granted to members for the treatment of HR-positive, HER2-negative recurrent, advanced, or metastatic breast cancer when Kisqali is used in combination with an aromatase inhibitor, fulvestrant, or tamoxifen.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy for an indication outlined in section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Kisqali [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2018.

Reference number(s)
1639-A

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SPECIALTY GUIDELINE MANAGEMENT

KISQALI FEMARA CO-PACK (ribociclib tablets; letrozole tablets)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

The Kisqali Femara Co-Pack is indicated as initial endocrine-based therapy for the treatment of pre/perimenopausal or postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of hormone receptor (HR) and human epidermal growth factor receptor 2 (HER2) status is necessary to initiate the prior authorization review.

III. CRITERIA FOR INITIAL APPROVAL

Breast cancer

Authorization of 12 months may be granted to members for the treatment of HR-positive, HER2-negative recurrent, advanced or metastatic breast cancer.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy for an indication outlined in section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Kisqali Femara Co-Pack [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; February 2019.

SPECIALTY GUIDELINE MANAGEMENT

KORLYM (mifepristone)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Korlym is a cortisol receptor blocker indicated to control hyperglycemia secondary to hypercortisolism in adult patients with endogenous Cushing's syndrome who have type 2 diabetes mellitus or glucose intolerance and have failed surgery or are not candidates for surgery.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

- A. For initial requests: pretreatment hemoglobin A1C level
- B. For continuation of therapy: current hemoglobin A1C level

III. CRITERIA FOR INITIAL APPROVAL

Cushing's syndrome/disease

Authorization of 6 months may be granted for treatment of Cushing's syndrome/disease when all of the following criteria are met:

- A. Member has type 2 diabetes mellitus or glucose intolerance
- B. Korlym is being prescribed to control hyperglycemia secondary to hypercortisolism
- C. Member has failed to achieve adequate glycemic control despite individualized diabetic management
- D. Member has had surgery that was not curative OR member is not a candidate for surgery
- E. If the member is able to become pregnant, a negative pregnancy test is required before initiating therapy

IV. CONTINUATION OF THERAPY

Cushing's syndrome/disease

Authorization of 12 months for continuation of therapy may be granted if the member has experienced improved glycemic control as evidenced by decreased hemoglobin A1C levels.

V. REFERENCES

1. Korlym [package insert]. Menlo Park, CA: Corcept Therapeutics Incorporated; May 2017.
2. Nieman LK, Biller B, Findling JW, et al. Treatment of Cushing's Syndrome: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2015;100:2807-2831.

SPECIALTY GUIDELINE MANAGEMENT

KRYSTEXXA (pegloticase)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Krystexxa is indicated for the treatment of chronic gout in adult patients refractory to conventional therapy.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Chronic gout

Authorization of 12 months may be granted for members with a diagnosis of chronic gout when all of the following criteria are met:

- A. Krystexxa will not be used concomitantly with oral urate-lowering therapies
- B. Member has at least 3 gout flares in the previous 18 months that were inadequately controlled by colchicine or NSAIDs or at least 1 gout tophus or gouty arthritis
- C. Member has had an inadequate response to or a clinical reason for not completing at least a three-month trial (see Appendix) with the following medications at the medically appropriate maximum doses:
 1. Allopurinol or febuxostat
 2. Probenecid (alone or in combination with allopurinol or febuxostat)

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) with a diagnosis of chronic gout that meet all initial authorization criteria and have not had two consecutive uric acid levels above 6 mg/dL since starting treatment with Krystexxa.

IV. APPENDIX: Clinical reasons for not completing a three-month trial with allopurinol, febuxostat, and probenecid (examples):

- A. Member experienced a severe allergic reaction to the medication
- B. Member experienced toxicity with the medication
- C. Member could not tolerate the medication
- D. Member's current medication regimen has a significant drug interaction
- E. Member has severe renal dysfunction (allopurinol)
- F. Member has known blood dyscrasias or uric acid kidney stones (probenecid)
- G. Member has renal insufficiency (i.e., glomerular filtration rate 30 mL/minute or less) (probenecid)
- H. Member has end stage renal impairment (febuxostat)

Reference number
1803-A

V. REFERENCES

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2. DRUGDEX® System (electronic version). Truven Health Analytics, Ann Arbor, Michigan. Available at <http://www.micromedexsolutions.com>. Accessed February 22, 2018.
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8. Probenecid [package insert]. Morgantown, WV: Mylan Pharmaceuticals Inc.; March 2006.

SPECIALTY GUIDELINE MANAGEMENT

KUVAN (sapropterin dihydrochloride)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Kuvan is indicated to reduce blood phenylalanine (Phe) levels in patients with hyperphenylalaninemia (HPA) due to tetrahydrobiopterin- (BH4-) responsive phenylketonuria (PKU). Kuvan is to be used in conjunction with a Phe-restricted diet.

B. Compendial Uses

1. Autosomal dominant guanine triphosphate cyclohydrolase deficiency (Segawa disease)
2. Autosomal recessive guanine (GTP) cyclohydrolase deficiency
3. 6-pyruvoyl-tetrahydropterin synthase (6-PTS) deficiency
4. Sepiapterin reductase deficiency
5. Dihydropteridine reductase (DHPR) deficiency
6. Pterin-4a-carbinolamine dehydratase deficiency (also called primapterinuria)

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: enzyme assay or genetic testing results supporting diagnosis.

III. CRITERIA FOR INITIAL APPROVAL

A. **Phenylketonuria (PKU)**

Authorization of 60 days may be granted for members with a diagnosis of phenylketonuria who have a baseline phenylalanine level over 360 micromol/L (6mg/dL) with dietary interventions alone.

B. **Biopterin Metabolic Defects**

Authorization of indefinite approval may be granted for members who have any of the following biopterin metabolic defects:

1. Autosomal dominant guanine triphosphate cyclohydrolase deficiency (Segawa disease)
2. Autosomal recessive guanine (GTP) cyclohydrolase deficiency
3. 6-pyruvoyl-tetrahydropterin synthase (6-PTS) deficiency
4. Sepiapterin reductase deficiency
5. Dihydropteridine reductase (DHPR) deficiency
6. Pterin-4a-carbinolamine dehydratase deficiency (also called primapterinuria)

IV. CONTINUATION OF THERAPY

A. Phenylketonuria (PKU)

Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for phenylketonuria (PKU) who meet any of the following criteria:

1. Achieve or maintain a 30% decrease in phenylalanine levels from baseline; or
2. Phenylalanine levels are in an acceptable range (less than 360 micromol/L or 6mg/dL); or
3. Demonstrate an improvement in neuropsychiatric symptoms.

B. Biopterin Metabolic Defects

Authorization of indefinite approval may be granted for continued treatment in members requesting reauthorization for any biopterin metabolic defect listed in Section III who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

V. REFERENCES

1. Kuvan [package insert]. Novato, CA: BioMarin Pharmaceutical Inc.; August 2016.
2. Vockley J, Andersson HC, Antshel KM, et al. Phenylalanine hydroxylase deficiency: diagnosis and management guideline. *Genet Med*. 2014;16(2):188-200.
3. Singh RH, Rohr F, Frazier D, et al. Recommendations for the nutrition management of phenylalanine hydroxylase deficiency. *Genet Med*. 2014;16(2):121-131.

SPECIALTY GUIDELINE MANAGEMENT

KYMRIAH (tisagenlecleucel)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Pediatric and Young Adult Relapsed or Refractory (r/r) B-cell Acute Lymphoblastic Leukemia (ALL)
Patients up to 25 years of age with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse.
2. Adult Relapsed or Refractory (r/r) Diffuse Large B-cell Lymphoma
Adult patients with relapsed or refractory (r/r) large B-cell lymphoma after two or more lines of systemic therapy including diffuse large B-cell lymphoma (DLBCL) not otherwise specified (NOS), high grade B-cell lymphoma and DLBCL arising from follicular lymphoma.

Limitation of Use: Kymriah is not indicated for treatment of patients with primary central nervous system lymphoma.

B. Compendial Uses

1. Acquired immunodeficiency syndrome (AIDS)-related diffuse large B-cell lymphoma
2. Diffuse large B-cell lymphoma
3. Human herpesvirus 8 (HHV8)-positive diffuse large B-cell lymphoma, NOS
4. Monomorphic post-transplant lymphoproliferative disorder (B-cell type)
5. Primary mediastinal large B-cell lymphoma

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Testing or analysis confirming CD19 protein on the surface of the B-cell

III. CRITERIA FOR INITIAL APPROVAL

A. **Pediatric and Young Adult Relapsed or Refractory (r/r) B-cell Acute Lymphoblastic Leukemia (ALL)**

Authorization of 3 months may be granted for treatment of B-cell precursor acute lymphoblastic leukemia (ALL) in patients less than or equal to 25 years of age when all of the following criteria are met:

1. The disease is refractory to treatment or in second or later relapse.
2. The member has not received a previous treatment course of Kymriah or another CD19-directed chimeric antigen receptor (CAR) T-cell therapy.
3. The B-cells must be CD19-positive as confirmed by testing or analysis

4. Member meets one of the following:
 - a. Member has Philadelphia chromosome-positive disease and failed at least two tyrosine kinase inhibitors (TKI) (e.g., imatinib, dasatinib, nilotinib, bosutinib, ponatinib).
 - b. Member has Philadelphia chromosome-negative disease.

B. Adult B-cell Lymphomas

Authorization of 3 months may be granted for treatment of B-cell lymphomas in members 18 years of age or older when all of the following criteria are met:

1. Member has any of the following B-cell lymphoma subtypes:
 - a. Diffuse large B-cell lymphoma (DLBCL) arising from follicular lymphoma (also known as follicular lymphoma with histologic transformation to DLBCL)
 - b. Diffuse large B-cell lymphoma
 - c. Primary mediastinal large B-cell lymphoma
 - d. High-grade B-cell lymphoma (high-grade B-cell lymphoma with translocations of MYC and BCL2 and/or BCL6 [double/triple hit lymphoma], high-grade B-cell lymphoma, NOS)
 - e. Acquired immunodeficiency syndrome (AIDS)-related diffuse large B-cell lymphoma
 - f. Human herpesvirus 8 (HHV8)-positive diffuse large B-cell lymphoma, NOS
 - g. Monomorphic post-transplant lymphoproliferative disorder (B-cell type)
2. The member does not have primary central nervous system lymphoma.
3. The member has not received a previous treatment course of Kymriah or another CD19-directed chimeric antigen receptor (CAR) T-cell therapy.
4. The B-cells must be CD19-positive as confirmed by testing or analysis
5. For diffuse large B-cell lymphoma arising from follicular lymphoma: member received prior treatment with two or more chemoimmunotherapy regimens which included at least one anthracycline or anthracenedione-based regimen, unless contraindicated.
6. For all other B-cell lymphoma subtypes: member has partial response following second-line therapy OR the disease is in second relapse or greater.

IV. REFERENCES

1. Kymriah [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; May 2018.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed April 17, 2019.
3. The NCCN Clinical Practice Guidelines in Oncology® Acute Lymphoblastic Leukemia (Version 1.2019).© 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed April 17, 2019.
4. The NCCN Clinical Practice Guidelines in Oncology® B-Cell Lymphomas (Version 2.2019).© 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed April 17, 2019.

SPECIALTY GUIDELINE MANAGEMENT

KYNAMRO (mipomersen)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Kynamro is indicated as an adjunct to lipid-lowering medications and diet to reduce low density lipoprotein-cholesterol (LDL-C), apolipoprotein B (apo B), total cholesterol, and non-high density lipoprotein-cholesterol (non-HDL-C) in patients with homozygous familial hypercholesterolemia (HoFH).

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of documentation supporting the diagnosis of homozygous familial hypercholesterolemia per Appendix A or B is necessary to initiate the prior authorization review.

III. CRITERIA FOR INITIAL APPROVAL

Homozygous familial hypercholesterolemia (HoFH)

Authorization for 6 months may be granted for members who meet all of the criteria listed below:

- A. Member has a documented diagnosis of HoFH confirmed by genetic analysis or clinical criteria (See Appendices).
- B. Prior to initiation of treatment with Kynamro, patient is/was receiving a combination lipid-lowering regimen consisting of a high-intensity statin, ezetimibe, and evolocumab (Repatha), unless the member has known LDL-receptor negative mutations in both alleles.
- C. Prior to initiation of treatment with Kynamro, patient is/was experiencing an inadequate response to such a combination regimen, as demonstrated a treated LDL-C of greater than or equal to 100 mg/dL (or greater than or equal to 70 mg/dL with clinical atherosclerotic cardiovascular disease [ASCVD]), unless the member has known LDL-receptor negative mutations in both alleles.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members (including new members) who meet all initial authorization criteria and have achieved or maintained a LDL-C reduction greater than 20% from the levels immediately prior to initiation of treatment with Kynamro.

V. APPENDICES

APPENDIX A. Diagnosis of Homozygous Familial Hypercholesterolemia

- Genetic confirmation
 - Mutations in both alleles at LDL receptor, ApoB, PCSK9 or LDL receptor adaptor protein gene locus
- Clinical diagnosis
 - Untreated LDL-C > 500 mg/dL OR unknown untreated LDL-C with treated LDL-C > 300 mg/dL **plus**
 - One of the following:
 - Tendon or cutaneous xanthomas at age 10 or younger
 - Diagnosis of familial hypercholesterolemia (FH) by Simon-Broome Diagnostic Criteria or Dutch Lipid Clinic Network Criteria (See Appendix B) in both parents
 - Evidence of FH in both parents with a history including any of the following:
 - Total cholesterol \geq 310 mg/dL
 - Premature ASCVD (before 55 years in men and 60 years in women)
 - Tendon xanthoma
 - Sudden premature cardiac death

APPENDIX B: Diagnosis of familial hypercholesterolemia (FH)

A diagnosis of FH is made when one of the following diagnostic criteria is met:

- Genetic confirmation
 - An LDL-receptor mutation, familial defective apo B-100, or a PCSK9 gain-of-function mutation
- Simon-Broome Diagnostic Criteria for FH
 - Total cholesterol > 290 mg/dL or LDL-C > 190 mg/dL in patients over 16 years of age or total cholesterol > 260 mg/dL or LDL-C > 155 mg/dL in patients less than 16 years of age and one of the following
 - Tendon xanthomas in the patient, first (parent, sibling or child) or second degree relative (grandparent, uncle or aunt)
 - Family history of myocardial infarction in a first degree relative before the age of 60 or in a second degree relative before the age of 50
 - Total cholesterol greater than 290 mg/dL in an adult first or second degree relative
 - Total cholesterol greater than 260 mg/dL in a child, brother, or sister aged younger than 16 years
- Dutch Lipid Clinic Network Criteria for FH
 - Total score > 5 points

VI. REFERENCES

1. Kynamro [package insert]. Cambridge, MA: Genzyme Corporation, Inc.; May 2016.
2. Nordestgaard BG, Chapman MJ, Humphries SE, et al. Familial hypercholesterolaemia is underdiagnosed and undertreated in the general population: guidance for clinicians to prevent coronary heart disease. Consensus Statement of the European Atherosclerosis Society. *Eur Heart J*. 2013;34:3478–3490.
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4. National Institute for Health and Clinical Excellence (2008). Identification and management of familial hypercholesterolaemia. NICE clinical guideline 71.
5. Raal JF, Santos RD, Blom DJ, et al. Mipomersen, an apolipoprotein B Synthesis inhibitor, for lowering of LDL cholesterol concentrations in patients with homozygous familial hypercholesterolaemia: a randomized, double-blind, placebo-controlled trial. *Lancet*. 2010;375:998-1006.
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7. Raal JF, Santos RD. Homozygous familial hypercholesterolemia: current perspectives on diagnosis and treatment. *Atherosclerosis*. 2012;223:262-268.

8. Liposorber System [package insert]. New York, NY: Kaneka Pharma America, LLC. Available at <http://www.liposorber.com/physician/prescribe/prescribe.htm>. Accessed: December 6, 2017.
9. Moriarty PM. LDL-apheresis therapy: current therapeutic practice and potential future use. *Future Lipidol*. 2006;3:299-308.
10. Bays HE, Jones PH, Orringer CE, et al. National Lipid Annual Summary of Clinical Lipidology 2016. *J Clin Lipidol* 2016; 10:S1-S43.
11. Lloyd-Jones DM, Morris PB, Ballantyne CM, Birtcher KK, Daly DD Jr., DePalma SM, Minissian MB, Orringer CE, Smith SC Jr. 2017 focused update of the 2016 ACC expert consensus decision pathway on the role of non-statin therapies for LDL-cholesterol lowering in the management of atherosclerotic cardiovascular disease risk: a report of the American College of Cardiology Task Force on Clinical Expert Consensus Documents. *J Am Coll Cardiol* 2017;70:1785–822.

SPECIALTY GUIDELINE MANAGEMENT

KYPROLIS (carfilzomib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Kyprolis is indicated in combination with dexamethasone or with lenalidomide plus dexamethasone for the treatment of patients with relapsed or refractory multiple myeloma who have received one to three lines of therapy.
2. Kyprolis is indicated as a single agent for the treatment of patients with relapsed or refractory multiple myeloma who have received one or more lines of therapy.

B. Compendial Uses

Waldenström macroglobulinemia/lymphoplasmacytic lymphoma

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Multiple Myeloma**

Authorization of 12 months may be granted for treatment of multiple myeloma when the requested medication will be used in any of the following regimens:

1. In combination with dexamethasone
2. In combination with cyclophosphamide and dexamethasone
3. In combination with lenalidomide and dexamethasone
4. In combination with panobinostat for members who have received at least two prior therapies, including bortezomib and an immunomodulatory agent
5. In combination with pomalidomide and dexamethasone for patients who have received at least two prior therapies, including an immunomodulatory agent and a proteasome inhibitor
6. As a single agent when the member has received one or more lines of therapy

B. **Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma**

Authorization of 12 months may be granted for treatment of Waldenström macroglobulinemia/lymphoplasmacytic lymphoma when the requested medication will be used as a component of the CaRD (carfilzomib, rituximab, and dexamethasone) regimen.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Kyprolis [package insert]. Thousand Oaks, CA: Onyx Pharmaceuticals, Inc.; February 2019.
2. The NCCN Drugs & Biologics Compendium 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 29, 2019.
3. The NCCN Clinical Practice Guidelines in Oncology Multiple Myeloma (Version 1.2019) 2018 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed March 29, 2019.
4. The NCCN Clinical Practice Guidelines in Oncology Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma (Version 2.2019) 2018 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed March 29, 2019.

SPECIALTY GUIDELINE MANAGEMENT

LARTRUVO (olaratumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Lartruvo is indicated, in combination with doxorubicin, for the treatment of adult patients with soft tissue sarcoma (STS) with a histologic subtype for which an anthracycline-containing regimen is appropriate and which is not amenable to curative treatment with radiotherapy or surgery.

Initiating therapy with olaratumab (Lartruvo) in new patients is considered experimental/investigational and not medically necessary.

All other indications are considered experimental/investigational and not medically necessary.

In January 2019, Eli Lilly and Company reported that the results of ANNOUNCE did not confirm the clinical benefit of olaratumab in combination with doxorubicin as compared to doxorubicin. Specifically, the study did not meet the primary endpoints of overall survival (OS) in the full study population or in the leiomyosarcoma (LMS) sub-population; there was no difference in survival between the study arms for either population.

II. CRITERIA FOR INITIAL APPROVAL

Initiating therapy with olaratumab (Lartruvo) in new members is considered experimental/investigational and not medically necessary.

III. CONTINUATION OF THERAPY

Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for soft tissue sarcomas who are experiencing clinical benefit to therapy or who have not experienced an unacceptable toxicity. The member must be enrolled in the Lartruvo Patient Access Program (PAP) by July 31, 2019.

IV. REFERENCES

1. Lartruvo [package insert]. Indianapolis, IN: Eli Lilly and Company; August 2018.

SPECIALTY GUIDELINE MANAGEMENT

LEMTRADA (alemtuzumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Lemtrada is indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS). Because of its safety profile, the use of Lemtrada should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR APPROVAL

A. First Course – Relapsing forms of multiple sclerosis

Authorization of 30 days (5 doses) may be granted to members with a diagnosis of a relapsing form of multiple sclerosis who have had an inadequate response to two or more drugs indicated for multiple sclerosis.

B. Subsequent Courses – Relapsing forms of multiple sclerosis

Authorization of 30 days (3 doses) may be granted to members with a diagnosis of a relapsing form of multiple sclerosis who have completed at least one previous course of therapy.

III. OTHER CRITERIA

Members will not use Lemtrada concomitantly with other medications used for the treatment of multiple sclerosis, excluding Ampyra.

For subsequent courses, members must have received the previous course of Lemtrada treatment at least 12 months prior to the planned date of the first dose of Lemtrada course of treatment.

IV. REFERENCE

1. Lemtrada [package insert]. Cambridge, MA: Genzyme Corporation; July 2019.

SPECIALTY GUIDELINE MANAGEMENT

LENVIMA (lenvatinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Lenvima is indicated for the treatment of patients with locally recurrent or metastatic, progressive, radioactive iodine-refractory differentiated thyroid cancer (DTC).
2. Lenvima is indicated in combination with everolimus, for the treatment of patients with advanced renal cell carcinoma (RCC) following one prior anti-angiogenic therapy.
3. Lenvima is indicated for the first-line treatment of patients with unresectable hepatocellular carcinoma (HCC).
4. Lenvima is indicated in combination with pembrolizumab, for the treatment of patients with advanced endometrial carcinoma that is not microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR), who have disease progression following prior systemic therapy and are not candidates for curative surgery or radiation.

B. Compendial Uses

Medullary, follicular, Hurthle cell or papillary thyroid carcinoma

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review for endometrial carcinoma:

Documentation of laboratory report confirming MSI-H or mismatch repair deficient (dMMR) tumor status.

III. CRITERIA FOR INITIAL APPROVAL

A. **Thyroid carcinoma (follicular, Hürthle cell, papillary)**

Authorization of 12 months may be granted for the treatment of radioiodine refractory follicular, Hürthle cell, or papillary thyroid carcinoma.

B. **Medullary thyroid carcinoma**

Authorization of 12 months may be granted for the treatment of medullary thyroid carcinoma if the member has progressed on vandetanib (Caprelsa) or cabozantinib (Cometriq) OR these therapies are inappropriate.

C. **Renal Cell Carcinoma**

Authorization of 12 months may be granted for the treatment of advanced or metastatic renal cell carcinoma when used in combination with everolimus (Afinitor) AND either of the following is met:

1. The disease is predominantly clear cell and the member has used prior therapy OR

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1865-A

2. The disease is non-clear cell

D. Hepatocellular Carcinoma

Authorization of 12 months may be granted for the treatment of unresectable hepatocellular carcinoma.

E. Endometrial Carcinoma

Authorization of 12 months may be granted for the treatment of endometrial carcinoma when used in combination with pembrolizumab for advanced endometrial carcinoma that is not MSI-H or dMMR when the member has disease progression following prior systemic therapy and is not a candidate for curative surgery or radiation.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy for an indication outlined in Section III when there is no evidence of unacceptable toxicity or disease progression on the current regimen.

V. REFERENCES

1. Lenvima [package insert]. Woodcliff Lake, NJ: Eisai Inc.; September 2019.
2. The NCCN Drugs & Biologics Compendium 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed May 16, 2019.
3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology Thyroid Carcinoma (Version 1.2018). <http://www.nccn.org>. Accessed November 5, 2018.
4. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology Kidney Cancer (Version 2.2019). <http://www.nccn.org>. Accessed November 5, 2018.

SPECIALTY GUIDELINE MANAGEMENT

LEUKINE (sargramostim)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

- A. Use Following Induction Chemotherapy in Acute Myelogenous Leukemia
Leukine is indicated for use following induction chemotherapy in adult patients 55 years and older with acute myelogenous leukemia (AML) to shorten time to neutrophil recovery and to reduce the incidence of severe and life-threatening infections and infections resulting in death.
- B. Autologous Peripheral Blood Progenitor Cells Mobilization and Collection
Leukine is indicated in adult patients with cancer undergoing autologous hematopoietic stem cell transplantation for the mobilization of hematopoietic progenitor cells into peripheral blood for collection by leukapheresis.
- C. Autologous Peripheral Blood Progenitor Cell and Bone Marrow Transplantation
Leukine is indicated for acceleration of myeloid reconstitution following autologous peripheral blood progenitor cell (PBPC) or bone marrow transplantation in adult and pediatric patients 2 years of age and older with non-Hodgkin's lymphoma (NHL), acute lymphoblastic leukemia (ALL) and Hodgkin's lymphoma (HL).
- D. Allogeneic Bone Marrow Transplantation (BMT)
Leukine is indicated for acceleration of myeloid reconstitution in adult and pediatric patients 2 years of age and older undergoing allogeneic BMT from human leukocyte antigens (HLA)-matched related donors.
- E. Allogeneic or Autologous Bone Marrow Transplantation: Treatment of Delayed Neutrophil recovery or Graft Failure
Leukine is indicated for the treatment of adult and pediatric patients 2 years and older who have undergone allogeneic or autologous BMT in whom neutrophil recovery is delayed or failed.
- F. Acute Exposure to Myelosuppressive Doses of Radiation (H-ARS)
Leukine is indicated to increase survival in adult and pediatric patients from birth to 17 years of age acutely exposed to myelosuppressive doses of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome [H-ARS]).

B. Compendial Uses

1. Prophylaxis and treatment of chemotherapy-induced febrile neutropenia in non-myeloid malignancies
2. Treatment of neutropenia and anemia in patients with myelodysplastic syndromes (MDS)
3. Acute myeloid leukemia
4. Agranulocytosis (non-chemotherapy drug induced)
5. Aplastic anemia
6. Neutropenia related to HIV/AIDS
7. Stem cell transplantation-related indications
8. Neuroblastoma
9. Severe chronic neutropenia (congenital, cyclic, or idiopathic)

10. Radiation therapy/injury

All other indications are considered experimental/investigational and are not a covered benefit.

II. REQUIRED DOCUMENTATION

Primary Prophylaxis of Febrile Neutropenia

- A. Documentation must be provided of the member's diagnosis and chemotherapeutic regimen.
- B. If chemotherapeutic regimen has an intermediate risk of febrile neutropenia (10-19% [See Appendix B]), documentation must be provided outlining the patient's risk factors that confirm the member is at high risk for febrile neutropenia.

III. CRITERIA FOR INITIAL APPROVAL

A. Neutropenia in cancer patients receiving myelosuppressive chemotherapy

Authorization of 6 months may be granted for prevention or treatment of febrile neutropenia when all of the following criteria are met (1, 2, and 3):

1. The requested medication will not be used in combination with other colony stimulating factors within any chemotherapy cycle.
2. The member will not be receiving concurrent chemotherapy and radiation therapy.
3. One of the following criteria is met (i, ii, or iii):
 - i. The requested medication will be used for primary prophylaxis in members with solid tumors or non-myeloid malignancies who have received, are currently receiving, or will be receiving myelosuppressive anti-cancer therapy that is expected to result in 20% or higher incidence of FN (*See Appendix A*) OR 10 – 19% risk of FN (*See Appendix B*) and who are considered to be at high risk of FN because of bone marrow compromise or co-morbidity, including any of the following (not an all-inclusive list):
 - a. Active infections, open wounds, or recent surgery
 - b. Age greater than or equal to 65 years
 - c. Bone marrow involvement by tumor producing cytopenias
 - d. Previous chemotherapy or radiation therapy
 - e. Poor nutritional status
 - f. Poor performance status
 - g. Previous episodes of FN
 - h. Other serious co-morbidities, including renal dysfunction, liver dysfunction, HIV infection, cardiovascular disease
 - i. Persistent neutropenia
 - ii. The requested medication will be used for secondary prophylaxis in members with solid tumors or non-myeloid malignancies who experienced a febrile neutropenic complication or a dose-limiting neutropenic event (a nadir or day of treatment count impacting the planned dose of chemotherapy) from a prior cycle of similar chemotherapy, with the same dose and schedule planned for the current cycle (for which primary prophylaxis was not received).
 - iii. The requested medication will be used for treatment of high risk FN in members who have any of the following prognostic factors that are predictive of clinical deterioration:
 - a. Age greater than 65 years
 - b. Being hospitalized at the time of the development of fever
 - c. Sepsis syndrome
 - d. Invasive fungal infection
 - e. Pneumonia or other clinically documented infection
 - f. Prolonged (neutropenia expected to last greater than 10 days) or profound (absolute neutrophil count less than $1 \times 10^9/L$) neutropenia

- g. Prior episodes of febrile neutropenia

B. Other indications

Authorization of 6 months may be granted for members with any of the following indications:

1. Myelodysplastic syndrome (anemia or neutropenia)
2. Acute myeloid leukemia
3. Agranulocytosis (non-chemotherapy drug induced)
4. Aplastic anemia
5. Neutropenia related to HIV/AIDS
6. Stem cell transplantation-related indications
7. Neuroblastoma
Use with dinutuxin (Unituxin), interleukin-2 (aldesleukin (Proleukin)), and isotretinoin (13-cis-retinoic acid (RA)), for the treatment of high-risk neuroblastoma.
8. Severe chronic neutropenia (congenital, cyclic, or idiopathic)
9. Radiation therapy/injury
 - i. Manage neutropenia in members acutely exposed to myelosuppressive doses of radiation therapy
 - ii. Treatment of radiation injury

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. APPENDIX

A. APPENDIX A: Selected Chemotherapy Regimens with an Incidence of Febrile Neutropenia of 20% or Higher

1. Acute Lymphoblastic Leukemia:
Select ALL regimens as directed by treatment protocol (see NCCN guidelines)
2. Bladder Cancer:
 - i. Dose dense MVAC (methotrexate, vinblastine, doxorubicin, cisplatin)
 - ii. CBDCa/Pac (carboplatin, paclitaxel)
3. Bone Cancer
 - i. VAI (vincristine, doxorubicin or dactinomycin, ifosfamide)
 - ii. VDC-IE (vincristine, doxorubicin or dactinomycin, and cyclophosphamide alternating with ifosfamide and etoposide)
 - iii. Cisplatin/doxorubicin
 - iv. VDC (cyclophosphamide, vincristine, doxorubicin or dactinomycin)
 - v. VIDE (vincristine, ifosfamide, doxorubicin or dactinomycin, etoposide)
4. Breast Cancer:
 - i. Docetaxel + trastuzumab
 - ii. Dose-dense AC (doxorubicin, cyclophosphamide) + paclitaxel (or dose dense paclitaxel)
 - iii. TAC (docetaxel, doxorubicin, cyclophosphamide)
 - iv. AT (doxorubicin, docetaxel)
 - v. Doc (docetaxel)
 - vi. TC (docetaxel, cyclophosphamide)
 - vii. TCH (docetaxel, carboplatin, trastuzumab)
5. Colorectal Cancer:

- FOLFOXIRI (fluorouracil, leucovorin, oxaliplatin, irinotecan)
6. Esophageal and Gastric Cancers:
Docetaxel/cisplatin/fluorouracil
 7. Head and Neck Squamous Cell Carcinoma
TPF (docetaxel, cisplatin, fluorouracil)
 8. Hodgkin Lymphoma:
 - i. Brentuximab vedotin + AVD (doxorubicin, vinblastine, dacarbazine)
 - ii. Escalated BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone)
 9. Kidney Cancer:
Doxorubicin/gemcitabine
 10. Non-Hodgkin's Lymphoma:
 - i. Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin)
 - ii. ICE (ifosfamide, carboplatin, etoposide)
 - iii. Dose-dense CHOP-14 (cyclophosphamide, doxorubicin, vincristine, prednisone) + rituximab
 - iv. MINE (mesna, ifosfamide, novantrone, etoposide)
 - v. DHAP (dexamethasone, cisplatin, cytarabine)
 - vi. ESHAP (etoposide, methylprednisolone, cisplatin, cytarabine (Ara-C))
 - vii. HyperCVAD + rituximab (cyclophosphamide, vincristine, doxorubicin, dexamethasone + rituximab)
 - viii. VAPEC-B (vincristine, doxorubicin, prednisolone, etoposide, cyclophosphamide, bleomycin)
 11. Melanoma:
Dacarbazine-based combination with IL-2, interferon alpha (dacarbazine, cisplatin, vinblastine, IL-2, interferon alpha)
 12. Multiple myeloma:
 - i. DT-PACE (dexamethasone/ thalidomide/ cisplatin/ doxorubicin/ cyclophosphamide/ etoposide) + bortezomib (VTD-PACE)
 - ii. DT-PACE
(dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide)
 13. Ovarian Cancer:
 - i. Topotecan
 - ii. Docetaxel
 14. Pancreatic Cancer:
FOLFIRINOX (fluorouracil, leucovorin, irinotecan, oxaliplatin)
 15. Soft Tissue Sarcoma:
 - i. MAID (mesna, doxorubicin, ifosfamide, dacarbazine)
 - ii. Doxorubicin
 - iii. Ifosfamide/doxorubicin
 16. Small Cell Lung Cancer:
 - i. Top (topotecan)
 - ii. CAV (cyclophosphamide, doxorubicin, vincristine)
 17. Testicular cancer:
 - i. VeIP (vinblastine, ifosfamide, cisplatin)
 - ii. VIP (etoposide, ifosfamide, cisplatin)
 - iii. TIP (paclitaxel, ifosfamide, cisplatin)

B. APPENDIX B: Selected Chemotherapy Regimens with an Incidence of Febrile Neutropenia of 10% to 19%

Reference number(s)
1929-A

1. Occult primary – adenocarcinoma:
Gemcitabine/docetaxel
2. Breast cancer:
 - i. Docetaxel
 - ii. CMF classic (cyclophosphamide, methotrexate, fluorouracil)
 - iii. CA (doxorubicin, cyclophosphamide) (60 mg/m²) (hospitalized)
 - iv. AC (doxorubicin, cyclophosphamide) + sequential docetaxel (taxane portion only)
 - v. AC + sequential docetaxel + trastuzumab
 - vi. A (doxorubicin) (75 mg/m²)
 - vii. AC (doxorubicin, cyclophosphamide)
 - viii. CapDoc (capecitabine, docetaxel)
 - ix. Paclitaxel every 21 days
3. Cervical Cancer:
 - i. Irinotecan
 - ii. Cisplatin/topotecan
 - iii. Paclitaxel/cisplatin
 - iv. Topotecan
4. Colorectal:
 - i. FL (fluorouracil, leucovorin)
 - ii. CPT-11 (irinotecan) (350 mg/m² q 3 wk)
 - iii. FOLFOX (fluorouracil, leucovorin, oxaliplatin)
5. Esophageal and Gastric Cancers:
 - i. Irinotecan/cisplatin
 - ii. Epirubicin/cisplatin/fluorouracil
 - iii. Epirubicin/cisplatin/capecitabine
6. Non-Hodgkin's lymphomas:
 - i. EPOCH-IT chemotherapy
 - ii. GDP (gemcitabine, dexamethasone, cisplatin/carboplatin)
 - iii. GDP (gemcitabine, dexamethasone, cisplatin/carboplatin) + rituximab
 - iv. FMR (fludarabine, mitoxantrone, rituximab)
 - v. CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) including regimens with pegylated liposomal doxorubicin
 - vi. CHOP + rituximab (cyclophosphamide, doxorubicin, vincristine, prednisone, rituximab) including regimens with pegylated liposomal doxorubicin
 - vii. CHP (cyclophosphamide, doxorubicin, prednisone) + brentuximab vedotin
 - viii. Bendamustine
7. Non-Small Cell Lung Cancer:
 - i. Cisplatin/paclitaxel
 - ii. Cisplatin/vinorelbine
 - iii. Cisplatin/docetaxel
 - iv. Cisplatin/etoposide
 - v. Carboplatin/paclitaxel
 - vi. Docetaxel
8. Ovarian cancer:
Carboplatin/docetaxel
9. Prostate cancer:
Cabazitaxel
10. Small Cell Lung Cancer:
Etoposide/carboplatin
11. Testicular Cancer:
 - i. BEP (bleomycin, etoposide, cisplatin)

Reference number(s)
1929-A

- ii. Etoposide/cisplatin
- 12. Uterine sarcoma:
Docetaxel

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SPECIALTY GUIDELINE MANAGEMENT

leuprolide acetate injection

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Prostate cancer: Leuprolide acetate is indicated in the palliative treatment of advanced prostate cancer.
2. Central precocious puberty (CPP): Leuprolide acetate is indicated in the treatment of children with central precocious puberty.

B. Compendial Uses

1. Use as a stimulation test to confirm the diagnosis of CPP
2. Use in combination with growth hormone for children with growth failure and advancing puberty
3. Prostate cancer
4. Inhibition of premature luteinizing hormone (LH) surges in women undergoing assisted reproductive technology
5. Metastatic androgen receptor positive salivary gland tumors
6. Triggering of follicle maturation and ovulation in assisted reproductive technology cycle

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Central precocious puberty (CPP)**

1. Authorization up to age 12 may be granted for the treatment of CPP in a female member when all of the following criteria are met:
 - a. Intracranial tumor has been evaluated by appropriate lab tests and diagnostic imaging, such as computed tomography (CT scan), magnetic resonance imaging (MRI), or ultrasound.
 - b. The diagnosis of CPP has been confirmed by a pubertal response to a gonadotropin releasing hormone (GnRH) agonist test or a pubertal level of a third generation luteinizing hormone (LH) assay.
 - c. The assessment of bone age versus chronological age supports the diagnosis of CPP.
 - d. The member was less than 8 years of age at the onset of secondary sexual characteristics.
2. Authorization up to age 13 may be granted for the treatment of CPP in a male member when all of the following criteria are met:
 - a. Intracranial tumor has been evaluated by appropriate lab tests and diagnostic imaging, such as CT scan, MRI, or ultrasound.
 - b. The diagnosis of CPP has been confirmed by a pubertal response to a GnRH agonist test or a pubertal level of a third generation LH assay.
 - c. The assessment of bone age versus chronological age supports the diagnosis of CPP.
 - d. The member was less than 9 years of age at the onset of secondary sexual characteristics.

B. Stimulation test for CPP diagnosis

Authorization of one dose may be granted for use as a stimulation test to confirm the diagnosis of CPP.

C. Advancing puberty and growth failure

Authorization of 12 months may be granted for the treatment of advancing puberty and growth failure in a pediatric member when leuprolide acetate is used in combination with growth hormone.

D. Prostate cancer

Authorization of 12 months may be granted for treatment of prostate cancer.

E. Salivary gland tumors

Authorization of 12 months may be granted for treatment of metastatic salivary gland tumors when the tumor is androgen receptor positive.

F. Inhibition of premature luteinizing hormone (LH) surge[‡]

Authorization of 12 months may be granted for the inhibition of premature LH surge in a member undergoing ovulation induction or assisted reproductive technology (ART).

G. Oocyte maturation and ovulation trigger[‡]

Authorization of 12 months may be granted for members undergoing ovulation induction or assisted reproductive technology (ART)

[‡] Specialty Guideline Management coverage review will be bypassed for leuprolide if it is being requested for a procedure that has been approved under a member's medical benefit plan. Such members will be exempt from the requirements in Section II. A medical authorization number and confirmation of the approved procedure(s) will be required. *NOTE: Some plans may opt-out of medical benefit alignment. Members receiving coverage under such plans must meet the requirements in Section II.*

III. CONTINUATION OF THERAPY

A. Central precocious puberty (CPP)

1. Authorization up to age 12 may be granted for continuation of therapy for CPP in a female member if the member is currently less than 12 years of age.
2. Authorization up to age 13 may be granted for continuation of therapy for CPP in a male member if the member is currently less than 13 years of age.

B. Prostate cancer, stimulation test for CPP diagnosis, advancing puberty and growth failure, salivary gland tumors, inhibition of premature LH surge, and oocyte maturation and ovulation trigger.

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

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SPECIALTY GUIDELINE MANAGEMENT

FUSILEV (levoleucovorin) powder KHAPZORY (levoleucovorin) powder levoleucovorin solution

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications¹⁻³

1. Levoleucovorin/Fusilev/Khapzory is indicated for rescue after high-dose methotrexate therapy in osteosarcoma.
2. Levoleucovorin/Fusilev/Khapzory is indicated for diminishing the toxicity and counteracting the effects of impaired methotrexate elimination and of inadvertent overdosage of folic acid antagonists.
3. Fusilev is indicated for use in combination chemotherapy with 5-fluorouracil in the palliative treatment of patients with advanced metastatic colorectal cancer.
4. Khapzory is indicated for use in combination chemotherapy with fluorouracil for treatment of metastatic colorectal cancer.

B. Compendial Uses⁴⁻²⁰

1. Rescue treatment after high-dose methotrexate therapy in osteosarcoma, dedifferentiated chondrosarcoma, high-grade undifferentiated pleomorphic sarcoma, peripheral T-cell lymphomas, adult T-cell leukemia/lymphoma, nasal type extranodal NK/T-cell lymphoma, mantle cell lymphoma, AIDS-related B-cell lymphomas, Burkitt lymphoma, acute lymphoblastic leukemia, primary CNS lymphoma, brain metastases, leptomeningeal metastases, gestational trophoblastic neoplasia, follicular lymphoma, diffuse large B-cell lymphoma, high-grade B-cell lymphoma, rhabdomyosarcoma, chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), and hepatosplenic gamma-delta T-cell lymphoma.
2. Used in combination with fluorouracil based regimens for colorectal cancer, gastric adenocarcinoma, esophageal/esophagogastric junction cancer, pancreatic cancer, thymomas/thymic carcinomas, cervical cancer, anal adenocarcinoma, occult primary, mucinous ovarian carcinomas, bladder cancer, and neuroendocrine and adrenal tumors when leucovorin is not an available option.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL¹⁻²⁰

Authorization of 3 months may be granted for any of the indications listed below when leucovorin is not an appropriate/available option at this time:

- A. Rescue treatment after high-dose methotrexate therapy
- B. Treatment of a folate antagonist overdose
- C. Combination therapy with fluorouracil based chemotherapy regimens

Reference number(s)
1661-A

III. REFERENCES

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SPECIALTY GUIDELINE MANAGEMENT

LIBTAYO (cemiplimab-rwlc)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Libtayo is indicated for the treatment of patients with metastatic cutaneous squamous cell carcinoma (CSCC) or locally advanced CSCC who are not candidates for curative surgery or curative radiation.

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

Coverage will not be provided for members who have experienced disease progression while on programmed death receptor-1 (PD-1) or programmed death ligand 1 (PD-L1) inhibitor therapy.

III. CRITERIA FOR INITIAL APPROVAL

Cutaneous squamous cell carcinoma

Authorization of 6 months may be granted for treatment of cutaneous squamous cell carcinoma when all of the following criteria are met:

- A. The disease is metastatic or locally advanced
- B. The member is not a candidate for curative surgery or curative radiation

IV. CONTINUATION OF THERAPY

Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES

1. Libtayo [package insert]. Tarrytown, NY: Regeneron Pharmaceuticals, Inc.; September 2018.

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	LONG ACTING INSULIN /GLP-1 AGONIST
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BRAND NAME (generic)	
---------------------------------	--

	SOLIQUA (insulin glargine/lixisenatide injection)
--	--

	XULTOPHY (insulin degludec/liraglutide injection)
--	--

Status: CVS Caremark Criteria Type: Initial Prior Authorization
--

POLICY

FDA-APPROVED INDICATIONS

Soliqua

Soliqua is a combination of insulin glargine and lixisenatide and is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use

- Soliqua has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.
- Soliqua is not recommended for use in combination with any other product containing a GLP-1 receptor agonist.
- Soliqua is not indicated for use in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis.
- Soliqua has not been studied in patients with gastroparesis and is not recommended in patients with gastroparesis.
- Soliqua has not been studied in combination with prandial insulin.

Xultophy

Xultophy is a combination of insulin degludec and liraglutide, and is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use

- Xultophy is not recommended as first line therapy for patients who have inadequate glycemic control on diet and exercise because of the uncertain relevance of the rodent C-cell tumor findings to humans.
- Xultophy is not recommended for use in combination with any other product containing liraglutide or another GLP-1 receptor agonist.
- Xultophy is not indicated for use in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis.
- Xultophy has not been studied in combination with prandial insulin.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has been receiving the requested drug for at least 3 months and has demonstrated a reduction in A1c (hemoglobin A1c) since starting combination insulin and GLP-1 Agonist therapy

OR

- The patient has a diagnosis of type 2 diabetes mellitus

AND

- The patient has experienced an inadequate treatment response, intolerance, or contraindication to metformin

OR

- The patient requires combination therapy AND has an A1c (hemoglobin A1c) of 7.5 percent or greater

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PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	LONG ACTING INSULIN /GLP-1 AGONIST
-------------------	---

BRAND NAME (generic)	SOLIQUA (insulin glargine/lixisenatide injection)
	XULTOPHY (insulin degludec/liraglutide injection)

Status: CVS Caremark Criteria

Type: Initial Prior Authorization with Quantity Limit

POLICY

FDA-APPROVED INDICATIONS

Soliqua

Soliqua is a combination of insulin glargine and lixisenatide and is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use

- Soliqua has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.
- Soliqua is not recommended for use in combination with any other product containing a GLP-1 receptor agonist.
- Soliqua is not indicated for use in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis.
- Soliqua has not been studied in patients with gastroparesis and is not recommended in patients with gastroparesis.
- Soliqua has not been studied in combination with prandial insulin.

Xultophy

Xultophy is a combination of insulin degludec and liraglutide, and is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use

- Xultophy is not recommended as first line therapy for patients who have inadequate glycemic control on diet and exercise because of the uncertain relevance of the rodent C-cell tumor findings to humans.
- Xultophy is not recommended for use in combination with any other product containing liraglutide or another GLP-1 receptor agonist.
- Xultophy is not indicated for use in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis.
- Xultophy has not been studied in combination with prandial insulin.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has been receiving the requested drug for at least 3 months and has demonstrated a reduction in A1c (hemoglobin A1c) since starting combination insulin and GLP-1 Agonist therapy.

OR

- The patient has a diagnosis of type 2 diabetes mellitus

AND

- The patient has experienced an inadequate treatment response, intolerance, or contraindication to metformin

OR

- The patient requires combination therapy AND has an A1c (hemoglobin A1c) of 7.5 percent or greater

Quantity Limits apply.

At maximum approved dosing for Soliqua 10 prefilled pens (2 packages of 5 x 3mL), a total of 10 pens (30mL) will be allowed for a 30 day supply. At maximum approved dosing for Xultophy 5 prefilled pens (1 package of 5 x 3mL), a total of 5 pens (15mL) will be allowed for a 30 day supply.

REFERENCES

1. Soliqua [package insert]. Bridgewater, NJ: Sanofi-aventis U.S. LLC; March 2019.
2. Xultophy [package insert]. Plainsboro, NJ: Novo Nordisk U.S. LLC; February 2019.
3. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed July 2019.
4. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed July 2019.
5. American Diabetes Association (ADA) Standards of Medical Care in Diabetes-2019—*Diabetes Care*. 2019; 42(Supplement 1).
6. Garber AJ, et al. AACE/ACE Consensus Statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the Comprehensive Type 2 Diabetes Management Algorithm 2019, *Endocr Pract*. 2019; 25 (No 1). 69-100

SPECIALTY GUIDELINE MANAGEMENT

LONSURF (trifluridine and tipiracil)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Lonsurf is indicated for the treatment of adult patients with metastatic colorectal cancer previously treated with fluoropyrimidine-, oxaliplatin-and irinotecan-based chemotherapy, an anti-VEGF biological therapy, and if RAS wild-type, an anti-EGFR therapy.

Lonsurf is indicated for the treatment of adult patients with metastatic gastric or gastroesophageal junction adenocarcinoma previously treated with at least two prior lines of chemotherapy that included a fluoropyrimidine, a platinum, either a taxane or irinotecan, and if appropriate, HER2/neu-targeted therapy.

B. Compendial Uses

1. Unresectable advanced or metastatic colon cancer
2. Rectal cancer
3. Esophageal and esophagogastric junction cancers
4. Gastric cancer

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Colorectal cancer (CRC)**

Authorization of 12 months may be granted for treatment of unresectable advanced or metastatic colorectal cancer in members when the following criteria are met:

1. Member was previously treated with fluoropyrimidine-, oxaliplatin-and irinotecan-based chemotherapy;
AND
2. An anti-VEGF biological therapy; AND
3. If member is RAS wild type, failure of a cetuximab or panitumumab-containing regimen.

B. **Gastric or Gastroesophageal Junction Adenocarcinoma**

Authorization of 12 months may be granted for treatment of unresectable locally advanced, recurrent, or metastatic gastric or gastroesophageal junction adenocarcinoma when the member has been previously treated with at least two prior lines of chemotherapy.

III. CONTINUATION OF THERAPY

Reference number(s)
1896-A

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced disease progression or an unacceptable toxicity.

IV. REFERENCES

1. Lonsurf [package insert]. Princeton, NJ: Taiho Oncology, Inc.; February 2019.
2. The NCCN Drugs & Biologics Compendium 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed July 10, 2019.

SPECIALTY GUIDELINE MANAGEMENT

LORBRENA (lorlatinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Lorbrena is a kinase inhibitor indicated for the treatment of patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC) whose disease has progressed on:

- Crizotinib and at least one other ALK inhibitor for metastatic disease; or
- Alectinib as the first ALK inhibitor therapy for metastatic disease; or
- Ceritinib as the first ALK inhibitor therapy for metastatic disease

This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

B. Compendial Uses

Single-agent therapy for recurrent, advanced or metastatic NSCLC in patients with:

1. ALK rearrangement-positive tumors, following disease progression on:
 - a. Brigatinib as the first ALK inhibitor therapy for metastatic disease or
 - b. Crizotinib as the first ALK inhibitor therapy for metastatic disease and subsequent therapy with crizotinib for asymptomatic disease or isolated systemic lesion; or
2. ROS1 rearrangement-positive tumors, following disease progression on crizotinib, entrectinib or ceritinib

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Chart documentation indicating ALK mutation status or ROS-1 rearrangement status as applicable to Section III.

III. CRITERIA FOR INITIAL APPROVAL

Non-small cell lung cancer (NSCLC)

- A. Authorization of 12 months may be granted for treatment of recurrent, advanced or metastatic NSCLC as a single-agent therapy when all of the following criteria are met:
 1. The disease is ALK-positive
 2. The disease has progressed on any of the following: alectinib, brigatinib, ceritinib, or crizotinib.

Reference number(s)
2787-A

- B. Authorization of 12 months may be granted for treatment of recurrent, advanced or metastatic NSCLC as a single-agent therapy when all of the following criteria are met:
1. The disease is ROS1 rearrangement-positive
 2. The disease has progressed on any of the following: certinib, crizotinib, or entrectinib.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES

1. Lorbrena [package insert]. New York, NY: Pfizer, Inc.; November 2018.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed September 12, 2019.
3. The NCCN Clinical Practice Guidelines in Oncology® Non-Small Cell Lung Cancer. (Version 7.2019). © 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed September 12, 2019.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

LOTRONEX
(alosecron)

Status: CVS Caremark Criteria

Type: Initial Prior Authorization

Ref # 129-A

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated*

FDA-APPROVED INDICATIONS

Lotronex is indicated only for women with severe diarrhea-predominant irritable bowel syndrome (IBS) who have:

- chronic IBS symptoms (generally lasting six months or longer),
- had anatomic or biochemical abnormalities of the gastrointestinal tract excluded, and
- not responded adequately to conventional therapy

Diarrhea-predominant IBS is severe if it includes diarrhea and one or more of the following:

- frequent and severe abdominal pain/discomfort
- frequent bowel urgency or fecal incontinence
- disability or restriction of daily activities due to IBS

Because of infrequent but serious gastrointestinal adverse events associated with Lotronex, the indication is restricted to those patients for whom the benefit-to-risk balance is most favorable.

Clinical studies have not been performed to adequately confirm the benefits of Lotronex in men.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for a biological female or a person that self-identifies as a female with a diagnosis of severe diarrhea-predominant irritable bowel syndrome (IBS) AND all of the following apply: A) Chronic IBS symptoms lasting at least 6 months, B) Gastrointestinal tract abnormalities have been ruled out, C) Inadequate response to conventional therapy

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Lotronex is indicated only for women with severe diarrhea-predominant irritable bowel syndrome (IBS) who have: chronic IBS symptoms (generally lasting six months or longer), had anatomic or biochemical abnormalities of the gastrointestinal tract excluded, and not responded adequately to conventional therapy

Diarrhea-predominant IBS is severe if it includes diarrhea and one or more of the following: frequent and severe abdominal pain/discomfort, frequent bowel urgency or fecal incontinence, disability or restriction of daily activities due to IBS.

REFERENCES

1. Lotronex [package insert]. San Diego, CA: Prometheus Laboratories Inc.; July 2016.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed September 2018.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed September 2018.

Written by: UM Development (LS)
Date Written: 09/2003
Revised: (JG) 11/2002; (MG) 08/2003; (CM) 09/2004; (JG) 10/2005; (CT) 06/2006, 05/2007, 06/2008, 06/2009, 06/2010, 07/2011, 07/2012; 10/2012 (extended duration), 08/2013; (JH) 08/2014, 08/2015; (KM) 08/2016 (removed safety question, removed female from question 1), 09/2016 (updated wording of criteria for approval to not discriminate for TGC patients); (DS) 08/2017 (no clinical changes); (JG) 09/2018 (no clinical changes)
Reviewed: Medical Affairs 02/11/2000, 08/2000, 11/2002, 08/2003; (MM) 10/2004, 10/2005, 06/2006; (WF) 05/2007, 06/2008, 06/2009; (KP) 06/2010, 07/2011, (LB) 07/2012; (KP) 08/2013; (KC) 08/2014; (MC) 08/2015; (ME) 08/2016
External Review: 02/2003, 10/2003, 11/2004, 12/2006, 12/2007, 12/2008, 12/2009, 02/2011, 02/2012, 04/2013, 12/2013, 12/2014, 12/2015, 12/2016, 11/2017, 12/2018

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for a biological female or a person that self-identifies as a female with a diagnosis of severe diarrhea-predominant irritable bowel syndrome (IBS) AND do all of the following apply: A) Chronic IBS symptoms lasting at least 6 months, B) Gastrointestinal tract abnormalities have been ruled out, C) Inadequate response to conventional therapy?	Yes	No
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Mapping Instructions			
	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Approve, 36 months	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you are a biological female or you self-identify as female with severe diarrhea-predominant irritable bowel syndrome (IBS) and all of the following:</p> <ul style="list-style-type: none"> – You have had IBS symptoms for at least 6 months – Gastrointestinal tract abnormalities have been ruled out – Other therapies did not work for you <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No approvable diagnosis]</p>

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

LOTRONEX
(alosectron)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

Ref# 129-A
Ref# 690-A

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Lotronex is indicated only for women with severe diarrhea-predominant irritable bowel syndrome (IBS) who have:

- chronic IBS symptoms (generally lasting six months or longer),
- had anatomic or biochemical abnormalities of the gastrointestinal tract excluded, and
- not responded adequately to conventional therapy

Diarrhea-predominant IBS is severe if it includes diarrhea and one or more of the following:

- frequent and severe abdominal pain/discomfort
- frequent bowel urgency or fecal incontinence
- disability or restriction of daily activities due to IBS

Because of infrequent but serious gastrointestinal adverse events associated with Lotronex, the indication is restricted to those patients for whom the benefit-to-risk balance is most favorable.

Clinical studies have not been performed to adequately confirm the benefits of Lotronex in men.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for a biological female or a person that self-identifies as a female with a diagnosis of severe diarrhea-predominant irritable bowel syndrome (IBS)

AND

- The patient has experienced chronic irritable bowel syndrome (IBS) symptoms lasting at least 6 months

AND

- Gastrointestinal tract abnormalities have been ruled out

AND

- The patient has had an inadequate response to conventional therapy

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Lotronex is indicated only for women with severe diarrhea-predominant irritable bowel syndrome (IBS) who have: chronic IBS symptoms (generally lasting six months or longer), had anatomic or biochemical abnormalities of the gastrointestinal tract excluded, and not responded adequately to conventional therapy.

Because of infrequent but serious gastrointestinal adverse events associated with Lotronex, the indication is restricted to those patients for whom the benefit-to-risk balance is most favorable. Clinical studies have not been performed to adequately confirm the benefits of Lotronex in men.

REFERENCES

1. Lotronex [package insert]. Roswell, GA: Sebela Pharmaceuticals Inc.; April 2019.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed August 2019.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed August 2019.

Written by: UM Development (LS)
 Date Written: 09/2003
 Revised: (JG) 11/2002; (MG) 08/2003; (CM) 09/2004; (JG) 10/2005; (CT) 06/2006, 05/2007, 06/2008, 06/2009, 06/2010, 07/2011, 07/2012; 10/2012 (extended duration), 08/2013; (JH) 08/2014, 08/2015; (KM) 08/2016 (removed safety question, removed female from question 1), 09/2016 (updated wording of criteria for approval to not discriminate for TGC patients); (DS) 08/2017 (no clinical changes); (JG) 09/2018 (no clinical changes); (DS) 09/2019 (no clinical changes; combined criteria; removed MDC)
 Reviewed: Medical Affairs 02/11/2000, 08/2000, 11/2002, 08/2003; (MM) 10/2004, 10/2005, 06/2006; (WF) 05/2007, 06/2008, 06/2009; (KP) 06/2010, 07/2011, (LB) 07/2012; (KP) 08/2013; (KC) 08/2014; (MC) 08/2015; (ME) 08/2016; (CHART) 09/26/2019
 External Review: 02/2003, 10/2003, 11/2004, 12/2006, 12/2007, 12/2008, 12/2009, 02/2011, 02/2012, 04/2013, 12/2013, 12/2014, 12/2015, 12/2016, 12/2017, 12/2018, 12/2019

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for a biological female or a person that self-identifies as a female with a diagnosis of severe diarrhea-predominant irritable bowel syndrome (IBS)?	Yes	No
2	Has the patient experienced chronic irritable bowel syndrome (IBS) symptoms lasting at least 6 months?	Yes	No
3	Have gastrointestinal tract abnormalities been ruled out?	Yes	No
4	Has the patient had an inadequate response to conventional therapy?	Yes	No

Mapping Instructions (129-A)

	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you are a biological female or you self-identify as female with severe diarrhea-predominant irritable bowel syndrome (IBS). Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
2.	Go to 3	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have had IBS symptoms for at least 6 months. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
3.	Go to 4	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have had gastrointestinal tract abnormalities ruled out. Your request has been denied based on the information we have.

			[Short Description: No approvable diagnosis]
4.	Approve, 36 months	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when other therapies did not work for you.</p> <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No approvable diagnosis]</p>

Mapping Instructions (690-A)			
	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you are a biological female or you self-identify as female with severe diarrhea-predominant irritable bowel syndrome (IBS).</p> <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No approvable diagnosis]</p>
2.	Go to 3	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you have had IBS symptoms for at least 6 months.</p> <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No approvable diagnosis]</p>
3.	Go to 4	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you have had gastrointestinal tract abnormalities ruled out.</p> <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No approvable diagnosis]</p>
4.	Approve, 12 months	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when other therapies did not work for you.</p> <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No approvable diagnosis]</p>

PRIOR AUTHORIZATION CRITERIA

BRAND NAME LUCENTIS
(generic) (ranibizumab)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

MDC
Ref # 883-A

FDA-APPROVED INDICATIONS¹

Lucentis is indicated for the treatment of patients with: neovascular (wet) age-related macular degeneration (AMD), macular edema following retinal vein occlusion (RVO), diabetic macular edema (DME), diabetic retinopathy (DR), or myopic choroidal neovascularization (mCNV).

CRITERIA FOR APPROVAL

1	Does the patient have a diagnosis of neovascular (wet) age-related macular degeneration (AMD)? [If yes, no further questions.]	Yes	No
2	Does the patient have a diagnosis of macular edema following retinal vein occlusion (RVO)? [If yes, no further questions.]	Yes	No
3	Does the patient have a diagnosis of diabetic macular edema (DME)? [If yes, no further questions.]	Yes	No
4	Does the patient have a diagnosis of diabetic retinopathy (DR)? [If yes, no further questions.]	Yes	No
5	Does the patient have a diagnosis of myopic choroidal neovascularization (mCNV)?	Yes	No

Guidelines for Approval

Duration of Approval				12 Months	
Set 1: AMD		Set 2: Macular edema RVO		Set 3: DME	
Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)
1	None	2	1	3	1
					2
Set 4: DR		Set 5: mCNV			
Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)		
4	1	5	1		
	2		2		
	3		3		
			4		

Mapping Instructions

	Yes	No
1.	Approve, 12 months	Go to 2

Mapping Instructions		
	Yes	No
2.	Approve, 12 months	Go to 3
3.	Approve, 12 months	Go to 4
4.	Approve, 12 months	Go to 5
5.	Approve, 12 months	Deny

RATIONALE

These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to ensure that patients follow selection elements noted in labeling and/or practice guidelines in order to decrease the potential for inappropriate utilization.

REFERENCES

1. Lucentis [package insert]. South San Francisco, CA: Genentech, Inc.; March 2018.

DOCUMENT HISTORY

Written: Specialty Clinical Development (AS) 01/2007
Revised: AC (adapted from SGM) 09/2012; WH 02/2013, 09/2013 (adapted from SGM); KF 01/2014, KF09/2014 (CMS), TS 02/2015, TS 08/2015 (CMS), PK 02/2016, TS 06/2016 (CMS), CN 04/2017 (label update), PK 07/2017 (CMS), TE 02/2018, TE 07/2018 (CMS), DG 06/2019 (CMS)
Reviewed: CDPR/KP 03/2012; DNC 09/2012, 02/2013; LMS 09/2013; DNC 01/2014, 03/2015, LCB 02/2016, SD 04/2017, LMS 02/2018
External Review: 04/2012, 06/2013, 04/2014, 04/2015, 04/2016, 05/2017, 05/2018

SPECIALTY GUIDELINE MANAGEMENT

LUCENTIS (ranibizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

- A. Diabetic macular edema
- B. Neovascular (wet) age-related macular degeneration
- C. Macular edema following retinal vein occlusion
- D. Diabetic retinopathy
- E. Myopic choroidal neovascularization

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Diabetic Macular Edema

Authorization of 6 months may be granted for treatment of diabetic macular edema.

B. Neovascular (Wet) Age-Related Macular Degeneration

Authorization of 6 months may be granted for treatment of neovascular (wet) age-related macular degeneration.

C. Macular Edema Following Retinal Vein Occlusion

Authorization of 6 months may be granted for treatment of macular edema following retinal vein occlusion.

D. Diabetic Retinopathy

Authorization of 6 months may be granted for treatment of diabetic retinopathy.

E. Myopic Choroidal Neovascularization

Authorization of 6 months may be granted for treatment of myopic choroidal neovascularization.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment of an indication listed in Section II for members who have demonstrated a positive clinical response to therapy (e.g., improvement or maintenance in best corrected visual acuity [BCVA] or visual field, or a reduction in the rate of vision decline or the risk of more severe vision loss).

IV. REFERENCES

1. Lucentis [package insert]. South San Francisco, CA: Genentech, Inc.; March 2018.
2. American Academy of Ophthalmology Retinal/Vitreous Panel. Preferred Practice Pattern® Guidelines. Age-Related Macular Degeneration. San Francisco, CA: American Academy of Ophthalmology; 2015. Available at: <https://www.aao.org/preferred-practice-pattern/age-related-macular-degeneration-ppp-2015>
3. American Academy of Ophthalmology Retinal/Vitreous Panel. Preferred Practice Pattern® Guidelines. Diabetic Retinopathy. San Francisco, CA: American Academy of Ophthalmology; 2017. Available at: <https://www.aao.org/preferred-practice-pattern/diabetic-retinopathy-ppp-updated-2017>
4. American Academy of Ophthalmology Retinal/Vitreous Panel. Preferred Practice Pattern® Guidelines. Retinal Vein Occlusions. San Francisco, CA: American Academy of Ophthalmology; 2015. Available at: <https://www.aao.org/preferred-practice-pattern/retinal-vein-occlusions-ppp-2015>
5. Larsen M, Waldstein SM, Boscia F, et al.; CRYSTAL Study Group. Individualized ranibizumab regimen driven by stabilization criteria for central retinal vein occlusion: twelve-month results of the CRYSTAL study. Ophthalmology. 2016 May;123(5):1101-11. URL: <https://www.ncbi.nlm.nih.gov/pubmed/?term=26896124>. Accessed May 26, 2017.
6. Sepah YJ, Sadiq MA, Boyer D, et al.; READ-3 Study Group. Twenty-four-month outcomes of the ranibizumab for edema of the macula in diabetes – Protocol 3 with high dose (READ-3) study. Ophthalmology. 2016 Dec;123(12):2581-2587. URL: <https://www.ncbi.nlm.nih.gov/pubmed/?term=27707550>. Accessed May 26, 2017.
7. Tadayoni R, Waldstein SM, Boscia F, et al; BRIGHTER study group. Individualized stabilization criteria-driven ranibizumab versus laser in branch retinal vein occlusion: six-month results of BRIGHTER. Ophthalmology. 2016 Jun;123(6):1332-44. URL: <https://www.ncbi.nlm.nih.gov/pubmed/?term=27039022>. Accessed May 26, 2017.

SPECIALTY GUIDELINE MANAGEMENT

LUMIZYME (alglucosidase alfa)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Lumizyme is indicated for patients with Pompe disease (acid alpha-glucosidase [GAA] deficiency).

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: acid alpha-glucosidase enzyme assay or genetic testing results supporting diagnosis.

III. CRITERIA FOR INITIAL APPROVAL

Pompe disease

Authorization of 12 months may be granted for treatment of Pompe disease when the diagnosis of Pompe disease was confirmed by enzyme assay demonstrating a deficiency of acid alpha-glucosidase enzyme activity or by genetic testing.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for Pompe disease who are responding to therapy (e.g., improvement, stabilization, or slowing of disease progression for motor function, walking capacity, cardiorespiratory function, decrease in left ventricular mass index (LVMI), delay in death).

V. REFERENCES

1. Lumizyme [package insert]. Cambridge, MA: Genzyme Corporation; August 2014.

SPECIALTY GUIDELINE MANAGEMENT

LUMOXITI (moxetumomab pasudotox-tdfk)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Lumoxiti is a CD22-directed cytotoxin indicated for the treatment of adult patients with relapsed or refractory hairy cell leukemia (HCL) who received at least two prior systemic therapies, including treatment with a purine nucleoside analog (PNA).

Limitations of use

Lumoxiti is not recommended in patients with severe renal impairment ($\text{CrCl} \leq 29 \text{ mL/min}$).

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Hairy Cell Leukemia

Authorization of 6 months may be granted for treatment of relapsed or refractory hairy cell leukemia when all of the following criteria are met:

- A. Member has received at least two prior systemic therapies, including treatment with a purine nucleoside analog.
- B. Member has not previously received 6 or more cycles of treatment with the requested medication.

III. CONTINUATION OF THERAPY

Authorization of up to 6 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when all of the following criteria are met:

- A. Member has not previously received 6 or more cycles of treatment with the requested medication.
- B. Member has not experienced disease progression or an unacceptable toxicity.

IV. REFERENCES

1. Lumoxiti [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; January 2019.

SPECIALTY GUIDELINE MANAGEMENT

LUPANETA PACK-1 Month 3.75 mg LUPANETA PACK-3 Month 11.25 mg (leuprolide acetate for depot suspension/norethindrone acetate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Lupaneta Pack is indicated for initial management of the painful symptoms of endometriosis and for management of recurrence of symptoms.

Limitations of Use: Duration of use is limited due to concerns about adverse impact on bone mineral density. The initial treatment course of Lupaneta Pack is limited to six months. A single retreatment course of not more than six months may be administered after the initial course of treatment if symptoms recur. Use of Lupaneta Pack for longer than a total of 12 months is not recommended.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Endometriosis

Authorization of up to 6 months (one treatment course) may be granted to members for initial treatment of endometriosis.

III. CONTINUATION OF THERAPY

Endometriosis

Authorization of up to 6 months (for a lifetime maximum of 12 months total) may be granted for retreatment of endometriosis when all of the following criteria are met:

- A. The member has had a recurrence of symptoms
- B. The member has a bone mineral density within normal limits

IV. REFERENCES

1. Lupaneta Pack [package insert]. North Chicago, IL: AbbVie Inc.; June 2015.

SPECIALTY GUIDELINE MANAGEMENT

LUPRON DEPOT 3.75 mg LUPRON DEPOT-3 Month 11.25 mg (leuprolide acetate for depot suspension)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Lupron Depot 3.75 mg and Lupron Depot-3 Month 11.25 mg are indicated for management of endometriosis, including pain relief and reduction of endometriotic lesions. Lupron Depot 3.75 mg monthly and Lupron Depot-3 Month 11.25 mg with norethindrone acetate 5 mg daily are also indicated for initial management of endometriosis and for management of recurrence of symptoms. Duration of initial treatment or retreatment should be limited to six months.
2. When used concomitantly with iron therapy, Lupron Depot 3.75 mg and Lupron Depot-3 Month 11.25 mg are indicated for the preoperative hematologic improvement of patients with anemia caused by uterine leiomyomata. The clinician may wish to consider a one-month trial period on iron alone inasmuch as some of the patients will respond to iron alone. Lupron may be added if the response to iron alone is considered inadequate. Recommended duration of therapy is up to 3 months, either given as Lupron Depot 3.75 mg monthly or as a single injection of Lupron Depot-3 Month 11.25 mg. Lupron Depot-3 Month 11.25 mg is indicated only for women for whom three months of hormonal suppression is deemed necessary.

Experience with Lupron Depot in females has been limited to women 18 years of age and older, and experience with the Lupron Depot-3 Month 11.25 mg formulation has been limited to treatment for no more than six months.

B. Compendial Uses

1. Breast cancer
2. Ovarian Cancer
 - a. Epithelial ovarian cancer/fallopian tube cancer/primary peritoneal cancer
 - b. Malignant sex cord-stromal tumors
3. Preoperative use in uterine leiomyomata (fibroids) to facilitate surgery
4. Gender dysphoria (also known as gender non-conforming or transgender persons)

NOTE: Some plans may opt-out of coverage for gender dysphoria.
5. Preservation of ovarian function^{9,10}
6. Prevention of recurrent menstrual related attacks in acute porphyria

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Endometriosis

Authorization of up to 6 months (one treatment course) may be granted to members for initial treatment of endometriosis.

B. Uterine leiomyomata (fibroids)

Authorization of up to 3 months may be granted for initial treatment of uterine leiomyomata (fibroids) when either of the following criteria is met:

1. Member has anemia due to uterine leiomyomata, or
2. Lupron Depot will be used prior to surgery for uterine leiomyomata.

C. Breast cancer

Authorization of 12 months may be granted for treatment of hormone receptor-positive breast cancer.

D. Ovarian cancer

1. Authorization of 12 months may be granted for treatment of epithelial ovarian cancer, fallopian tube cancer, or primary peritoneal cancer.
2. Authorization of 12 months may be granted for treatment of malignant sex cord-stromal tumors.

E. Gender dysphoria

1. Authorization of 12 months may be granted for pubertal suppression in preparation for gender reassignment in an adolescent member when all of the following criteria are met:
 - a. The member has a diagnosis of gender dysphoria.
 - b. The member has reached Tanner stage 2 of puberty.
2. Authorization of 12 months may be granted for gender reassignment in an adult member when all of the following criteria are met:
 - a. The member has a diagnosis of gender dysphoria.
 - b. The member will receive Lupron Depot concomitantly with cross sex hormones.

F. Preservation of ovarian function

Authorization of 3 months may be granted for preservation of ovarian function when the member is premenopausal and undergoing chemotherapy.

G. Prevention of recurrent menstrual related attacks in acute porphyria

Authorization of 12 months may be granted for prevention of recurrent menstrual related attacks in members with acute porphyria when the requested medication is prescribed by or in consultation with a physician experienced in the management of porphyrias.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria in addition to the following diagnosis-specific criteria (if applicable).

A. Endometriosis

Authorization of up to 6 months (for a lifetime maximum of 12 months total) may be granted for retreatment of endometriosis when all of the following criteria are met:

1. The member has had a recurrence of symptoms.
2. The member has a bone mineral density within normal limits.

B. Uterine leiomyomata (fibroids)

Authorization of up to 3 months (for a lifetime maximum of 6 months total) may be granted when either of the following criteria is met:

1. Member has anemia due to uterine leiomyomata, or
2. Lupron Depot will be used prior to surgery for uterine leiomyomata.

C. All other indications

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Lupron Depot 3.75 mg [package insert]. North Chicago, IL: AbbVie Inc.; October 2013.
2. Lupron Depot-3 Month 11.25 mg [package insert.]. North Chicago, IL: AbbVie Inc.; April 2018.
3. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed May 22, 2019.
4. Alternatives to hysterectomy in the management of leiomyomas. ACOG Practice Bulletin No. 96. American College of Obstetricians and Gynecologists. *Obstet Gynecol*. 2008;112:387-400.
5. Marret H, Fritel X, Ouldamer L, et al. Therapeutic management of uterine fibroid tumors: updated French guidelines. *European Journal of Obstetrics and Gynecology and Reproductive Biology*. 2012;165:156-164.
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7. Gender Identity Research and Education Society. Guidance for GPs and other clinicians on the treatment of gender variant people. UK Department of Health. Published March 10, 2008.
8. Standards of care for the health of transsexual, transgender, and gender-nonconforming people, 7th version. ©2012 World Professional Association for Transgender Health. Available at <http://www.wpath.org>.
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11. Stein P, Badminton M, Barth J, Rees D, Stewart MF; British and Irish Porphyria Network. Best practice guidelines on clinical management of acute attacks of porphyria and their complications. *Ann Clin Biochem*. 2013 May;50(Pt 3):217-23.
12. Innala, E, Bäckström, T, Bixo, M, Andersson, C. Evaluation of gonadotrophin-releasing hormone agiist treatment for prevention of menstrual-related attacks in acute porphyria. *Acta Obstet Gynecol* 2010;89:95–100.

SPECIALTY GUIDELINE MANAGEMENT

LUPRON DEPOT 1-Month 7.5 mg LUPRON DEPOT 3-Month 22.5 mg LUPRON DEPOT 4-Month 30 mg LUPRON DEPOT 6-Month 45 mg (leuprolide acetate for depot suspension)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Lupron Depot 7.5 mg, Lupron Depot 3-Month 22.5 mg, Lupron Depot 4-Month 30 mg, and Lupron Depot 6-Month 45 mg are indicated in the palliative treatment of advanced prostate cancer.

B. Compendial Uses

1. Prostate cancer
2. Metastatic androgen receptor positive salivary gland tumor
3. Gender dysphoria (also known as gender non-conforming or transgender persons)

NOTE: Some plans may opt-out of coverage for gender dysphoria.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Prostate cancer

Authorization of 12 months may be granted for treatment of prostate cancer.

B. Gender dysphoria

1. Authorization of 12 months may be granted for pubertal suppression in preparation for gender reassignment in an adolescent member when all of the following criteria are met:
 - a. The member has a diagnosis of gender dysphoria.
 - b. The member has reached Tanner stage 2 of puberty.
2. Authorization of 12 months may be granted for gender reassignment in an adult member when all of the following criteria are met:
 - a. The member has a diagnosis of gender dysphoria.
 - b. The member will receive Lupron Depot concomitantly with cross sex hormones.

C. Salivary gland tumor

Authorization of 12 months may be granted for treatment of metastatic salivary gland tumors when the tumor is androgen receptor positive.

Reference number(s)
1971-A, 2087-A

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Lupron Depot 7.5 mg, 22.5, 30mg, 45mg [package insert]. North Chicago, IL: AbbVie Inc.; December 2018.
2. The NCCN Drugs & Biologics Compendium® © 2018 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed October 11, 2018.
3. National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology: prostate cancer. Version 4.2018. http://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed October 11, 2018.
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5. Gender Identity Research and Education Society. Guidance for GPs and other clinicians on the treatment of gender variant people. UK Department of Health. Published March 10, 2008.
6. Standards of care for the health of transsexual, transgender, and gender-nonconforming people, 7th version. ©2012 World Professional Association for Transgender Health. Available at <http://www.wpath.org>.
7. The NCCN Drugs & Biologics Compendium® © 2018 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed October 11, 2018.
8. National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology: head and neck tumors. Version 2.2018. http://www.nccn.org/professionals/physician_gls/pdf/head-and-neck.pdf. Accessed October 11, 2018.

SPECIALTY GUIDELINE MANAGEMENT

Lupron Depot-PED (leuprolide acetate for depot suspension)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Lupron Depot-PED is indicated for the treatment of children with central precocious puberty (CPP).

B. Compendial Use

Gender dysphoria (also known as gender non-conforming or transgender persons)

NOTE: Some plans may opt-out of coverage for gender dysphoria.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Central precocious puberty (CPP)**

1. Authorization up to age 12 may be granted for the treatment of CPP in a female member when all of the following criteria are met:
 - a. Intracranial tumor has been evaluated by appropriate lab tests and diagnostic imaging, such as computed tomography (CT scan), magnetic resonance imaging (MRI), or ultrasound.
 - b. The diagnosis of CPP has been confirmed by a pubertal response to a gonadotropin releasing hormone (GnRH) agonist test or a pubertal level of a third generation luteinizing hormone (LH) assay.
 - c. The assessment of bone age versus chronological age supports the diagnosis of CPP.
 - d. The member was less than 8 years of age at the onset of secondary sexual characteristics.
2. Authorization up to age 13 may be granted for the treatment of CPP in a male member when all of the following criteria are met:
 - a. Intracranial tumor has been evaluated by appropriate lab tests and diagnostic imaging, such as CT scan, MRI, or ultrasound.
 - b. The diagnosis of CPP has been confirmed by a pubertal response to a GnRH agonist test or a pubertal level of a third generation LH assay.
 - c. The assessment of bone age versus chronological age supports the diagnosis of CPP.
 - d. The member was less than 9 years of age at the onset of secondary sexual characteristics.

B. **Gender dysphoria**

1. Authorization of 12 months may be granted for pubertal suppression in preparation for gender reassignment in an adolescent member when all of the following criteria are met:
 - a. The member has a diagnosis of gender dysphoria.
 - b. The member has reached Tanner stage 2 of puberty.

2. Authorization of 12 months may be granted for gender reassignment in an adult member when all of the following criteria are met:
 - a. The member has a diagnosis of gender dysphoria.
 - b. The member will receive Lupron Depot-PED concomitantly with cross sex hormones.

III. CONTINUATION OF THERAPY

A. Central precocious puberty (CPP)

1. Authorization up to age 12 may be granted for continuation of therapy for CPP in a female member if the member is currently less than 12 years of age.
2. Authorization up to age 13 may be granted for continuation of therapy for CPP in a male member if the member is currently less than 13 years of age.

B. Gender Dysphoria

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Lupron Depot-PED [package insert]. North Chicago, IL: AbbVie Inc.; May 2017.
2. Kletter GB, Klein KO, Wong YY. A pediatrician's guide to central precocious puberty. *Clin Pediatr*. 2015;54:414-424.
3. Carel J, Eugster EA, Rogol A, et al. Consensus statement on the use of gonadotropin-releasing hormone analogs in children. *Pediatrics*. 2009;123:e752-e762.
4. Houk CP, Kunselman AR, Lee PA. Adequacy of a single unstimulated luteinizing hormone level to diagnose central precocious puberty in girls. *Pediatrics*. 2009;123:e1059-e1063.
5. Kaplowitz P, Bloch C, the Section on Endocrinology. Evaluation and referral of children with signs of early puberty. *Pediatrics*. 2016;137:e20153732.
6. Hembree WC, Cohen-Kettenis PT, Gooren L, et al. Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*. 2017;102(11):3869–3903.
7. Gender Identity Research and Education Society. Guidance for GPs and other clinicians on the treatment of gender variant people. UK Department of Health. Published March 10, 2008.
8. Standards of care for the health of transsexual, transgender, and gender-nonconforming people, 7th version. ©2012 World Professional Association for Transgender Health. Available at <http://www.wpath.org>.
9. Bangalor Krishna K, Fuqua JS, Rogol AD, et al. Use of gonadotropin-releasing hormone analogs in children: Update by an international consortium. *Horm Res Paediatr*. 2019 Jul 18:1-16. doi: 10.1159/000501336. [Epub ahead of print]

SPECIALTY GUIDELINE MANAGEMENT

LUTATHERA (lutetium Lu 177 dotatate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Treatment of somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs), including foregut, midgut, and hindgut neuroendocrine tumors in adults.

B. Compendial Uses

1. Carcinoid syndrome
2. Neuroendocrine tumors (NETs) of the lung and thymus (carcinoid tumors)
3. Pheochromocytoma/paraganglioma

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
Somatostatin receptor status as detected by somatostatin receptor-based imaging

III. CRITERIA FOR INITIAL APPROVAL

A. **Neuroendocrine tumors (NETs)**

1. Tumors of the gastrointestinal (GI) tract (carcinoid tumors)
Authorization of 12 months and 4 doses total may be granted for treatment of somatostatin receptor-positive NETs of the gastrointestinal tract when both of the following criteria are met:
 - a. Member has clinically significant tumor burden or progressive locoregional advanced disease and/or distant metastases.
 - b. Member experienced disease progression on octreotide or lanreotide.
2. Tumors of the pancreas
Authorization of 12 months and 4 doses total may be granted for treatment of somatostatin receptor-positive NETs of the pancreas when both of the following criteria are met:
 - a. Member has progressive locoregional advanced disease and/or distant metastases.
 - b. Member experienced disease progression on octreotide or lanreotide.
3. Neuroendocrine tumors (NETs) of the lung and thymus (carcinoid tumors)
Authorization of 12 months and 4 doses total may be granted for treatment of somatostatin receptor-positive NETs of the lung and thymus when all of the following criteria are met:
 - a. Member has locoregional unresectable or distant metastatic disease.

- b. Member experienced disease progression on octreotide or lanreotide.

B. Carcinoid Syndrome

Authorization of 12 months and 4 doses total may be granted for treatment of poorly controlled carcinoid syndrome when all of the following criteria are met:

1. Member has somatostatin receptor-positive neuroendocrine tumors of the gastrointestinal tract, lung or thymus.
2. Member experienced progression on octreotide or lanreotide.
3. Lutathera will be used in combination with either a) octreotide LAR or lanreotide for persistent symptoms (i.e., flushing, diarrhea) or b) telotristat for persistent diarrhea.

C. Pheochromocytoma/paraganglioma

Authorization of 12 months and 4 doses total may be granted for treatment of somatostatin receptor-positive pheochromocytoma/paraganglioma when the member has locally unresectable disease or distant metastases.

IV. REFERENCES

1. Lutathera [package insert]. Millburn, NJ: Advanced Accelerator Applications USA, Inc.; July 2018.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. Available at: <https://www.nccn.org>. Accessed September 12, 2019.
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SPECIALTY GUIDELINE MANAGEMENT

LUXTURNA (voretigene neparvovec-rzyl)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication¹

Luxturna is indicated for the treatment of patients with confirmed biallelic RPE65 mutation-associated retinal dystrophy. Patients must have viable retinal cells as determined by the treating physician(s).

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Testing or analysis confirming a genetic diagnosis of pathogenic/likely pathogenic biallelic RPE65 gene mutations.

III. CRITERIA FOR INITIAL APPROVAL

Biallelic RPE65 mutation-associated retinal dystrophy

Authorization of 90 days for a one-time administration per eye may be granted for treatment of biallelic RPE65 mutation-associated retinal dystrophy when all of the following criteria are met:

- A. The member has bi-allelic pathogenic and/or likely pathogenic RPE65 mutations via genetic testing (single gene test or multi gene panel test if medically necessary).
- B. The RPE65 gene mutations classifications are based on the current American College of Medical Genetics and Genomics (ACMG) standards and guidelines for the interpretation of sequence variants.
- C. Pathogenic and/or likely pathogenic classification of the RPE65 mutations has been affirmed within the last 12 months.
- D. The member is at least 12 months of age but less than 65 years of age.
- E. The member has viable retinal cells in each eye to be treated as determined by optical coherence tomography (OCT) and/or ophthalmoscopy; and must have any of the following:
 1. An area of retina within the posterior pole of greater than 100 µm thickness shown on OCT
 2. Greater than or equal to 3 disc areas of retina without atrophy or pigmentary degeneration within the posterior pole
 3. Remaining visual field within 30 degrees of fixation as measured by a III4e isopter or equivalent
- F. The member has not received a previous treatment course of Luxturna.

IV. REFERENCES

1. Luxturna [package insert]. Philadelphia, PA: Spark Therapeutics, Inc.; December 2017.

Reference number(s)
2458-A

2. Russel S, Bennet J, Wellman JA, et al. Efficacy and safety of voretigene neparvovec (AAV2-hRPE65v2) in patients with RPE65-mediated inherited retinal dystrophy: a randomized, controlled, open-label phase 3 trial. *Lancet* 2017; 390:849-860.
3. Richards S, Aziz N, Bale S, et al; ACMG Laboratory Quality Assurance Committee. Standards and guidelines for the interpretation of sequence variants: A joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. *Genet Med*. 2015;17(5):405-24.

SPECIALTY GUIDELINE MANAGEMENT

LYNPARZA (olaparib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Ovarian Cancer

a. First-Line Maintenance Treatment of *BRCA*-mutated Advanced Ovarian Cancer

Lynparza is indicated for the maintenance treatment of adult patients with deleterious or suspected deleterious germline or somatic *BRCA*-mutated (*gBRCAm* or *sBRCAm*) advanced epithelial ovarian, fallopian tube or primary peritoneal cancer who are in complete or partial response to first-line platinum-based chemotherapy. Select patients for therapy based on an FDA- approved companion diagnostic test for Lynparza.

b. Maintenance Treatment of Recurrent Ovarian Cancer

Lynparza is indicated for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer, who are in complete or partial response to platinum-based chemotherapy.

c. Advanced *gBRCA*-mutated Ovarian Cancer After 3 or More Lines of Chemotherapy

Lynparza is indicated for the treatment of adult patients with deleterious or suspected deleterious germline *BRCA*-mutated (*gBRCAm*) advanced ovarian cancer who have been treated with three or more prior lines of chemotherapy. Select patients for therapy based on an FDA- approved companion diagnostic test for Lynparza.

2. Breast Cancer

Lynparza is indicated in patients with deleterious or suspected deleterious *gBRCAm*, HER2-negative metastatic breast cancer, who have been treated with chemotherapy in the neoadjuvant, adjuvant, or metastatic setting. Patients with hormone receptor (HR)-positive breast cancer should have been treated with a prior endocrine therapy or be considered inappropriate for endocrine therapy. Select patients for therapy based on an FDA- approved companion diagnostic test for Lynparza.

3. Pancreatic Cancer

Lynparza is indicated in patients with deleterious or suspected deleterious *gBRCAm* metastatic pancreatic adenocarcinoma whose disease has not progressed on at least 16 weeks of a first-line platinum-based chemotherapy regimen. Select patients for therapy based on an FDA- approved companion diagnostic test for Lynparza.

B. Compendial uses

1. Breast cancer

Recurrent or metastatic HER2-negative, *BRCA* 1/2-germline mutated breast cancer that is hormone receptor-negative or hormone receptor-positive and endocrine therapy refractory.

2. Ovarian Cancer

Reference number
1810-A

As a single-agent maintenance therapy for patients with BRCA1/2 germline or somatic mutations who are in a complete clinical remission (no definitive evidence of disease) or in a partial remission after primary treatment for stage II-IV disease

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
Documentation of laboratory report confirming BRCA mutation status, where applicable.

III. CRITERIA FOR INITIAL APPROVAL

A. Epithelial ovarian, fallopian tube, or primary peritoneal cancer

1. Authorization of 12 months may be granted for treatment of epithelial ovarian, fallopian tube, or primary peritoneal cancer as a single agent when all of the following criteria are met:
 - a. Tumor has deleterious BRCA mutation (germline, somatic, or both) as detected by an FDA-approved companion diagnostic test
 - b. Member has received three or more prior chemotherapies
2. Authorization of 12 months may be granted for the maintenance treatment of recurrent disease as a single agent when all of the following criteria are met:
 - a. Member is in complete or partial response to platinum based chemotherapy
 - b. Member has received at least two prior platinum-containing regimens
3. Authorization of 12 months may be granted for the maintenance treatment of BRCA mutated-Stage II-IV disease as a single agent when all of the following criteria are met:
 - a. Member is in complete or partial response to platinum based chemotherapy
 - b. Member has a deleterious BRCA mutation (germline, somatic, or both) as detected by an FDA-approved companion diagnostic test

B. Breast Cancer

Authorization of 12 months may be granted for the treatment of human epidermal growth factor receptor 2 (HER2)-negative recurrent or metastatic breast cancer as a single agent in members with deleterious or suspected deleterious germline BRCA mutations.

C. Pancreatic Cancer

Authorization of 12 months may be granted for the maintenance treatment of deleterious or suspected deleterious germline BRCA-mutated metastatic pancreatic adenocarcinoma as a single agent, in members whose disease has not progressed on at least 16 weeks of a first-line platinum-based chemotherapy regimen.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced disease progression or an unacceptable toxicity. For the first-line maintenance treatment of BRCA-mutated advanced ovarian cancer in a complete response, the maximum treatment duration is 2 years.

Reference number
1810-A

V. REFERENCES

1. Lynparza® Tablets [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; December 2019.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed January 07, 2020.
3. The NCCN Clinical Practice Guidelines in Oncology® Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer (Version 3.2019). © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed January 07, 2020.
4. The NCCN Clinical Practice Guidelines in Oncology® Breast Cancer (Version 3.2019). © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed January 07, 2020.
5. The NCCN Clinical Practice Guidelines in Oncology® Pancreatic Adenocarcinoma (Version 01.2020). © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed January 07, 2020.

SPECIALTY GUIDELINE MANAGEMENT

MACUGEN (pegaptanib sodium injection)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Macugen is indicated for the treatment of neovascular (wet) age-related macular degeneration.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Neovascular (wet) age-related macular degeneration

Authorization of 6 months may be granted for treatment of neovascular (wet) age-related macular degeneration.

III. CONTINUATION OF THERAPY

Authorization of 12 months (with a maximum of 2 years of treatment for each eye) may be granted for continued treatment in members requesting reauthorization for neovascular (wet) age-related macular degeneration who have demonstrated a positive clinical response to Macugen therapy (e.g., improvement or maintenance in best corrected visual acuity [BCVA], or visual field, or a reduction in the rate of vision decline or the risk of more severe vision loss).

IV. REFERENCES

1. Macugen [package insert]. Palm Beach Gardens, FL: Eyetech Inc.; July 2016.

SPECIALTY GUIDELINE MANAGEMENT

MAVENCLAD (cladribine)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Mavenclad is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include relapsing-remitting disease and active secondary progressive disease, in adults. Because of its safety profile, use of Mavenclad is generally recommended for patients who have had an inadequate response to, or are unable to tolerate, an alternative drug indicated for the treatment of MS.

Limitations of Use

Mavenclad is not recommended for use in patients with clinically isolated syndrome (CIS) because of its safety profile.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Multiple Sclerosis

A. Initial requests

Authorization of 45 days may be granted for treatment of relapsing forms of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapses) and when all of the following criteria are met:

1. Inadequate response or unable to tolerate an alternative drug indicated for the treatment of multiple sclerosis.
2. Member does not have clinically isolated syndrome (CIS).
3. Member has not received 2 courses (i.e., 4 cycles) of Mavenclad.
4. Members will not use Mavenclad concomitantly with other medications used for the treatment of multiple sclerosis, excluding Ampyra.

B. Subsequent requests

Authorization of 45 days may be granted for treatment of relapsing forms of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapses) and when all of the following criteria are met:

1. Member has not received 2 courses (i.e., 4 cycles) of Mavenclad.
2. Members will not use Mavenclad concomitantly with other medications used for the treatment of multiple sclerosis, excluding Ampyra.
3. The member has not received Mavenclad in the last 43 weeks.

III. REFERENCES

Reference number(s)
2975-A

1. Mavenclad [package insert]. Rockland, MA: EMD Serono; April 2019.
2. Giovannoni, G., Comi, G., Cook, S., et al. A Placebo-Controlled Trial of Oral Cladribine for Relapsing Multiple Sclerosis. N Engl J Med 2010;362:416-426.

SPECIALTY GUIDELINE MANAGEMENT

MAVYRET (glecaprevir and pibrentasvir)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Mavyret is indicated for the treatment of adult patients 12 years and older or weighing at least 45 kg with chronic hepatitis C virus (HCV) genotype (GT) 1, 2, 3, 4, 5 or 6 infection without cirrhosis or with compensated cirrhosis (Child-Pugh A). Mavyret is also indicated for the treatment of adult and pediatric patients 12 years and older or weighing at least 45 kg with HCV genotype 1 infection, who previously have been treated with a regimen containing an HCV NS5A inhibitor or an NS3/4A protease inhibitor (PI), but not both.

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

Coverage will not be provided for members with decompensated cirrhosis/moderate or severe hepatic impairment (Child Turcotte Pugh Class B or C)

Note: When the requested drug is being used in a combination therapy regimen, exclusions to the other antiviral drugs also apply.

III. CRITERIA FOR INITIAL APPROVAL

A. Chronic hepatitis C virus infection

1. Genotype 1 infection

- a. Authorization of up to 8 weeks total may be granted for treatment-naïve members without cirrhosis or with compensated cirrhosis.
- b. Authorization of up to 16 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who failed prior treatment with an NS5A inhibitor and who have not received an NS3/4A protease inhibitor.
- c. Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who failed prior treatment with an NS3/4A protease inhibitor (e.g., simeprevir, boceprevir or telaprevir in combination with peginterferon and ribavirin, simeprevir with sofosbuvir) and who have not received an NS5A inhibitor.
- d. Authorization of up to 8 weeks total may be granted for members without cirrhosis who failed prior treatment with peginterferon-alfa (PEG-IFN) and ribavirin (RBV) and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.
- e. Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.

- f. Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who failed prior treatment with a sofosbuvir (Sovaldi)-containing regimen (e.g., sofosbuvir and ribavirin with or without PEG-IFN) and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.

2. Genotype 2 infection

- a. Authorization of up to 8 weeks total may be granted for treatment-naïve members without cirrhosis or with compensated cirrhosis.
- b. Authorization of up to 8 weeks total may be granted for members without cirrhosis who failed prior treatment with PEG-IFN and RBV and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.
- c. Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.
- d. Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who failed prior treatment with sofosbuvir (Sovaldi) and ribavirin with or without PEG-IFN and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.

3. Genotype 3 infection

- a. Authorization of up to 8 weeks total may be granted for treatment-naïve members without cirrhosis or with compensated cirrhosis.
- b. Authorization of up to 16 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.
- c. Authorization of up to 16 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who failed prior treatment with sofosbuvir (Sovaldi) and RBV with or without PEG-IFN and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.

4. Genotype 4, 5, or 6 infection

- a. Authorization of up to 8 weeks total may be granted for treatment-naïve members without cirrhosis or with compensated cirrhosis.
- b. Authorization of up to 8 weeks total may be granted for members without cirrhosis who failed prior treatment with PEG-IFN and RBV and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.
- c. Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.
- d. Authorization of up to 8 weeks total may be granted for members without cirrhosis who failed prior treatment with sofosbuvir (Sovaldi) and ribavirin with or without PEG-IFN and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.
- e. Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with sofosbuvir (Sovaldi) and ribavirin with or without PEG-IFN and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.

5. Recurrent HCV infection post liver transplantation

- a. Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis and recurrent HCV genotype 1, 2, 3, 4, 5 or 6 infection post liver transplantation.
- b. Authorization of up to 16 weeks total may be granted for members with recurrent HCV genotype 1 infection post liver transplantation without cirrhosis or with compensated cirrhosis who failed prior treatment with an NS5A inhibitor and who have not received an NS3/4A protease inhibitor.

- c. Authorization of up to 16 weeks total may be granted for members with recurrent HCV genotype 3 infection post liver transplantation without cirrhosis or with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.
- d. Authorization of up to 16 weeks total may be granted for members with recurrent HCV genotype 3 infection post liver transplantation without cirrhosis or with compensated cirrhosis who failed prior treatment with sofosbuvir (Sovaldi) and RBV with or without PEG-IFN and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.

6. Kidney transplant recipients

- a. Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who have HCV genotype 1, 2, 3, 4, 5 or 6 infection.
- b. Authorization of up to 16 weeks total may be granted for members with HCV genotype 1 infection without cirrhosis or with compensated cirrhosis who failed prior treatment with an NS5A inhibitor and who have not received an NS3/4A protease inhibitor.
- c. Authorization of up to 16 weeks total may be granted for members with HCV genotype 3 infection without cirrhosis or with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.
- d. Authorization of up to 16 weeks total may be granted for members with HCV genotype 3 infection without cirrhosis or with compensated cirrhosis who failed prior treatment with sofosbuvir (Sovaldi) and RBV with or without PEG-IFN and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.

B. HCV and HIV Coinfection

Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in Section A above are met.

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. REFERENCES

1. Mavyret [package insert]. North Chicago, IL: AbbVie Inc.; September 2019.
2. AASLD/IDSA/IAS–USA. Recommendations for testing, managing, and treating hepatitis C. <http://www.hcvguidelines.org>. Last changes made May 24, 2018. Accessed August 02, 2018.

SPECIALTY GUIDELINE MANAGEMENT

MAYZENT (siponimod)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Mayzent is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease and active secondary progressive disease, in adults.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Relapsing forms of multiple sclerosis

Authorization of 12 months may be granted to members who have been diagnosed with a relapsing form of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse).

B. Clinically isolated syndrome

Authorization of 12 months may be granted to members for the treatment of clinically isolated syndrome.

III. CONTINUATION OF THERAPY

For all indications: Authorization of 12 months may be granted for members who are experiencing disease stability or improvement while receiving Mayzent.

IV. OTHER CRITERIA

Members will not use Mayzent concomitantly with other medications used for the treatment of multiple sclerosis, excluding Ampyra.

V. REFERENCES

1. Mayzent [package insert]. East Hanover, NJ: Novartis; March 2019.

SPECIALTY GUIDELINE MANAGEMENT

MEKINIST (trametinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Mekinist is indicated, as a single agent or in combination with dabrafenib, for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test.
2. Mekinist is indicated, in combination with dabrafenib, for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) with BRAF V600E mutation as detected by an FDA-approved test.
3. Mekinist is indicated, in combination with dabrafenib, for the adjuvant treatment of patients with melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test, and involvement of lymph node(s), following complete resection.
4. Mekinist is indicated, in combination with dabrafenib, for the treatment of patients with locally advanced or metastatic anaplastic thyroid cancer (ATC) with BRAF V600E mutation and no satisfactory locoregional treatment options.

B. Compendial Uses

1. Melanoma (including brain metastases), BRAF V600 activating mutation-positive
2. Glioma, BRAF V600 activating mutation-positive
3. Meningioma, BRAF V600 activating mutation-positive
4. Astrocytoma, BRAF V600 activating mutation-positive
5. Uveal melanoma as a single agent
6. Colorectal cancer, BRAF V600E activating mutation-positive

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of BRAF mutation documentation is necessary to initiate the prior authorization review for applicable indications as outlined in section III.

III. CRITERIA FOR INITIAL APPROVAL

A. **Melanoma**

1. Authorization of 12 months may be granted for treatment of unresectable or metastatic cutaneous melanoma with a BRAF V600 activating mutation as a single agent or in combination with dabrafenib (Tafinlar).
2. Authorization of 12 months may be granted for treatment of brain metastases from melanoma with a BRAF V600 activating mutation in combination with dabrafenib (Tafinlar).

Reference number(s)
1681-A

3. Authorization of 12 months may be granted for adjuvant treatment of cutaneous melanoma with a BRAF V600 activating mutation in combination with dabrafenib (Tafinlar).
4. Authorization of 12 months may be granted for treatment of metastatic or unresectable uveal melanoma as a single agent.

B. Non-Small Cell Lung Cancer (NSCLC)

Authorization of 12 months may be granted for treatment of BRAF V600E mutation-positive NSCLC in combination with dabrafenib (Tafinlar).

C. Anaplastic Thyroid Cancer (ATC)

Authorization of 12 months may be granted for treatment of metastatic BRAF V600E mutation-positive ATC in combination with dabrafenib (Tafinlar).

D. Central Nervous System Cancer

Authorization of 12 months may be granted for treatment of BRAF V600 mutation-positive gliomas, meningiomas, or astrocytomas.

E. Colorectal Cancer

Authorization of 12 months may be granted for treatment of unresectable advanced or metastatic colorectal cancer when the following criteria are met:

1. Mekinist is used in combination with dabrafenib (Tafinlar) and either cetuximab or panitumumab
2. Tumor is positive for BRAF V600E mutation.
3. Will be used as subsequent therapy

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy for an indication outlined in section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen. For patients using Mekinist for adjuvant treatment of cutaneous melanoma, only 12 months of therapy total will be approved.

V. REFERENCES

1. Mekinist [package insert]. East Hanover, NJ: Novartis Pharmaceutical Corporation; May 2018.
2. The NCCN Drugs & Biologics Compendium 2018 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed July 30, 2019.
3. The NCCN Clinical Practice Guidelines in Oncology Non-Small Cell Lung Cancer (Version 1.2019). 2018 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed November 19, 2018.
4. The NCCN Clinical Practice Guidelines in Oncology Cutaneous Melanoma (Version 1.2019). 2018 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed November 19, 2018.
5. The NCCN Clinical Practice Guidelines in Oncology Uveal Melanoma (Version 1.2018). 2018 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed November 19, 2018.
6. The NCCN Clinical Practice Guidelines in Oncology Central Nervous System Cancers (Version 1.2018). 2018 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed November 19, 2018.
7. Usabalieva A, Pierson CR, Kavran CA, et al. Primary Meningeal Pleomorphic Xanthoastrocytoma With Anaplastic Features: A Report of 2 Cases, One With *BRAFV600E* Mutation and Clinical Response to the *BRAF* Inhibitor Dabrafenib. *J Neuropathol Exp Neurol*. 2015;74(10):960-969. doi:10.1097/NEN.0000000000000240.
8. Mordechai O, Postovsky S, Vlodavsky E, et al. Metastatic Rhabdoid Meningioma with *BRAF* V600E Mutation and Good Response to Personalized Therapy: Case Report and Review of the Literature. *Pediatr Hematol Oncol*. 2015; 32:3, 207-211, DOI: 10.3109/08880018.2014.936058

Reference number(s)
1681-A

9. Lassaletta, A, Guerreiro Stucklin, A, Ramaswamy, V, et al. Profound clinical and radiological response to BRAF inhibition in a 2-month-old diencephalic child with hypothalamic/chiasmatic glioma. *Pediatric Blood and Cancer*. 2016; 63: 2038-2041. doi:10.1002/pbc.26086.
10. Meletah SK, Pavlick D, Brennan T, et al. Personalized Treatment for a Patient with a BRAF V600E Mutation using Dabrafenib and a Tumor Treatment Fields Device in a High-Grade Glioma Arising from Ganglioglioma. *J Natl Compr Canc Netw*. 2016; 14(11): 1345-1350.

SPECIALTY GUIDELINE MANAGEMENT

MEKTOVI (binimetinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Mektovi is indicated, in combination with encorafenib, for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation, as detected by an FDA-approved test.

B. Compendial Uses

1. Glioma, BRAF V600 activating mutation-positive
2. Meningioma, BRAF V600 activating mutation-positive
3. Astrocytoma, BRAF V600 activating mutation-positive
4. Colorectal cancer, BRAF V600E activating mutation-positive

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of BRAF mutation documentation is necessary to initiate the prior authorization review.

III. CRITERIA FOR INITIAL APPROVAL

A. **Melanoma**

Authorization of 12 months may be granted for treatment of unresectable or metastatic melanoma when all of the following criteria are met:

1. Mektovi is used in combination with encorafenib (Braftovi)
2. Tumor is positive for BRAF V600E or V600K mutation.

B. **Central Nervous System Cancer**

Authorization of 12 months may be granted for treatment of BRAF V600 mutation-positive gliomas, meningiomas, or astrocytomas.

C. **Colorectal Cancer**

Authorization of 12 months may be granted for treatment of unresectable advanced or metastatic colorectal cancer when the following criteria are met:

1. Mektovi is used in combination with encorafenib (Braftovi) and either cetuximab or panitumumab
2. Tumor is positive for BRAF V600E mutation.
3. Will be used as subsequent therapy

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy for an indication outlined in section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Mektovi [package insert]. Boulder, CO: Array BioPharma, Inc.; January 2019.
2. The NCCN Drugs & Biologics Compendium 2018 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed July 30, 2019
3. Usabalieva A, Pierson CR, Kavran CA, et al. Primary Meningeal Pleomorphic Xanthoastrocytoma With Anaplastic Features: A Report of 2 Cases, One With *BRAFV600E* Mutation and Clinical Response to the *BRAF* Inhibitor Dabrafenib. *Journal of neuropathology and experimental neurology*. 2015;74(10):960-969. doi:10.1097/NEN.0000000000000240.
4. Mordechai O, Postovsky S, Vlodavsky E, et al. Metastatic Rhabdoid Meningioma with *BRAF V600E* Mutation and Good Response to Personalized Therapy: Case Report and Review of the Literature. *Pediatric Hematology and Oncology*. 2015; 32:3, 207-211, DOI: 10.3109/08880018.2014.936058
5. Lassaletta, A, Guerreiro Stucklin, A, Ramaswamy, V, et al. Profound clinical and radiological response to BRAF inhibition in a 2-month-old diencephalic child with hypothalamic/chiasmatic glioma. *Pediatric Blood and Cancer*. 2016; 63: 2038-2041. doi:10.1002/pbc.26086.
6. Meletah SK, Pavlick D, Brennan T, et al. Personalized Treatment for a Patient with a BRAF V600E Mutation using Dabrafenib and a Tumor Treatment Fields Device in a High-Grade Glioma Arising from Ganglioglioma. *Journal of the National Comprehensive Cancer Network*. 2016; 14(11): 1345-1350.

SPECIALTY GUIDELINE MANAGEMENT

MENOPUR (menotropins for injection)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Menopur is indicated for development of multiple follicles and pregnancy in ovulatory women as part of an assisted reproductive technology (ART) cycle.

All other indications are considered experimental/investigational and not medically necessary.

II. MEDICAL BENEFIT ALIGNMENT

Specialty Guideline Management coverage review will be bypassed for drug(s) being requested for a procedure that has been approved under a member's medical benefit plan. Such members will be exempt from the requirements in Sections III and IV. A medical authorization number and confirmation of the approved procedure(s) will be required.

NOTE: Some plans may opt-out of medical benefit alignment. Members receiving coverage under such plans must meet the requirements in Sections III and IV.

III. CRITERIA FOR INITIAL APPROVAL

Follicle stimulation

Authorization of 12 months may be granted for members undergoing ovulation induction or assisted reproductive technology who meet any of the following criteria:

1. Member has completed three or more previous cycles of clomiphene, or
2. Member has a risk factor for poor ovarian response to clomiphene, or
3. Member has a contraindication or exclusion to clomiphene, or
4. Member is 37 years of age or older

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. REFERENCES

1. Menopur [package insert]. Parsippany, NJ: Ferring Pharmaceuticals Inc.; May 2018.

Reference number(s)
1991-A, 1992-A

2. Practice Committee of the American Society of Reproductive Medicine. Use of clomiphene citrate in infertile women: a committee opinion. *Fertil & Steril*. 2013;100:341-348.

SPECIALTY GUIDELINE MANAGEMENT

MEPSEVII (vestronidase alfa-vjbk)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Mepsevii is indicated in pediatric and adult patients for the treatment of mucopolysaccharidosis VII (MPS VII, Sly syndrome).

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: beta-glucuronidase enzyme assay or genetic testing results supporting diagnosis.

III. CRITERIA FOR INITIAL APPROVAL

Mucopolysaccharidosis VII (MPS VII, Sly syndrome)

Authorization of 12 months may be granted for treatment of MPS VII (Sly syndrome) when both of the following criteria are met:

- A. Diagnosis of MPS VII was confirmed by enzyme assay demonstrating a deficiency of beta-glucuronidase enzyme activity or by genetic testing; AND
- B. Elevated urinary glycosaminoglycan (uGAG) excretion at a minimum of 2-fold over the mean normal for age at initiation of treatment with Mepsevii.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for mucopolysaccharidosis VII (MPS VII, Sly syndrome) who are responding to therapy (e.g., improvement, stabilization, or slowing of disease progression for motor function, pulmonary function, reduction in liver volume, reduction in spleen volume).

V. REFERENCES

1. Mepsevii [package insert]. Novato, CA: Ultragenyx; November 2017.
2. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). Identifier NCT01856218. An OpenLabel Phase 1/2 Study to Assess the Safety, Efficacy and Dose of Study Drug UX003 Recombinant Human Beta- glucuronidase (rhGUS) Enzyme Replacement Therapy in Patients With Mucopolysaccharidosis Type 7 (MPS 7); January 31, 2018. Available at: <https://clinicaltrials.gov/ct2/show/NCT01856218?term=NCT01856218&rank=1>.

3. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). Identifier NCT02230566. A Phase 3 Study of UX003 Recombinant Human Betaglucuronidase (rhGUS) Enzyme Replacement Therapy in Patients With Mucopolysaccharidosis Type 7 (MPS 7); February 16, 2018. Available at: <https://clinicaltrials.gov/ct2/show/NCT02230566?term=NCT02230566&rank=1>.
4. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). Identifier NCT02432144. A LongTerm Open-Label Treatment and Extension Study of UX003 rhGUS Enzyme Replacement Therapy in Subjects With MPS 7; November 6, 2017. Available at: <https://clinicaltrials.gov/ct2/show/NCT02432144?term=NCT02432144&rank=1>.
5. Harmatz P, et al. A novel Blind Start study design to investigate vestronidase alfa for mucopolysaccharidosis VII, an ultra-rare genetic disease. Mol Genet Metab. 2018 Apr;123(4):488-494.

SPECIALTY GUIDELINE MANAGEMENT

ZAVESCA (miglustat) miglustat (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Zavesca is indicated as monotherapy for the treatment of adult patients with mild to moderate type 1 Gaucher disease for whom enzyme replacement therapy is not a therapeutic option (e.g. due to allergy, hypersensitivity, or poor venous access).

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: beta-glucocerebrosidase enzyme assay or genetic testing results supporting diagnosis

III. CRITERIA FOR INITIAL APPROVAL

Gaucher disease type 1

Authorization of 12 months may be granted for treatment of Gaucher disease type 1 when the diagnosis of Gaucher disease was confirmed by enzyme assay demonstrating a deficiency of beta-glucocerebrosidase (glucosidase) enzyme activity or by genetic testing, and the member has a documented inadequate response or intolerable adverse events with enzyme replacement therapy.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for Gaucher disease type 1 who are not experiencing an inadequate response or any intolerable adverse events from therapy.

V. REFERENCES

1. Zavesca [package insert]. South San Francisco, CA: Actelion Pharmaceuticals US, Inc.; November 2017.
2. miglustat [package insert]. Horsham, PA: Patriot Pharmaceuticals, LLC.; November 2017.

Reference number
2098-A

SPECIALTY GUIDELINE MANAGEMENT

MIRCERA (methoxy polyethylene glycol-epoetin beta)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Mircera is indicated for the treatment of anemia associated with chronic kidney disease (CKD) in:

- Adult patients on dialysis and adult patients not on dialysis.
- Pediatric patients 5 to 17 years of age on hemodialysis who are converting from another erythropoiesis-stimulating agent (ESA) after their hemoglobin level was stabilized with an ESA.

All other indications are considered experimental/investigational and are not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Note: Requirements regarding hemoglobin level exclude values due to recent transfusion. All members must be assessed for iron deficiency anemia and have adequate iron stores or are receiving iron therapy before starting Mircera. Members may not use Mircera concomitantly with other erythropoiesis stimulating agents.

Anemia Due to Chronic Kidney Disease

Authorization of 12 weeks may be granted for the treatment of anemia due to chronic kidney disease when the pretreatment hemoglobin is less than 10 g/dL.

III. CONTINUATION OF THERAPY

Note: Requirements regarding current hemoglobin level exclude values due to recent transfusion. Members may not use Mircera concomitantly with other erythropoiesis stimulating agents.

Anemia Due to Chronic Kidney Disease

1. Authorization of 12 weeks may be granted for continuation of therapy when the current hemoglobin is ≤ 12 g/dL and the member has shown a response to therapy with a rise in hemoglobin of ≥ 1 g/dL after at least 12 weeks of ESA therapy.
2. Authorization of up to 12 weeks may be granted for continuation of therapy in members who have not completed 12 weeks of ESA therapy.

IV. REFERENCES

Reference number(s)
1618-A

1. Mircera [package insert]. South San Francisco, CA: Hoffmann-La Roche Inc.; June 2018.
2. Kidney Disease: Improving Global Outcomes (KDIGO) Anemia Work Group. KDIGO Clinical Practice Guideline for Anemia in Chronic Kidney Disease. *Kidney Int.* 2012;Suppl 2:279-335.
3. National Kidney Foundation. KDOQI Clinical Practice Guideline and Clinical Practice Recommendations for Anemia in Chronic Kidney Disease: 2007 Update of Hemoglobin Target. http://www2.kidney.org/professionals/KDOQI/guidelines_anemiaUP/. Accessed September 12, 2017.

EXCEPTION CRITERIA

DRUG CLASS

MISCELLANEOUS FORMULATIONS EXCEPTION

DRUG NAME

(brand/generic)

MISCELLANEOUS FORMULATIONS

[Use RxClaim List ID CMKCMPJTOP for target drug list]

Status: CVS Caremark Criteria

Type: Exception Criteria

Ref # 1267-A

COVERAGE CRITERIA

The requested drug will be covered with exception when the following criteria are met:

- The patient has a medical condition for which there are no FDA-approved drugs available
OR
- The patient had an inadequate treatment response, intolerance or contraindication to all available FDA-approved drugs for their medical condition

RATIONALE

The intent of the exception criteria is to provide a medical necessity review of products that are excluded from the pharmacy benefit. These products are manufactured commercially and have not been evaluated by the FDA for safety, efficacy or quality.

The requested drug will be covered if the patient has a medical condition for which there are no FDA-approved products available to treat. Coverage will also be provided if the patient had an inadequate treatment response, intolerance or contraindication to all available FDA-approved drugs for their condition.

If criteria for coverage are met, the requested product will be approved for 3 months. This short approval duration is in place to manage the use of products that may be marketed contrary to the Federal Food, Drug and Cosmetic Act.

Written by: UM Development (JK)
Date Written: 06/2015
Revised: 08/2015, (TM) 12/2016, (TM) 02/2017, (TM) 02/2018 (rephrased Q1), (TM) 02/2019 (no clinical changes), (TM) 02/2020 (no clinical changes)
Reviewed: Medical Affairs (WLF) 06/2015, 08/2015, (AN) 12/2016, (AN) 03/2017, 02/2018, (CHART) 02/27/20
External Review 02/2016, 02/2017, 04/2017, 04/2018, 04/2019, 04/2020

CRITERIA FOR APPROVAL

- | | | | |
|---|--|-----|----|
| 1 | Are there FDA-approved drugs available for the patient's medical condition?
[If no, then no further questions.] | Yes | No |
| 2 | Has the patient had an inadequate treatment response, intolerance or contraindication to all available FDA-approved drugs for their medical condition? | Yes | No |

Guidelines for Approval**Duration of Approval 3 Months**

Set 1		Set 2	
Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)
None	1	1	None
		2	

Mapping Instructions

	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Approve, 3 months	
2.	Approve, 3 months	Deny	<p>You do not meet the requirements of your plan.</p> <p>Your plan covers this drug when you meet one of these conditions:</p> <ul style="list-style-type: none"> - You have tried all available FDA-approved drugs for your medical condition and they did not work for you - You are unable to take FDA-approved drugs for your medical condition. <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No inadequate response, intolerance or contraindication to all available FDA-approved drugs]</p>

SPECIALTY GUIDELINE MANAGEMENT

Mitoxantrone

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications¹

1. Acute nonlymphocytic leukemia (ANLL)
Mitoxantrone in combination with other approved drug(s) is indicated in the initial therapy of ANLL in adults. This category includes myelogenous, promyelocytic, monocytic, and erythroid acute leukemias.
2. Multiple sclerosis
Mitoxantrone is indicated for reducing neurologic disability and/or the frequency of clinical relapses in patients with secondary (chronic) progressive, progressive relapsing, or worsening relapsing-remitting multiple sclerosis (MS) (i.e., patients whose neurologic status is significantly abnormal between relapses). Mitoxantrone is not indicated in the treatment of patients with primary progressive MS.
3. Prostate cancer
Mitoxantrone in combination with corticosteroids is indicated as initial chemotherapy for the treatment of patients with pain related to advanced hormone-refractory prostate cancer.

B. Compendial Uses

1. Acute lymphoblastic leukemia³
2. Breast cancer²
3. Hodgkin lymphoma^{3,4}
4. Liver carcinoma²
5. Malignant lymphoma, indolent²
6. Non-Hodgkin's lymphoma with following subtypes^{3,6,7}
 - a. AIDS-related B-cell lymphoma
 - b. Diffuse large B-cell lymphoma
 - c. Follicular lymphoma
 - d. Histologic transformation of marginal zone lymphoma to diffuse large B-cell lymphoma
 - e. Mantle cell lymphoma
 - f. T-cell prolymphocytic leukemia
 - g. Post-transplant proliferative disorders
7. Ovarian cancer²

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Acute lymphoblastic leukemia (ALL)³

Reference number(s)
1662-A

Authorization of 6 months may be granted for treatment of ALL.

B. Acute nonlymphocytic leukemia (ANLL)^{1-3, 5}

Authorization of 6 months may be granted for treatment of ANLL, including acute myeloid leukemia (AML) and acute promyelocytic leukemia (APL).

C. Multiple sclerosis¹

Authorization of 1 dose (3 months) may be granted for treatment of multiple sclerosis.

D. Prostate cancer^{1-3, 8}

Authorization of 6 months may be granted for treatment of prostate cancer.

E. Breast cancer²

Authorization of 6 months may be granted for treatment of breast cancer.

F. Hodgkin lymphoma^{3,4}

Authorization of 6 months may be granted for treatment of Hodgkin lymphoma.

G. Liver carcinoma²

Authorization of 6 months may be granted for treatment of liver carcinoma.

H. Non-Hodgkin's lymphoma (NHL)^{3,6,7}

Authorization of 6 months may be granted for treatment of one of the following subtypes of NHL:

1. AIDS-related B-cell lymphoma
2. Diffuse large B-cell lymphoma
3. Follicular lymphoma
4. Histologic transformation of marginal zone lymphoma to diffuse large B-cell lymphoma
5. Mantle cell lymphoma
6. T-cell prolymphocytic leukemia
7. Post-transplant proliferative disorders

I. Ovarian cancer²

Authorization of 6 months may be granted for treatment of ovarian cancer.

J. Malignant lymphoma, indolent²

Authorization of 6 months may be granted for treatment of malignant indolent lymphoma.

III. CONTINUATION OF THERAPY

A. Multiple Sclerosis

Authorization of 3 months may be granted for continued treatment in members requesting reauthorization for multiple sclerosis (MS) who experienced a benefit from therapy (e.g., reduced neurologic disability, reduced frequency of clinical relapses).

B. All Other Diagnoses (Excluding Multiple Sclerosis)

Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for all indications listed in Section II (excluding MS) who have not experienced an unacceptable toxicity.

IV. REFERENCES

Reference number(s)
1662-A

1. Mitoxantrone [package insert]. Irvine, CA: Teva Parenteral Medicines, Inc.; May 2012.
2. IBM Micromedex® DRUGDEX® System (electronic version). IBM Watson Health, Greenwood Village, Colorado. Available at <https://www.micromedexsolutions.com>. Accessed March 8, 2019.
3. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed March 8, 2019.
4. The NCCN Clinical Practice Guidelines in Oncology® Hodgkin Lymphoma (Version 1.2018). © 2018 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed March 8, 2019.
5. The NCCN Clinical Practice Guidelines in Oncology® Acute Myeloid Leukemia (Version 1.2018). © 2018 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed March 8, 2019.
6. The NCCN Clinical Practice Guidelines in Oncology® T-Cell Lymphomas (Version 3.2018). © 2018 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed March 8, 2019.
7. The NCCN Clinical Practice Guidelines in Oncology® B-Cell Lymphomas (Version 2.2018). © 2018 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed March 8, 2019.
8. The NCCN Clinical Practice Guidelines in Oncology® Prostate Cancer (Version 2.2018). © 2018 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed March 8, 2019.

GLOBAL EXCEPTION CRITERIA

MANAGED MEDICAID TEMPLATE GLOBAL EXCEPTION CRITERIA

Status: CVS Caremark Criteria

Type: Exception Criteria

Ref # 569-A

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested product is not being prescribed for an indication that is recognized as an excluded benefit by the applicable health plan's program (e.g., weight loss, erectile dysfunction, fertility, cosmetic, hair loss, medical foods)

AND

- The requested product is being used for an FDA-approved indication OR an indication supported in the compendia of current literature (examples: AHFS, Micromedex, current accepted guidelines)

AND

- The prescribed dose and quantity fall within the FDA-approved labeling or within dosing guidelines found in the compendia of current literature.

AND

- The request is for a formulary product for more than the initial limit

OR

- The request is for a non-formulary product and the patient is unable to take the preferred formulary alternatives for the given diagnosis due to a trial and inadequate treatment response, intolerance, expected adverse reaction, or contraindication.

AND

- If the request is for a combination product for which individual components are available at similar doses on formulary, then the patient must have had a trial and failure of the separate individual components due to an adverse event (examples: rash, nausea, vomiting, anaphylaxis) that is thought to be due to an inactive ingredient, **AND**
- If the request is for a brand name product that has a generic available on formulary, then the patient must have had a trial and failure of the generic agent due to an adverse event (examples: rash, nausea, vomiting, anaphylaxis) that is thought to be due to an inactive ingredient, **AND**
- If the request is for a product with an available alternative dosage form for the same active ingredient on formulary, then there must be a clinical reason why the patient is unable to take an applicable alternative formulary dosage form based on the patient's condition (e.g. age, indication)

OR

- The request is for a non-formulary product and the patient has a clinical condition or needs a specific dosage form for which there is no formulary alternative or the listed formulary alternatives are not recommended based on published guidelines or clinical literature OR the formulary alternatives will likely be ineffective or less effective for the patient OR the formulary alternatives will likely cause an adverse effect.

RATIONALE

The intent of the criteria is to ensure that patients follow selection elements noted in labeling and/or practice guidelines in order to decrease the potential for inappropriate utilization.

The intent of this program is to confirm the medical necessity of formulary medication quantity limits exceeding the initial limit, or to confirm the appropriate coverage of a non-formulary prescription medication for patients. These criteria apply to all medications subject to prior authorization not otherwise managed through drug-specific Prior Authorization criteria. Products excluded from the Managed Medicaid Template Formulary will not be covered under the prescription benefit as out lined in the applicable plan's program.

This policy is intended to ensure that medications subject to exception prior authorization by the Plan are utilized in accordance with FDA indications and uses found in the compendia of current literature including American Hospital Formulary Service Drug Information (AHFS), Micromedex, or current accepted guidelines. This policy also aims to ensure

MMT Global Exception 569-A 02-2020_7-10-20.docx

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that medications are approved within manufacturer's dosing guidelines or dosing guidelines of current compendia and to foster cost-effective, first-line use of available formulary/preferred drug list medications.

If the prescriber provides evidence of trial and failure of 3 formulary alternatives (generics and/or formulary brands) in a class with 3 or more alternatives available, the prior authorization will be approved. If the prescriber provides evidence of trial and failure of 2 formulary alternatives (generics and/or formulary brands) in a class with 2 alternatives available, the prior authorization will be approved. If the prescriber provides evidence of trial and failure of 1 formulary alternative (generic and/or formulary brands) in a class where only one alternative exists, the prior authorization will be approved.

If the request is for a non-formulary combination product for which individual components are available at similar doses on formulary, then the separate individual components of the combination product taken concurrently must be unable to be taken PLUS the remaining required number of alternatives, and the patient must have had a trial and failure of the separate individual components due to an adverse event (examples: rash, nausea, vomiting, anaphylaxis) that is thought to be due to an inactive ingredient.

If the request is for a non-formulary brand name product that has a generic available on formulary, then the formulary generic must be unable to be taken PLUS the remaining required number of alternatives, and the patient must have had a trial and failure of the generic agent due to an adverse event (examples: rash, nausea, vomiting, anaphylaxis) that is thought to be due to an inactive ingredient.

If the request is for a non-formulary product with an available alternative dosage form for the same active ingredient on formulary, then an alternative formulary dosage form of the requested product must be unable to be taken PLUS the remaining required number of formulary alternatives, and there must be a clinical reason why the patient is unable to take an applicable alternative formulary dosage form based on the patient's condition (e.g. age, indication).

If the patient has a clinical condition for which there is no formulary alternative or the listed formulary alternatives are not recommended based on published guidelines or clinical literature OR the formulary alternatives will likely be ineffective or less effective for the patient OR the formulary alternatives will likely cause an adverse effect, the claim should be approved. This includes if the request is for diabetic supply/insulin cartridge and visual impairment is noted, or if the request is for non-formulary test strips and the patient is on an insulin pump that requires the requested test strips.

REFERENCES

N/A

Written by: UM Development (NB)
Date Written: 10/2010
Revised: 09/2011, 03/2012, 09/2012, 07/2013, 09/2013, (TM) 02/2014, (NB) 02/2015, 02/2016 (updated excluded drug question, added combo product clarification), 02/2017 (moved dosing question up to question #3, combined #6 & #7); (JH) 02/2018 (aligned across other LOBs), (JK) 02/2019, 02/2020 (no clinical changes)
Reviewed: Medical Affairs (WF) 10/2010, 10/2011, 03/2012; (LB) 09/2012, (LS) 08/2013, 09/2013, (DC) 02/2014, (SS) 02/2015, 02/2016; (AA) 02/2018
External Review: 12/2010, 11/2011, 12/2012, 08/2013, 10/2013, 06/2014, 06/2015, 06/2016, 04/2016, 04/2017, 04/2018, 04/2019, 04/2020

CRITERIA FOR APPROVAL

- | | | | |
|---|---|-----|----|
| 1 | Is the requested product being prescribed for an indication that is recognized as an excluded benefit by the applicable health plan's program (e.g., weight loss, erectile dysfunction, fertility, cosmetic, hair loss, medical foods)?
[If yes, then no further questions.] | Yes | No |
| 2 | Is the requested product being used for an FDA-approved indication OR an indication supported in the compendia of current literature (examples: AHFS, Micromedex, current accepted guidelines)? | Yes | No |

3	Does the prescribed dose and quantity fall within the FDA-approved labeling or within dosing guidelines found in the compendia of current literature?	Yes	No
4	Is this a formulary product AND is the requested quantity more than the initial quantity limit? [If yes, then no further questions.]	Yes	No
5	Is the request for a combination product for which individual components are available at similar doses on formulary? [If no, then skip to question 7.]	Yes	No
6	Has the patient had a trial and failure of the separate individual components due to an adverse event (examples: rash, nausea, vomiting, anaphylaxis) that is thought to be due to an inactive ingredient? [If no, then no further questions.]	Yes	No
7	Is the request for a brand name product that has a generic available on formulary? [If no, then skip to question 9.]	Yes	No
8	Has the patient had a trial and failure of the generic agent due to an adverse event (examples: rash, nausea, vomiting, anaphylaxis) that is thought to be due to an inactive ingredient? [If no, then no further questions.]	Yes	No
9	Is the request for a product with an available alternative dosage form for the same active ingredient on formulary? [If no, then skip to question 11.]	Yes	No
10	Is there a clinical reason why the patient is unable to take an applicable alternative formulary dosage form based on the patient's condition (e.g. age, indication)? [If no, then no further questions.]	Yes	No
11	Is the patient unable to take the required number of formulary alternatives for the given diagnosis due to a trial and inadequate treatment response or intolerance or an expected adverse reaction or contraindication? [Tech Note: For formulary medications requiring step through a pre-requisite, only one alternative is required.]	Yes	No
(Requirement: 3 in a class with 3 or more alternatives, 2 in a class with 2 alternatives, or 1 in a class with only 1 alternative.)			
<i>If yes, documentation is required for approval. Provide documentation including name of medication(s) tried and reason for treatment failure(s), intolerance and/or contraindication whichever are applicable.</i>			
<i>If the requested drug is a combination product, then the separate individual components of the combination product taken concurrently must be unable to be taken PLUS the remaining required number of alternatives.</i>			
<i>If the requested drug is a brand product and has a formulary generic for the same active ingredient, then the formulary generic must be unable to be taken PLUS the remaining required number of alternatives.</i>			

If the requested drug has an available alternative formulary dosage form of the same active ingredient, then an alternative formulary dosage form of the requested product must be unable to be taken PLUS the remaining required number of formulary alternatives. Please note, requirement for alternative dosage forms apply only if clinically appropriate (e.g., same indication, age appropriateness.)

[If yes, then no further questions.]

[Tech Note: If yes, approve if for diabetic supply/insulin cartridge and visual impairment is noted OR if for non-formulary test strips and the patient is on an insulin pump that requires the requested test strips.]

- | | | | |
|----|---|-----|----|
| 12 | Does the patient have a clinical condition or need a specific dosage form for which there is no formulary alternative or the listed formulary alternatives are not recommended based on published guidelines or clinical literature OR the formulary alternatives will likely be ineffective or less effective for the patient OR the formulary alternatives will likely cause an adverse effect? | Yes | No |
|----|---|-----|----|

If yes, documentation is required for approval. Provide documentation including clinical condition, reason for specific dosage form (if applicable), and reason that formulary alternatives cannot be used.

[Tech Note: If yes, approve if for diabetic supply/insulin cartridge and visual impairment is noted OR if for non-formulary test strips and the patient is on an insulin pump that requires the requested test strips.]

Mapping Instructions			
	Yes	No	DENIAL REASONS
1.	Deny	Go to 2	<p>You do not meet the requirements of your plan. Your plan covers this drug when it is for a condition that is a covered benefit. Your request has been denied based on the information we have.</p> <p>[Short Description: Patient using drug for a condition not covered by benefit]</p>
2.	Go to 3	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when it is being used for an FDA-approved or compendia supported indication. Your request has been denied based on the information we have.</p> <p>[Short Description: No approvable diagnosis]</p>
3.	Go to 4	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when it is being used for an FDA-Approved or compendia supported dose and quantity. Your request has been denied based on the information we have.</p> <p>[Short Description: No approvable dose and quantity]</p>
4.	Approve, 12 months or appropriate duration for requested drug and for requested quantity	Go to 5	

5.	Go to 6	Go to 7	
6.	Go to 7	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you had an adverse reaction to the separate individual drugs due to an inactive ingredient. Your request has been denied based on the information we have.</p> <p>[Short Description: Patient did not have adverse reaction to the separate individual drugs caused by the inactive ingredient]</p>
7.	Go to 8	Go to 9	
8.	Go to 9	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you had an adverse reaction to the generic drug due to an inactive ingredient. Your request has been denied based on the information we have.</p> <p>[Short Description: Patient did not have adverse reaction to the generic drug caused by the inactive ingredient]</p>
9.	Go to 10	Go to 11	
10.	Go to 11	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when there is a reason you are unable to take an alternative formulary dosage form. Your request has been denied based on the information we have.</p> <p>[Short Description: Patient is able to take alternative dosage form]</p>
11.	Approve, 12 months or appropriate duration for requested drug	Go to 12	
12.	Approve, 12 months or appropriate duration for requested drug	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when your doctor provides documentation that you meet one of these conditions:</p> <ul style="list-style-type: none"> - You have a clinical condition for which there is no appropriate formulary alternative - You need a form of the drug that is not on the formulary - You tried the required number of preferred formulary alternatives on your formulary first. These drugs did not work for you or you cannot take them. <p>Your request has been denied based on the information we have.</p> <p>[Short Description: Patient has not tried appropriate formulary alternatives and/or documentation not provided]</p>

SPECIALTY GUIDELINE MANAGEMENT

MOZOBIL (plerixafor)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Mozobil is indicated in combination with granulocyte-colony stimulating factor (G-CSF) to mobilize hematopoietic stem cells (HSCs) to the peripheral blood for collection and subsequent autologous transplantation in patients with non-Hodgkin's lymphoma and multiple myeloma.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Hematopoietic Stem Cell Mobilization (HSCs)

Authorization of 6 months may be granted for treatment of non-Hodgkin's lymphoma (NHL) and multiple myeloma when all of the following criteria are met:

- A. Mozobil will be used to mobilize hematopoietic stem cells for collection prior to autologous transplantation.
- B. Mozobil will be used in combination with G-CSF (e.g., filgrastim).
- C. Mozobil will not be used beyond 4 consecutive days or after completion of stem cell harvest/apheresis.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Mozobil [package insert]. Cambridge, MA: Genzyme Corporation; May 2019.
2. The NCCN Drugs & Biologics Compendium™ © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed September 12, 2019.
3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology™ Hematopoietic Growth Factors (Version 2.2019) <https://www.nccn.org>. Accessed September 12, 2019.
4. Micromedex® (electronic version). IBM Watson Health, Greenwood Village, Colorado. Available at <https://www.micromedexsolutions.com> [available with subscription]. Accessed January 29, 2019.
5. AHFS DI (Adult and Pediatric) [database online]. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc.; http://online.lexi.com/lco/action/doc/retrieve/docid/complete_ashp [available with subscription]. Accessed January 29, 2019.
6. Sergio G, Costa L, Schriber J, et al. Optimizing autologous stem cell mobilization strategies to improve patient outcomes: consensus guidelines and recommendations. *Biol Blood Marrow Transplant*. 2014; 20(3):295-308.

SPECIALTY GUIDELINE MANAGEMENT

MULPLETA (lusutrombopag)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Mulpleta is indicated for the treatment of thrombocytopenia in adult patients with chronic liver disease who are scheduled to undergo a procedure.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: pretreatment platelet count

III. CRITERIA FOR APPROVAL

Thrombocytopenia in chronic liver disease

Authorization of 30 days may be granted for treatment of thrombocytopenia in members with chronic liver disease when all of the following criteria are met:

- A. Member has a baseline platelet count of less than $50 \times 10^9/L$ taken within 14 days of the request.
- B. Member is scheduled to undergo a procedure.
- C. Mulpleta will not be used in combination with other thrombopoietin receptor agonists (e.g., Doptelet, Promacta, Nplate) or with spleen tyrosine kinase inhibitors (e.g., Tavalisse).

IV. REFERENCES

1. Mulpleta [package insert]. Florham Park, NJ: Shionogi Inc.; July 2018.

SPECIALTY GUIDELINE MANAGEMENT

MULPLETA (lusutrombopag)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Mulpleta is indicated for the treatment of thrombocytopenia in adult patients with chronic liver disease who are scheduled to undergo a procedure.

B. Compendial Uses

Severe thrombocytopenia post cancer chemotherapy

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

- A. Thrombocytopenia in chronic liver disease: pretreatment platelet count
- B. Severe thrombocytopenia post cancer chemotherapy: pretreatment and current platelet counts

III. EXCLUSIONS

Coverage will not be provided for members with the following exclusion: concomitant use of Mulpleta with other thrombopoietin receptor agonists (e.g., Doptelet, Promacta, Nplate) or with spleen tyrosine kinase inhibitors (e.g., Tavalisse).

IV. CRITERIA FOR INITIAL APPROVAL

A. **Thrombocytopenia in chronic liver disease**

Authorization of 30 days may be granted for treatment of thrombocytopenia in members with chronic liver disease when both of the following criteria are met:

1. Member has a baseline platelet count of less than $50 \times 10^9/L$ taken within 14 days of the request.
2. Member is scheduled to undergo a procedure.

B. **Severe thrombocytopenia post cancer chemotherapy**

Authorization of 6 months may be granted for treatment of severe thrombocytopenia post cancer chemotherapy when the platelet count is less than $50 \times 10^9/L$.

V. CONTINUATION OF THERAPY

A. Thrombocytopenia in chronic liver disease

Continuation of therapy, defined as use beyond the initial approval for same procedure, is not approvable. All members (including new members) requesting authorization due to newly scheduled procedure must meet all initial authorization criteria.

B. Severe thrombocytopenia post cancer chemotherapy

Authorization of 6 months may be granted for continued treatment of severe thrombocytopenia post cancer chemotherapy in members who experience benefit from therapy (e.g., increased platelet counts, decreased bleeding events, reduced need for platelet transfusions) and the platelet count remains less than $100 \times 10^9/L$.

VI. REFERENCES

1. Mulpleta [package insert]. Florham Park, NJ: Shionogi Inc.; July 2018.
2. NCCN hematopoietic growth factors. Short-term recommendations specific to issues with COVID-19 (SARS-CoV-2). National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org/covid-19/pdf/HGF_COVID-19.pdf. Accessed April 16, 2020.

SPECIALTY GUIDELINE MANAGEMENT

MYALEPT (metreleptin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Myalept is indicated as an adjunct to diet as replacement therapy to treat the complications of leptin deficiency in patients with congenital or acquired generalized lipodystrophy.

Limitations of Use:

1. The safety and effectiveness of Myalept for the treatment of complications of partial lipodystrophy have not been established.
2. The safety and effectiveness of Myalept for the treatment of liver disease, including nonalcoholic steatohepatitis (NASH), have not been established.
3. Myalept is not indicated for use in patients with HIV-related lipodystrophy.
4. Myalept is not indicated for use in patients with metabolic disease, including diabetes mellitus and hypertriglyceridemia, without concurrent evidence of congenital or acquired generalized lipodystrophy.

B. Compendial Use

Partial lipodystrophy in patients with confirmed leptin deficiency and metabolic abnormalities

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: leptin level (for initial requests)

III. EXCLUSIONS

Coverage will not be provided for members with any of the following exclusions:

- A. HIV-related lipodystrophy
- B. Generalized obesity not associated with generalized lipodystrophy

IV. CRITERIA FOR INITIAL APPROVAL

Lipodystrophy

Reference number
1674-A

Authorization of 6 months may be granted for treatment of lipodystrophy when ALL of the following criteria are met:

- A. Member has a diagnosis of congenital generalized lipodystrophy (i.e., Berardinelli-Seip syndrome), acquired generalized lipodystrophy (i.e., Lawrence syndrome), or partial lipodystrophy
- B. Member has leptin deficiency confirmed by laboratory testing (i.e., less than 12ng/ml)⁷⁻⁹
- C. Member has at least one complication of lipodystrophy (e.g., diabetes mellitus, hypertriglyceridemia, increased fasting insulin level)

V. CONTINUATION OF THERAPY

Lipodystrophy

Authorization of 12 months may be granted to members requesting continuation of treatment for lipodystrophy when ALL of the following criteria are met:

- A. All initial authorization criteria are met
- B. Member has experienced an improvement from baseline in metabolic control (e.g., improved glycemic control, decrease in triglycerides, decrease in hepatic enzyme levels)

VI. REFERENCES

1. Myalept [package insert]. Cambridge, MA: Aegerion Pharmaceuticals, Inc.; September 2015.
2. Brown RJ, Araujo-Vilar D, Cheung PT, et al. The diagnosis and management of lipodystrophy syndromes: A multi-society practice guideline. *J Clin Endocrinol Metab*. 2016;101(12):4500-4511.
3. Handelsman Y, Oral AE, Bloomgarden ZT, et al. The clinical approach to the detection of lipodystrophy – an AACE consensus statement. *Endocr Pract*. 2013;19:107-116.
4. Chan JL, Lutz K, Cochran E, et al. Clinical effects of long-term metreleptin treatment in patients with lipodystrophy. *Endocr Pract*. 2011;17:922-932.
5. Garg A. Lipodystrophies: genetic and acquired body fat disorders. *J Clin Endocrinol Metab*. 2011;96:3313-3325.
6. Rodriguez AJ, Mastronardi CA, Paz-Filho GJ. New advances in the treatment of generalized lipodystrophy: role of metreleptin. *Ther Clin Risk Manag*. 2015; 11:1391-1400.
7. Lee HL, Waldman MA, Auh S, et al. Effects of metreleptin on proteinuria in patients with lipodystrophy. *J Clin Endocrinol Metab*. 2019 Apr 16. pii: jc.2019-00200. doi: 10.1210/jc.2019-00200. [Epub ahead of print].
8. Oral EA, Gorden P, Cochran E, et al. Long-term effectiveness and safety of metreleptin in the treatment of patients with partial lipodystrophy. *Endocrine*. 2019 Feb 25. doi: 10.1007/s12020-019-01862-8. [Epub ahead of print].

SPECIALTY GUIDELINE MANAGEMENT

Mylotarg (gemtuzumab ozogamicin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

1. Newly diagnosed CD33-positive acute myeloid leukemia in adults
2. Relapsed or refractory CD33-positive AML in adults and pediatric patients 2 years and older

Compendial Use

Acute promyelocytic leukemia (APL)

1. In high risk patients with white blood cell count greater than 10,000/microliter
2. Following first relapse

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review (new starts only):
For AML: medical record documentation of CD33-positive tumor as confirmed by testing or analysis to identify the CD33 antigen.

III. CRITERIA FOR INITIAL APPROVAL

A. Acute Myeloid Leukemia (AML)

Authorization of 12 months may be granted for the treatment of AML when the tumor is CD33-positive as confirmed by testing or analysis to identify the CD33 antigen.

B. Acute Promyelocytic Leukemia (APL)

Authorization of 12 months may be granted for the treatment of APL when any of the following are met:

1. Member's white blood cell count is greater than 10,000/microliter.
2. The requested medication will be used for treatment after first relapse.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced disease progression or an unacceptable toxicity.

Reference number(s)
2299-A

V. REFERENCES

1. Mylotarg [package insert]. Philadelphia, PA: Pfizer; April 2018.
2. The NCCN Drugs & Biologics Compendium 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed July 17, 2019.

SPECIALTY GUIDELINE MANAGEMENT

MYOBLOC (rimabotulinumtoxin B)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

1. Treatment of cervical dystonia in adults to reduce the severity of abnormal head position and neck pain associated with cervical dystonia
2. Treatment of chronic sialorrhea in adults

B. Compendial Uses

1. Primary axillary and palmar hyperhidrosis
2. Upper limb spasticity

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

Coverage will not be provided for cosmetic use.

III. CRITERIA FOR INITIAL APPROVAL

A. **Cervical dystonia**

Authorization of 12 months may be granted for treatment of cervical dystonia (e.g., torticollis) when there is sustained head torsion and/or tilt with limited range of motion.

B. **Excessive salivation**

Authorization of 12 months may be granted for treatment of excessive salivation (chronic sialorrhea) when the member has been refractory to pharmacotherapy (e.g., anticholinergics).

C. **Primary axillary and palmar hyperhidrosis**

Authorization of 12 months may be granted for treatment of primary axillary or palmar hyperhidrosis when all of the following criteria are met:

1. Member is unresponsive or unable to tolerate pharmacotherapy prescribed for excessive sweating (e.g., anticholinergics, beta-blockers, or benzodiazepines); and
2. Significant disruption of professional and/or social life has occurred because of excessive sweating; and
3. Topical aluminum chloride or other extra-strength antiperspirants are ineffective or result in a severe rash.

D. Upper limb spasticity

Authorization of 12 months may be granted for treatment of upper limb spasticity.

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. REFERENCES

1. Myobloc [package insert]. South San Francisco, CA: Solstice Neurosciences, Inc.; August 2019.
2. DRUGDEX® System (electronic version). Truven Health Analytics, Ann Arbor, MI. Available at <http://www.micromedexsolutions.com>. Accessed August 08, 2019.
3. AHFS Drug Information. <http://online.lexi.com/lco>. Accessed August 12, 2019.
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5. Simpson DM, Hallett M, Ashman EJ et al. Practice guideline update summary: Botulinum neurotoxin for the treatment of blepharospasm, cervical dystonia, adult spasticity, and headache: Report of the Guideline Development Subcommittee of the American Academy of Neurology *Neurology* 2016; 86 (19) 1818-1826.
6. Lakraj AA, Moghimi N, Jabbari B. Sialorrhea: Anatomy, Pathophysiology and Treatment with Emphasis on the Role of Botulinum Toxins. *Toxins* 2013, 5, 1010-1031
7. Glader L, Delsing C, Hughes A et al. Sialorrhea in cerebral palsy. American Academy for Cerebral Palsy and Developmental Medicine Care Pathways. <https://www.aacpdm.org/publications/care-pathways/sialorrhea>. Accessed August 23, 2019.
8. Garuti G, Rao F, Ribuffo V et al. Sialorrhea in patients with ALS: current treatment options. *Degener Neurol Neuromuscul Dis*. 2019; 9: 19–26.

SPECIALTY GUIDELINE MANAGEMENT

NAGLAZYME (galsulfase)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Naglazyme is indicated for patients with mucopolysaccharidosis VI (MPS VI, Maroteaux-Lamy syndrome). Naglazyme has been shown to improve walking and stair-climbing capacity.

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: N-acetylgalactosamine 4-sulfatase (arylsulfatase B) enzyme assay or genetic testing results supporting diagnosis.

III. CRITERIA FOR INITIAL APPROVAL

Mucopolysaccharidosis VI (MPS VI)

Authorization of 12 months may be granted for treatment of MPS VI when the diagnosis of MPS VI was confirmed by enzyme assay demonstrating a deficiency of N-acetylgalactosamine 4-sulfatase (arylsulfatase B) enzyme activity or by genetic testing.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for mucopolysaccharidosis VI (MPS VI, Maroteaux-Lamy syndrome) who are responding to therapy (e.g., improvement, stabilization, or slowing of disease progression for 12-minute walk test [12-MWT] or 3-minute stair climb test [3-MSCT]).

V. REFERENCES

1. Naglazyme [package insert]. Novato, CA: BioMarin Pharmaceutical Inc.; March 2013.

SPECIALTY GUIDELINE MANAGEMENT

NATPARA (parathyroid hormone)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Natpara is indicated as an adjunct to calcium and vitamin D to control hypocalcemia in patients with hypoparathyroidism.

Limitations of Use:

- *Because of the potential risk of osteosarcoma, Natpara is recommended only for patients who cannot be well-controlled on calcium supplements and active forms of vitamin D alone.*
- *Natpara was not studied in patients with hypoparathyroidism caused by calcium-sensing receptor mutations.*
- *Natpara was not studied in patients with acute post-surgical hypoparathyroidism.*

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

Coverage will not be provided for members with the following exclusion:

Acute postsurgical hypoparathyroidism (within 6 months of surgery) and expected recovery from the hypoparathyroidism

III. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review:

- A. Lab results confirming serum parathyroid hormone concentrations below the lower limit of normal for the laboratory reference range on 2 separate days (at least 21 days apart) within the last 12 months
- B. Lab results confirming magnesium levels within normal laboratory limits
- C. Lab results confirming 25-hydroxyvitamin D concentration above the lower limit of normal laboratory range
- D. Lab results confirming serum calcium is above 7.5mg/dL prior to initiating therapy with the requested medication

IV. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for members who are initiating treatment with Natpara for the treatment of hypocalcemia associated with hypoparathyroidism who meet all of the following:

- A. Member has hypocalcemia and concomitant serum parathyroid hormone concentrations below the lower limit of normal for the laboratory reference range on at least 2 separate dates at least 21 days apart within the last 12 months
- B. Member is receiving vitamin D metabolite/analog therapy with calcitriol greater than or equal to 0.25 mcg per day or alphacalcidol greater than or equal to 0.5 mcg/day (or equivalent)
- C. Member is receiving supplemental calcium treatment greater than or equal to 1000 mg/day over and above normal dietary calcium intake
- D. Serum magnesium levels within normal laboratory limits
- E. Serum 25-hydroxyvitamin D concentration above the lower limit of normal laboratory range
- F. Serum calcium is greater than 7.5mg/dL prior to initiating therapy with the requested medication

V. CONTINUATION OF THERAPY

Authorization of 12 months will be granted for continued treatment in members requesting reauthorization for an indication listed in Section IV who are experiencing benefit from therapy as evidenced by having an increase in calcium and parathyroid hormone level from baseline.

VI. REFERENCES

1. Natpara [package insert]. Bedminster, NJ: NPS Pharmaceuticals, Inc.; December 2018.
2. Khan MI, Waguespack SG, Hu MI. Medical management of postsurgical hypoparathyroidism. *Endocr Pract.* 2011;17(Suppl 1): 18-25.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

NAYZILAM
(midazolam nasal spray)

Status: CVS Caremark Criteria

Type: Initial Prior Authorization

Ref # 3102-C

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Nayzilam is indicated for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from a patient's usual seizure pattern in patients with epilepsy 12 years of age and older.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from the patient's usual seizure pattern in a patient with epilepsy

AND

- The patient is 12 years of age or older

Quantity Limits apply.

RATIONALE

Nayzilam is indicated for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from a patient's usual seizure pattern in patients with epilepsy 12 years of age and older. Patients and caregivers should be instructed on what is and is not an intermittent and stereotypic episode of increased seizure activity (i.e., seizure cluster) that is appropriate for treatment, and the timing of administration in relation to the onset of the episode. The initial dose of Nayzilam is one spray (5 mg dose) administered into one nostril. If needed, one additional spray (5 mg dose) may be administered into the opposite nostril after 10 minutes if the patient has not responded to the initial dose. A second dose of Nayzilam should not be administered if the patient has trouble breathing or if there is excessive sedation that is uncharacteristic of the patient during a seizure cluster episode. Do not use more than 2 doses of Nayzilam to treat a single episode. It is recommended that Nayzilam be used to treat no more than 1 episode every three days and no more than 5 episodes per month.

Nayzilam is supplied as a solution of midazolam. Each single-dose nasal spray unit delivers 5 mg of midazolam in 0.1 mL of solution. Nayzilam is supplied in boxes of 2 nasal spray units, each contained within an individual blister pack. Because it is not recommended to treat more than 5 episodes per month and each episode could require up to 2 doses, the limit will be set at 5 boxes, 10 nasal spray units.

REFERENCES

1. Nayzilam [package insert]. Plymouth, MN: Proximagen, LLC; May 2019.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed May 2019.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed May 2019.

Written by: UM Development (DS)
 Date Written: 06/2019
 Revised:
 Reviewed: Medical Affairs (GAD) 07/2019
 External Review: 10/2019

CRITERIA FOR APPROVAL

- | | | | |
|---|--|-----|----|
| 1 | Is the requested drug being prescribed for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from the patient's usual seizure pattern in a patient with epilepsy? | Yes | No |
| 2 | Is the patient 12 years of age or older? | Yes | No |
| 3 | Does the patient require more than the plan allowance of 10 nasal spray units per month? | Yes | No |
- [RPh Note: If yes, then deny and enter a partial approval for 10 nasal spray units per month of Nayzilam.]

Mapping Instructions

	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Deny	<p>You do not meet the requirements of your plan.</p> <p>Your plan covers this drug when you meet all of the following:</p> <ul style="list-style-type: none"> - You have epilepsy - The requested drug is being used for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from your usual seizure pattern <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No approvable diagnosis]</p>
2.	Go to 3	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you are 12 years of age or older.</p> <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No approvable diagnosis]</p>
3.	Deny	Approve, 12 months, 10 nasal spray units (5 boxes)/month	<p>You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 10 nasal spray units/month of the requested drug and strength. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied.</p> <p>[Short Description: Over max quantity]</p>

Reference number(s)
2178-A

SPECIALTY GUIDELINE MANAGEMENT

NERLYNX (neratinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Nerlynx is indicated for the extended adjuvant treatment of adult patients with early stage human epidermal growth factor receptor (HER)2-overexpressed/amplified breast cancer, to follow adjuvant trastuzumab based therapy.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of human epidermal growth factor receptor 2 (HER2) status is necessary to initiate the prior authorization review.

III. CRITERIA FOR INITIAL APPROVAL

Breast cancer

Authorization of up to 12 months total may be granted for the treatment of early stage HER2-positive breast cancer when Nerlynx will be initiated after completing adjuvant trastuzumab-based therapy.

IV. CONTINUATION OF THERAPY

Authorization of 12 months total may be granted for continuation of therapy for an indication outlined in section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Nerlynx [package insert]. Los Angeles, CA: Puma Biotechnology; June 2018.
2. Chan A, Delaloge S, Holmes FA, et al. Neratinib after trastuzumab-based adjuvant therapy in patients with HER2-positive breast cancer (ExteNET): a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Oncol.* 2016; 17(3):367-77.
3. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed August 15, 2019.

SPECIALTY GUIDELINE MANAGEMENT

NEULASTA (pegfilgrastim) FULPHILA (pegfilgrastim-jmdp) UDENYCA (pegfilgrastim-cbqv) ZIEXTENZO (pegfilgrastim-bmez)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Neulasta

1. Patients with Cancer Receiving Myelosuppressive Chemotherapy
Neulasta is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.
2. Hematopoietic Syndrome of Acute Radiation Syndrome
Neulasta is indicated to increase survival in patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome).

Fulphila

Patients with Cancer Receiving Myelosuppressive Chemotherapy
Fulphila is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia

Udenyca

Patients with Cancer Receiving Myelosuppressive Chemotherapy
Udenyca is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.

Ziextenzo

Patients with Cancer Receiving Myelosuppressive Chemotherapy
Ziextenzo is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.

Limitations of Use: Ziextenzo is not indicated for the mobilization of peripheral blood progenitor cells for hematopoietic stem cell transplantation.

B. Compendial Use

Reference number(s)
1931-A

1. Stem cell transplantation-related indications
2. Prophylaxis for chemotherapy-induced febrile neutropenia in patients with solid tumors
3. Radiation therapy/injury
4. Hairy cell leukemia
5. Chronic Myeloid Leukemia (CML), treatment of resistant neutropenia due to tyrosine kinases inhibitor therapy

All other indications are considered experimental/investigational and are not a covered benefit.

II. REQUIRED DOCUMENTATION

A. Primary Prophylaxis of Febrile Neutropenia

1. Documentation must be provided of the member's diagnosis and chemotherapeutic regimen.
2. If chemotherapeutic regimen has an intermediate risk of febrile neutropenia (10-19% [See Appendix B]), documentation must be provided outlining the patient's risk factors that confirm the member is at high risk for febrile neutropenia.

III. CRITERIA FOR INITIAL APPROVAL

A. Prevention of neutropenia in cancer patients receiving myelosuppressive chemotherapy¹⁻⁶

Authorization of 6 months may be granted for prevention of febrile neutropenia when all of the following criteria are met (1, 2, 3, and 4):

1. The requested medication will not be used in combination with other colony stimulating factors within any chemotherapy cycle.
2. The member will not be receiving concurrent chemotherapy and radiation therapy.
3. The requested medication will not be administered with weekly chemotherapy regimens.
4. One of the following criteria is met (i or ii):
 - i. The requested medication will be used for primary prophylaxis in members with a solid tumor or non-myeloid malignancies who have received, are currently receiving, or will be receiving myelosuppressive anti-cancer therapy that is expected to result in 20% or higher incidence of FN (*See Appendix A*) OR 10 – 19% risk of FN (*See Appendix B*) and who are considered to be at high risk of FN because of bone marrow compromise or co-morbidity, including any of the following (not an all-inclusive list):
 - a. Active infections, open wounds, or recent surgery
 - b. Age greater than or equal to 65 years
 - c. Bone marrow involvement by tumor producing cytopenias
 - d. Previous chemotherapy or radiation therapy
 - e. Poor nutritional status
 - f. Poor performance status
 - g. Previous episodes of FN
 - h. Other serious co-morbidities, including renal dysfunction, liver dysfunction, HIV infection, cardiovascular disease
 - i. Persistent neutropenia
 - ii. The requested medication will be used for secondary prophylaxis in members with solid tumors or non-myeloid malignancies who experienced a febrile neutropenic complication or a dose-limiting neutropenic event (a nadir or day of treatment count impacting the planned dose of chemotherapy) from a prior cycle of similar chemotherapy, with the same dose and scheduled planned for the current cycle (for which primary prophylaxis was not received).

B. Other indications

Authorization of 6 months may be granted for members with any of the following indications:

1. Stem cell transplantation-related indications

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2. Radiation therapy/injury
 - i. Manage neutropenia in members acutely exposed to myelosuppressive doses of radiation therapy
 - ii. Treatment of radiation injury
3. Hairy cell leukemia
Individuals with hairy cell leukemia with neutropenic fever following chemotherapy.
4. Chronic Myeloid Leukemia
Individuals with Chronic Myeloid Leukemia (CML) for treatment of resistant neutropenia due to tyrosine kinase inhibitor therapy

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. APPENDIX

A. APPENDIX A: Selected Chemotherapy Regimens with an Incidence of Febrile Neutropenia of 20% or Higher

1. Acute Lymphoblastic Leukemia:
Select ALL regimens as directed by treatment protocol (see NCCN guidelines)
2. Bladder Cancer:
 - i. Dose dense MVAC (methotrexate, vinblastine, doxorubicin, cisplatin)
 - ii. CBDCA/Pac (carboplatin, paclitaxel)
3. Bone Cancer
 - i. VAI (vincristine, doxorubicin or dactinomycin, ifosfamide)
 - ii. VDC-IE (vincristine, doxorubicin or dactinomycin, and cyclophosphamide alternating with ifosfamide and etoposide)
 - iii. Cisplatin/doxorubicin
 - iv. VDC (cyclophosphamide, vincristine, doxorubicin or dactinomycin)
 - v. VIDE (vincristine, ifosfamide, doxorubicin or dactinomycin, etoposide)
4. Breast Cancer:
 - i. Docetaxel + trastuzumab
 - ii. Dose-dense AC (doxorubicin, cyclophosphamide) + paclitaxel (or dose dense paclitaxel)
 - iii. TAC (docetaxel, doxorubicin, cyclophosphamide)
 - iv. AT (doxorubicin, docetaxel)
 - v. Doc (docetaxel)
 - vi. TC (docetaxel, cyclophosphamide)
 - vii. TCH (docetaxel, carboplatin, trastuzumab)
5. Colorectal Cancer:
FOLFOXIRI (fluorouracil, leucovorin, oxaliplatin, irinotecan)
6. Esophageal and Gastric Cancers:
Docetaxel/cisplatin/fluorouracil
7. Head and Neck Squamous Cell Carcinoma
TPF (docetaxel, cisplatin, fluorouracil)
8. Hodgkin Lymphoma:
 - i. Brentuximab vedotin + AVD (doxorubicin, vinblastine, dacarbazine)
 - ii. Escalated BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone)
9. Kidney Cancer:
Doxorubicin/gemcitabine
10. Non-Hodgkin's Lymphoma:

- i. Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin)
 - ii. ICE (ifosfamide, carboplatin, etoposide)
 - iii. Dose-dense CHOP-14 (cyclophosphamide, doxorubicin, vincristine, prednisone) + rituximab
 - iv. MINE (mesna, ifosfamide, novantrone, etoposide)
 - v. DHAP (dexamethasone, cisplatin, cytarabine)
 - vi. ESHAP (etoposide, methylprednisolone, cisplatin, cytarabine (Ara-C))
 - vii. HyperCVAD + rituximab (cyclophosphamide, vincristine, doxorubicin, dexamethasone + rituximab)
 - viii. VAPEC-B (vincristine, doxorubicin, prednisolone, etoposide, cyclophosphamide, bleomycin)
11. Melanoma:
Dacarbazine-based combination with IL-2, interferon alpha (dacarbazine, cisplatin, vinblastine, IL-2, interferon alpha)
12. Multiple myeloma:
- i. DT-PACE (dexamethasone/ thalidomide/ cisplatin/ doxorubicin/ cyclophosphamide/ etoposide) + bortezomib (VTD-PACE)
 - ii. DT-PACE
(dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide)
13. Ovarian Cancer:
- i. Topotecan
 - ii. Docetaxel
14. Pancreatic Cancer:
FOLFIRINOX (fluorouracil, leucovorin, irinotecan, oxaliplatin)
15. Soft Tissue Sarcoma:
- i. MAID (mesna, doxorubicin, ifosfamide, dacarbazine)
 - ii. Doxorubicin
 - iii. Ifosfamide/doxorubicin
16. Small Cell Lung Cancer:
- i. Top (topotecan)
 - ii. CAV (cyclophosphamide, doxorubicin, vincristine)
17. Testicular cancer:
- i. VeIP (vinblastine, ifosfamide, cisplatin)
 - ii. VIP (etoposide, ifosfamide, cisplatin)
 - iii. TIP (paclitaxel, ifosfamide, cisplatin)

B. APPENDIX B: Selected Chemotherapy Regimens with an Incidence of Febrile Neutropenia of 10% to 19%

- 1. Occult primary – adenocarcinoma:
Gemcitabine/docetaxel
- 2. Breast cancer:
 - i. Docetaxel
 - ii. CMF classic (cyclophosphamide, methotrexate, fluorouracil)
 - iii. CA (doxorubicin, cyclophosphamide) (60 mg/m²) (hospitalized)
 - iv. AC (doxorubicin, cyclophosphamide) + sequential docetaxel (taxane portion only)
 - v. AC + sequential docetaxel + trastuzumab
 - vi. A (doxorubicin) (75 mg/m²)
 - vii. AC (doxorubicin, cyclophosphamide)
 - viii. CapDoc (capecitabine, docetaxel)
 - ix. Paclitaxel every 21 days

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3. Cervical Cancer:
 - i. Irinotecan
 - ii. Cisplatin/topotecan
 - iii. Paclitaxel/cisplatin
 - iv. Topotecan
4. Colorectal:
 - i. FL (fluorouracil, leucovorin)
 - ii. CPT-11 (irinotecan) (350 mg/m² q 3 wk)
 - iii. FOLFOX (fluorouracil, leucovorin, oxaliplatin)
5. Esophageal and Gastric Cancers:
 - i. Irinotecan/cisplatin
 - ii. Epirubicin/cisplatin/fluorouracil
 - iii. Epirubicin/cisplatin/capecitabine
6. Non-Hodgkin's lymphomas:
 - i. EPOCH-IT chemotherapy
 - ii. GDP (gemcitabine, dexamethasone, cisplatin/carboplatin)
 - iii. GDP (gemcitabine, dexamethasone, cisplatin/carboplatin) + rituximab
 - iv. FMR (fludarabine, mitoxantrone, rituximab)
 - v. CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) including regimens with pegylated liposomal doxorubicin
 - vi. CHOP + rituximab (cyclophosphamide, doxorubicin, vincristine, prednisone, rituximab) including regimens with pegylated liposomal doxorubicin
 - vii. CHP (cyclophosphamide, doxorubicin, prednisone) + brentuximab vedotin
 - viii. Bendamustine
7. Non-Small Cell Lung Cancer:
 - i. Cisplatin/paclitaxel
 - ii. Cisplatin/vinorelbine
 - iii. Cisplatin/docetaxel
 - iv. Cisplatin/etoposide
 - v. Carboplatin/paclitaxel
 - vi. Docetaxel
8. Ovarian cancer:

Carboplatin/docetaxel
9. Prostate cancer:

Cabazitaxel
10. Small Cell Lung Cancer:

Etoposide/carboplatin
11. Testicular Cancer:
 - i. BEP (bleomycin, etoposide, cisplatin)
 - ii. Etoposide/cisplatin
12. Uterine sarcoma:

Docetaxel

VI. REFERENCES

1. Neulasta [package insert]. Thousand Oaks, CA: Amgen Inc.; April 2019.
2. Fulphila [package insert]. Zurich, Switzerland: Mylan; May 2019.
3. Udenyca [package insert]. Redwood City, California: Coherus BioSciences, Inc; September 2019.
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SPECIALTY GUIDELINE MANAGEMENT

NEUPOGEN (filgrastim) GRANIX (tbo-filgrastim) ZARXIO (filgrastim-sndz) NIVESTYM (filgrastim-aafi)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Neupogen

1. Patients with Cancer Receiving Myelosuppressive Chemotherapy
Neupogen is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever.
2. Patients With Acute Myeloid Leukemia Receiving Induction or Consolidation Chemotherapy
Neupogen is indicated for reducing the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of adults with acute myeloid leukemia.
3. Patients with Cancer Receiving Bone Marrow Transplant
Neupogen is indicated to reduce the duration of neutropenia and neutropenia-related clinical sequelae, (e.g., febrile neutropenia) in patients with non-myeloid malignancies undergoing myeloablative chemotherapy followed by marrow transplantation.
4. Patients Undergoing Autologous Peripheral Blood Progenitor Cell Collection and Therapy
Neupogen is indicated for the mobilization of autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.
5. Patients With Severe Chronic Neutropenia
Neupogen is indicated for chronic administration to reduce the incidence and duration of sequelae of neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia.
6. Hematopoietic Syndrome of Acute Radiation Syndrome
Neupogen is indicated to increase survival in patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome).

Nivestym

1. Patients with Cancer Receiving Myelosuppressive Chemotherapy

Reference number(s)
1930-A

Nivestym is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever.

2. **Patients With Acute Myeloid Leukemia Receiving Induction or Consolidation Chemotherapy**
Nivestym is indicated for reducing the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of adults with acute myeloid leukemia.
3. **Patients with Cancer Receiving Bone Marrow Transplant (BMT)**
Nivestym is indicated to reduce the duration of neutropenia and neutropenia-related clinical sequelae, (e.g., febrile neutropenia) in patients with non-myeloid malignancies undergoing myeloablative chemotherapy followed by marrow transplantation.
4. **Patients Undergoing Autologous Peripheral Blood Progenitor Cell Collection and Therapy**
Nivestym is indicated for the mobilization of autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.
5. **Patients With Severe Chronic Neutropenia**
Nivestym is indicated for chronic administration to reduce the incidence and duration of sequelae of neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia.

Granix

Granix is indicated to reduce the duration of severe neutropenia in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.

Zarxio

1. **Patients with Cancer Receiving Myelosuppressive Chemotherapy**
Zarxio is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever.
2. **Patients With Acute Myeloid Leukemia Receiving Induction or Consolidation Chemotherapy**
Zarxio is indicated for reducing the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of adults with acute myeloid leukemia.
3. **Patients with Cancer Undergoing Bone Marrow Transplant**
Zarxio is indicated to reduce the duration of neutropenia and neutropenia-related clinical sequelae, (e.g., febrile neutropenia) in patients with non-myeloid malignancies undergoing myeloablative chemotherapy followed by marrow transplantation.
4. **Patients Undergoing Autologous Peripheral Blood Progenitor Cell Collection and Therapy**
Zarxio is indicated for the mobilization of autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.
5. **Patients With Severe Chronic Neutropenia**
Zarxio is indicated for chronic administration to reduce the incidence and duration of sequelae of neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia.

B. Compendial Uses (Neupogen/Granix/Zarxio/Nivestym)

1. Treatment of chemotherapy-induced febrile neutropenia in patients with non-myeloid malignancies
2. Prophylaxis for chemotherapy-induced febrile neutropenia in patients with solid tumors
3. Treatment of anemia and neutropenia in patients with myelodysplastic syndromes (MDS)

Reference number(s)
1930-A

4. Stem cell transplantation-related indications
5. Agranulocytosis (non-chemotherapy drug induced)
6. Aplastic anemia
7. Neutropenia related to HIV/AIDS
8. Neutropenia related to renal transplantation
9. Acute myeloid leukemia
10. Severe chronic neutropenia (congenital, cyclic, or idiopathic)
11. Radiation therapy/injury
12. Supportive care for neutropenic patients with CAR T-cell-related toxicities
13. Hairy Cell Leukemia
14. Chronic Myeloid Leukemia
15. Glycogen Storage Disease (GSD) Type 1

All other indications are considered experimental/investigational and are not a covered benefit.

II. REQUIRED DOCUMENTATION

A. Primary Prophylaxis of Febrile Neutropenia

1. Documentation must be provided of the member's diagnosis and chemotherapeutic regimen.
2. If chemotherapeutic regimen has an intermediate risk of febrile neutropenia (10-19% [See Appendix B]), documentation must be provided outlining the patient's risk factors that confirm the member is at high risk for febrile neutropenia.

III. CRITERIA FOR INITIAL APPROVAL

A. Neutropenia in cancer patients receiving myelosuppressive chemotherapy¹⁻⁶

Authorization of 6 months may be granted for prevention or treatment of febrile neutropenia when all of the following criteria are met (1, 2, and 3):

1. The requested medication will not be used in combination with other colony stimulating factors within any chemotherapy cycle.
2. The member will not be receiving concurrent chemotherapy and radiation therapy.
3. One of the following criteria is met (i, ii, or iii):
 - i. The requested medication will be used for primary prophylaxis in members with solid tumors or non-myeloid malignancies who have received, are currently receiving, or will be receiving myelosuppressive anti-cancer therapy that is expected to result in 20% or higher incidence of FN (See Appendix A) OR 10 – 19% risk of FN (See Appendix B) and who are considered to be at high risk of FN because of bone marrow compromise or co-morbidity, including any of the following (not an all-inclusive list):
 - a. Active infections, open wounds, or recent surgery
 - b. Age greater than or equal to 65 years
 - c. Bone marrow involvement by tumor producing cytopenias
 - d. Previous chemotherapy or radiation therapy
 - e. Poor nutritional status
 - f. Poor performance status
 - g. Previous episodes of FN
 - h. Other serious co-morbidities, including renal dysfunction, liver dysfunction, HIV infection, cardiovascular disease
 - i. Persistent neutropenia
 - ii. The requested medication will be used for secondary prophylaxis in members with solid tumors or non-myeloid malignancies who experienced a febrile neutropenic complication or a dose-limiting

neutropenic event (a nadir or day of treatment count impacting the planned dose of chemotherapy) from a prior cycle of similar chemotherapy, with the same dose and schedule planned for the current cycle (for which primary prophylaxis was not received)

- iii. The requested medication will be used for treatment of high risk FN in members who have any of the following prognostic factors that are predictive of clinical deterioration:
 - a. Age greater than 65 years
 - b. Being hospitalized at the time of the development of fever
 - c. Sepsis syndrome
 - d. Invasive fungal infection
 - e. Pneumonia or other clinically documented infection
 - f. Prolonged (neutropenia expected to last greater than 10 days) or profound (absolute neutrophil count less than $1 \times 10^9/L$) neutropenia
 - g. Prior episodes of febrile neutropenia

B. Other indications

Authorization of 6 months may be granted for members with any of the following indications:

1. Myelodysplastic syndrome (anemia or neutropenia)
2. Stem cell transplantation-related indications
3. Agranulocytosis (non-chemotherapy drug induced)
4. Aplastic anemia
5. Neutropenia related to HIV/AIDS
6. Neutropenia related to renal transplantation
7. Acute myeloid leukemia
8. Severe chronic neutropenia (congenital, cyclic, or idiopathic)
9. Radiation therapy/injury
 - i. Manage neutropenia in members acutely exposed to myelosuppressive doses of radiation therapy
 - ii. Treatment of radiation injury
10. CAR T-cell-related toxicities
Supportive care for neutropenic patients with CAR T-cell-related toxicities
11. Hairy Cell Leukemia
Individuals with Hairy Cell Leukemia with neutropenic fever following chemotherapy.
12. Chronic Myeloid Leukemia
Individuals with Chronic Myeloid Leukemia (CML) for treatment of resistant neutropenia due to tyrosine kinase inhibitor therapy
13. Glycogen Storage Disease (GSD) Type 1
Individuals with GSD Type 1 for treatment of low neutrophil counts

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. APPENDIX

- A. APPENDIX A: Selected Chemotherapy Regimens with an Incidence of Febrile Neutropenia of 20% or Higher
 1. Acute Lymphoblastic Leukemia:
Select ALL regimens as directed by treatment protocol (see NCCN guidelines)

Reference number(s)
1930-A

2. Bladder Cancer:
 - i. Dose dense MVAC (methotrexate, vinblastine, doxorubicin, cisplatin)
 - ii. CBDCA/Pac (carboplatin, paclitaxel)
3. Bone Cancer
 - i. VAI (vincristine, doxorubicin or dactinomycin, ifosfamide)
 - ii. VDC-IE (vincristine, doxorubicin or dactinomycin, and cyclophosphamide alternating with ifosfamide and etoposide)
 - iii. Cisplatin/doxorubicin
 - iv. VDC (cyclophosphamide, vincristine, doxorubicin or dactinomycin)
 - v. VIDE (vincristine, ifosfamide, doxorubicin or dactinomycin, etoposide)
4. Breast Cancer:
 - i. Docetaxel + trastuzumab
 - ii. Dose-dense AC (doxorubicin, cyclophosphamide) + paclitaxel (or dose dense paclitaxel)
 - iii. TAC (docetaxel, doxorubicin, cyclophosphamide)
 - iv. AT (doxorubicin, docetaxel)
 - v. Doc (docetaxel)
 - vi. TC (docetaxel, cyclophosphamide)
 - vii. TCH (docetaxel, carboplatin, trastuzumab)
5. Colorectal Cancer:

FOLFOXIRI (fluorouracil, leucovorin, oxaliplatin, irinotecan)
6. Esophageal and Gastric Cancers:

Docetaxel/cisplatin/fluorouracil
7. Head and Neck Squamous Cell Carcinoma

TPF (docetaxel, cisplatin, fluorouracil)
8. Hodgkin Lymphoma:
 - i. Brentuximab vedotin + AVD (doxorubicin, vinblastine, dacarbazine)
 - ii. Escalated BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone)
9. Kidney Cancer:

Doxorubicin/gemcitabine
10. Non-Hodgkin's Lymphoma:
 - i. Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin)
 - ii. ICE (ifosfamide, carboplatin, etoposide)
 - iii. Dose-dense CHOP-14 (cyclophosphamide, doxorubicin, vincristine, prednisone) + rituximab
 - iv. MINE (mesna, ifosfamide, novantrone, etoposide)
 - v. DHAP (dexamethasone, cisplatin, cytarabine)
 - vi. ESHAP (etoposide, methylprednisolone, cisplatin, cytarabine (Ara-C))
 - vii. HyperCVAD + rituximab (cyclophosphamide, vincristine, doxorubicin, dexamethasone + rituximab)
 - viii. VAPEC-B (vincristine, doxorubicin, prednisolone, etoposide, cyclophosphamide, bleomycin)
11. Melanoma:

Dacarbazine-based combination with IL-2, interferon alpha (dacarbazine, cisplatin, vinblastine, IL-2, interferon alpha)
12. Multiple myeloma:
 - i. DT-PACE (dexamethasone/ thalidomide/ cisplatin/ doxorubicin/ cyclophosphamide/ etoposide) + bortezomib (VTD-PACE)
 - ii. DT-PACE
(dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide)

Reference number(s)
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13. Ovarian Cancer:
 - i. Topotecan
 - ii. Docetaxel
14. Pancreatic Cancer:
FOLFIRINOX (fluorouracil, leucovorin, irinotecan, oxaliplatin)
15. Soft Tissue Sarcoma:
 - i. MAID (mesna, doxorubicin, ifosfamide, dacarbazine)
 - ii. Doxorubicin
 - iii. Ifosfamide/doxorubicin
16. Small Cell Lung Cancer:
 - i. Top (topotecan)
 - ii. CAV (cyclophosphamide, doxorubicin, vincristine)
17. Testicular cancer:
 - i. VeIP (vinblastine, ifosfamide, cisplatin)
 - ii. VIP (etoposide, ifosfamide, cisplatin)
 - iii. TIP (paclitaxel, ifosfamide, cisplatin)

B. APPENDIX B: Selected Chemotherapy Regimens with an Incidence of Febrile Neutropenia of 10% to 19%

1. Occult primary – adenocarcinoma:
Gemcitabine/docetaxel
2. Breast cancer:
 - i. Docetaxel
 - ii. CMF classic (cyclophosphamide, methotrexate, fluorouracil)
 - iii. CA (doxorubicin, cyclophosphamide) (60 mg/m²) (hospitalized)
 - iv. AC (doxorubicin, cyclophosphamide) + sequential docetaxel (taxane portion only)
 - v. AC + sequential docetaxel + trastuzumab
 - vi. A (doxorubicin) (75 mg/m²)
 - vii. AC (doxorubicin, cyclophosphamide)
 - viii. CapDoc (capecitabine, docetaxel)
 - ix. Paclitaxel every 21 days
3. Cervical Cancer:
 - i. Irinotecan
 - ii. Cisplatin/topotecan
 - iii. Paclitaxel/cisplatin
 - iv. Topotecan
4. Colorectal:
 - i. FL (fluorouracil, leucovorin)
 - ii. CPT-11 (irinotecan) (350 mg/m² q 3 wk)
 - iii. FOLFOX (fluorouracil, leucovorin, oxaliplatin)
5. Esophageal and Gastric Cancers:
 - i. Irinotecan/cisplatin
 - ii. Epirubicin/cisplatin/fluorouracil
 - iii. Epirubicin/cisplatin/capecitabine
6. Non-Hodgkin's lymphomas:
 - i. EPOCH-IT chemotherapy
 - ii. GDP (gemcitabine, dexamethasone, cisplatin/carboplatin)
 - iii. GDP (gemcitabine, dexamethasone, cisplatin/carboplatin) + rituximab
 - iv. FMR (fludarabine, mitoxantrone, rituximab)
 - v. CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) including regimens with pegylated liposomal doxorubicin

Reference number(s)
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- vi. CHOP + rituximab (cyclophosphamide, doxorubicin, vincristine, prednisone, rituximab) including regimens with pegylated liposomal doxorubicin
- vii. CHP (cyclophosphamide, doxorubicin, prednisone) + brentuximab vedotin
- viii. Bendamustine
- 7. Non-Small Cell Lung Cancer:
 - i. Cisplatin/paclitaxel
 - ii. Cisplatin/vinorelbine
 - iii. Cisplatin/docetaxel
 - iv. Cisplatin/etoposide
 - v. Carboplatin/paclitaxel
 - vi. Docetaxel
- 8. Ovarian cancer:
 - Carboplatin/docetaxel
- 9. Prostate cancer:
 - Cabazitaxel
- 10. Small Cell Lung Cancer:
 - Etoposide/carboplatin
- 11. Testicular Cancer:
 - i. BEP (bleomycin, etoposide, cisplatin)
 - ii. Etoposide/cisplatin
- 12. Uterine sarcoma:
 - Docetaxel

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Reference number(s)
1930-A

MEDICAL NECESSITY CRITERIA

MEDICAL NECESSITY CRITERIA (NEW TO MARKET DRUGS)

Status: CVS Caremark Criteria

Type: Medical Necessity Criteria

Ref # 1175-A

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being used for an FDA-Approved indication OR an indication supported in the compendia of current literature (examples: AHFS, Micromedex, current accepted guidelines)

AND

- The prescribed quantity falls within the manufacturer's published dosing guidelines or within dosing guidelines found in the compendia of current literature (examples: package insert, AHFS, Micromedex, current accepted guidelines)

AND

- The patient had an inadequate treatment response or intolerance to all formulary alternatives for the given diagnosis (or to at least 1 agent within each of a given class of agents when more than 1 class is available for the diagnosis)

OR

- The patient has a contraindication to all formulary alternatives

OR

- This is the only FDA-Approved product for the patient's diagnosis.

RATIONALE

The intent of the criteria is to ensure that patients follow selection elements noted in labeling and/or practice guidelines in order to decrease the potential for inappropriate utilization. The intent of this Formulary Exception program is to confirm the appropriate coverage of a non-formulary prescription medication for patients. These criteria apply to all medications subject to formulary exception not otherwise managed through drug specific Prior Authorization criteria.

This policy is intended to ensure that medications subject to formulary exception under the CVS Health National Formulary are utilized in accordance with FDA indications and uses found in the compendia of current literature including American Hospital Formulary Service Drug Information (AHFS), Micromedex, or current accepted guidelines. This policy also aims to insure that non-formulary medications are approved within manufacturer's dosing guidelines or dosing guidelines of current compendia and to foster cost-effective, first-line use of available formulary/preferred drug list medications.

In addition, if the patient has tried and had an inadequate treatment response, intolerance, or contraindication to all formulary alternatives (generics and/or formulary brands), OR, there are no other FDA-Approved products for the patient's diagnosis, the prior authorization will be approved.

REFERENCES

N/A

Written by: UM Development (PL)

Date Written: 08/2014

Revised: (NB) 10/2014, 02/2015, 02/2016, (TM) 03/2016 (add Q1&2), (TM/JK) 06/2016 (add Q3, and e.g.), (NB) 09/2016 (moved #5, separated #6 & #7, reworded #8), (TM) 12/2016 (#3 e.g.), (changed duration to 12 mos), (TM, NB) 02/2017 (remove questions 1,2,3, changed reqd # to all), (TM) 02/2018 (no clinical changes), (TM) 02/2019 (no clinical changes)

Reviewed: Medical Affairs (LCB) 08/2014, 10/2014, (SS) 02/2015, 02/2016, (WF) 03/2016, (WF) 06/2016, (AN) 02/2017

External Review: 09/2014, 10/2014, 06/2015, 04/2016, 07/2016, 10/2016, 04/2017, 04/2018, 04/2019

CRITERIA FOR APPROVAL

- | | | | |
|---|--|-----|----|
| 1 | Is the requested drug being used for an FDA-Approved indication or an indication supported in the compendia of current literature (examples: AHFS, Micromedex, current accepted guidelines)? | Yes | No |
| 2 | Does the prescribed quantity fall within the manufacturer's published dosing guidelines or within dosing guidelines found in the compendia of current literature (examples: package insert, AHFS, Micromedex, current accepted guidelines)? | Yes | No |
| 3 | Has the patient had an inadequate treatment response or intolerance to all formulary alternatives for the given diagnosis (or to at least 1 agent within each of a given class of agents when more than 1 class is available for the diagnosis)?
[If yes, then no further questions.] | Yes | No |
| 4 | Does the patient have a contraindication to all formulary alternatives?
[If yes, then no further questions.] | Yes | No |
| 5 | Is this the only FDA-Approved product to treat the patient's diagnosis? | Yes | No |

Mapping Instructions

	Yes	No
1	Go to 2	Deny
2	Go to 3	Deny
3	Approve, 12 months	Go to 4
4	Approve, 12 months	Go to 5
5	Approve, 12 months	Deny

MEDICAL NECESSITY CRITERIA

MEDICAL NECESSITY CRITERIA (NEW TO MARKET DRUGS)

Status: CVS Caremark Criteria

Type: Medical Necessity Criteria

Ref # 1175-A

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being used for an FDA-approved indication OR an indication supported in the compendia of current literature (examples: AHFS, Micromedex, current accepted guidelines)

AND

- The prescribed dose and quantity fall within the FDA-approved labeling or within dosing guidelines found in the compendia of current literature

AND

- The patient had an inadequate treatment response or intolerance to the required number of formulary alternatives for the given diagnosis [Note: Requirement: 3 in a class with 3 or more alternatives, 2 in a class with 2 alternatives, or 1 in a class with only 1 alternative.]

OR

- The patient has a contraindication to all formulary alternatives

OR

- This is the only FDA-approved product for the patient's diagnosis

RATIONALE

The intent of the criteria is to ensure that patients follow selection elements noted in labeling and/or practice guidelines in order to decrease the potential for inappropriate utilization. The intent of this Formulary Exception program is to confirm the appropriate coverage of a non-formulary prescription medication for patients. These criteria apply to all medications subject to formulary exception not otherwise managed through drug specific Prior Authorization criteria.

This policy is intended to ensure that medications subject to formulary exception under the CVS Health National Formulary are utilized in accordance with FDA indications and uses found in the compendia of current literature including American Hospital Formulary Service Drug Information (AHFS), Micromedex, or current accepted guidelines. This policy also aims to insure that non-formulary medications are approved within manufacturer's dosing guidelines or dosing guidelines of current compendia and to foster cost-effective, first-line use of available formulary/preferred drug list medications.

In addition, if the patient has tried and had an inadequate treatment response, intolerance, or contraindication to the required number of formulary alternatives (generics and/or formulary brands), OR, there are no other FDA-approved products for the patient's diagnosis, the prior authorization will be approved.

REFERENCES

N/A

Written by: UM Development (PL)

Date Written: 08/2014

Revised: (NB) 10/2014, 02/2015, 02/2016, (TM) 03/2016 (add Q1&2), (TM/JK) 06/2016 (add Q3, and e.g.), (NB) 09/2016 (moved #5, separated #6 & #7, reworded #8), (TM) 12/2016 (#3 e.g.), (changed duration to 12 mos), (TM, NB) 02/2017 (remove questions 1,2,3, changed reqd # to all), (TM) 02/2018 (no clinical changes), (TM) 02/2019 (no clinical changes); (JK) 02/2020 (added denial reasons, changed T/F of all formulary alts to required number of alts)

Reviewed: Medical Affairs (LCB) 08/2014, 10/2014, (SS) 02/2015, 02/2016, (WF) 03/2016, (WF) 06/2016, (AN) 02/2017; (CHART) 02/27/2020
External Review: 09/2014, 10/2014, 06/2015, 04/2016, 07/2016, 10/2016, 04/2017, 04/2018, 04/2019, 04/2020

New To Market Drugs Medical Necessity 1175-A 02-2020_7-10-20.doc

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CRITERIA FOR APPROVAL

- | | | | |
|---|--|-----|----|
| 1 | Is the requested drug being used for an FDA-approved indication or an indication supported in the compendia of current literature (examples: AHFS, Micromedex, current accepted guidelines)? | Yes | No |
| 2 | Does the prescribed dose and quantity fall within the FDA-approved labeling or within dosing guidelines found in the compendia of current literature? | Yes | No |
| 3 | Has the patient had an inadequate treatment response or intolerance to the required number of formulary alternatives for the given diagnosis?
[Note: Requirement: 3 in a class with 3 or more alternatives, 2 in a class with 2 alternatives, or 1 in a class with only 1 alternative.]
[If yes, then no further questions.] | Yes | No |
| 4 | Does the patient have a contraindication to all formulary alternatives?
[If yes, then no further questions.] | Yes | No |
| 5 | Is this the only FDA-approved product to treat the patient's diagnosis? | Yes | No |

Mapping Instructions

	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when it is being used for an FDA-approved or compendia supported indication. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
2.	Go to 3	Deny	You do not meet the requirements of your plan. Your plan covers this drug when it is being used for an FDA-approved or compendia supported dose and quantity. Your request has been denied based on the information we have. [Short Description: No approvable dose and quantity]
3.	Approve, 12 months	Go to 4	
4.	Approve, 12 months	Go to 5	
5.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your request has been denied based on the information we have. Your plan covers this drug when you meet any of these conditions: - You tried the required number of formulary alternatives on your formulary first and these drugs did not work for you or you cannot tolerate them. - You cannot take all the formulary alternatives. - This is the only FDA-approved product to treat your diagnosis Your request has been denied based on the information we have. Short Description: No inadequate response, intolerance, contraindication to prerequisite drug or not the only product for the diagnosis]

SPECIALTY GUIDELINE MANAGEMENT

NEXAVAR (sorafenib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Hepatocellular carcinoma
Nexavar is indicated for the treatment of patients with unresectable hepatocellular carcinoma (HCC).
2. Renal cell carcinoma
Nexavar is indicated for the treatment of patients with advanced renal cell carcinoma (RCC).
3. Differentiated thyroid carcinoma
Nexavar is indicated for the treatment of locally recurrent or metastatic, progressive, differentiated thyroid carcinoma (DTC) that is refractory to radioactive iodine treatment.

B. Compendial Uses

1. Hepatocellular carcinoma (Child-Pugh Class A or B7)
 - a. Patients who have unresectable disease and are not a transplant candidate
 - b. Patients who are inoperable by performance status or comorbidity, or have local disease or local disease with minimal extrahepatic disease only
 - c. Patients who have metastatic disease or extensive liver tumor burden
 - d. Subsequent treatment as a single-agent for patients who have progressed after first-line lenvatinib
2. Acute myeloid leukemia
 - a. In combination with azacitidine or decitabine in patients age ≥ 60 years with FLT3-ITD mutation as low-intensity treatment induction when not a candidate for intensive induction therapy or declines intensive therapy
 - b. In combination with azacitidine or decitabine in patients age ≥ 60 years with FLT3-ITD mutation, as post-remission therapy following response to previous lower intensity therapy with the same regimen
 - c. A component of repeating the initial successful induction if late relapse (greater than or equal to 12 months) for relapsed or refractory disease
 - d. In combination with azacitidine or decitabine for relapsed or refractory disease
3. Soft tissue sarcoma subtypes
 - a. Angiosarcoma, as single agent therapy
 - b. Desmoid tumors (aggressive fibromatosis), primary, recurrent, or progressive disease
 - c. Solitary fibrous tumor, as single-agent therapy
 - d. Hemangiopericytoma, as single-agent therapy
 - e. Leiomyosarcoma
4. Gastrointestinal stromal tumors (GIST), treatment for disease progression after single-agent therapy with imatinib, sunitinib and regorafenib
5. Thyroid carcinoma (medullary carcinoma, papillary carcinoma, Hürthle cell carcinoma, or follicular)
6. Relapsed/refractory bone cancer, as second-line therapy as a single agent for the following subtypes:
 - a. Osteosarcoma

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2027-A

- b. Dedifferentiated chondrosarcoma
- c. High-grade undifferentiated pleomorphic sarcoma (UPS)
- 7. Recurrent chordoma
- 8. Epithelial ovarian cancer, fallopian tube cancer, and primary peritoneal cancer; if platinum-resistant, in combination with topotecan for persistent disease or recurrence

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: FLT3-ITD mutation testing results (where applicable)

III. CRITERIA FOR INITIAL APPROVAL

A. Hepatocellular Carcinoma

- 1. Authorization of 12 months may be granted for treatment of unresectable or metastatic hepatocellular carcinoma.
- 2. Authorization of 12 months may be granted for treatment of hepatocellular carcinoma for subsequent treatment as a single agent for members who progressed after first-line lenvatinib.

B. Acute Myeloid Leukemia

Authorization of 12 months may be granted for treatment of acute myeloid leukemia when either of the following criteria are met:

- 1. Nexavar will be used in combination with azacitidine or decitabine in members age 60 or older with FLT3-ITD mutation as low-intensity treatment induction or post-remission therapy; OR
- 2. Nexavar will be used for relapsed/refractory disease as either:
 - a. A component of repeating the initial successful induction if late relapse (greater than or equal to 12 months); OR
 - b. In combination with azacitidine or decitabine if the member is FLT3-ITD mutation positive.

C. Soft Tissue Sarcoma

- 1. Authorization of 12 months may be granted for treatment of leiomyosarcoma.
- 2. Authorization of 12 months may be granted for treatment of angiosarcoma, solitary fibrous tumor, or hemangiopericytoma as single agent therapy.
- 3. Authorization of 12 months may be granted for treatment of primary, recurrent, or progressive desmoid tumor/aggressive fibromatosis.

D. Gastrointestinal Stromal Tumor (GIST)

Authorization of 12 months may be granted for treatment of gastrointestinal stromal tumor for disease progression after single-agent therapy with imatinib, sunitinib, and regorafenib.

E. Renal Cell Carcinoma

Authorization of 12 months may be granted for treatment of advanced renal cell carcinoma.

F. Differentiated Thyroid Carcinoma

Authorization of 12 months may be granted for treatment of progressive and/or symptomatic radioiodine refractory papillary, Hürthle cell, or follicular thyroid carcinoma.

G. Medullary Thyroid Carcinoma

Reference number
2027-A

Authorization of 12 months may be granted for treatment of medullary thyroid carcinoma when either of the following criteria are met:

1. Member has an intolerance or contraindication to vandetanib (Caprelsa) AND cabozantinib (Cometriq), OR
2. Member has disease progression while on vandetanib (Caprelsa) or cabozantinib (Cometriq).

H. Bone Cancer

1. Authorization of 12 months may be granted for treatment as second-line therapy for relapsed/refractory or metastatic disease as a single agent for the following types of bone cancer:
 - a. Osteosarcoma
 - b. Dedifferentiated chondrosarcoma
 - c. High-grade undifferentiated pleomorphic sarcoma (UPS)

I. Chordoma

Authorization of 12 months may be granted for treatment of recurrent chordoma as a single agent.

J. Epithelial Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer

Authorization of 12 months may be granted for treatment of epithelial ovarian, fallopian tube, or primary peritoneal cancer if the disease is platinum-resistant and Nexavar is given in combination with topotecan for persistent disease or recurrence.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication in Section III who are clinically benefiting from therapy or who have not experienced an unacceptable toxicity.

V. REFERENCES

1. Nexavar [package insert]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc.; December 2018.
2. The NCCN Drugs & Biologic Compendium 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed May 28, 2019.
3. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Hepatobiliary Cancers. Version 2.2019. Accessed May 30, 2019. https://www.nccn.org/professionals/physician_gls/pdf/hepatobiliary.pdf.
4. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Acute Myeloid Leukemia. Version 3.2019. Accessed May 30, 2019. https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf.
5. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Kidney Cancer. Version 4.2019. Accessed May 30, 2019. https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf.
6. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Thyroid Carcinoma. Version 1.2019. Accessed May 30, 2019. https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf.
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Specialty Guideline Management

NINLARO (ixazomib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Ninlaro is indicated in combination with lenalidomide and dexamethasone for the treatment of patients with multiple myeloma who have received at least one prior therapy.

B. Compendial Uses

1. Multiple Myeloma

- In combination with lenalidomide and dexamethasone as primary therapy for active (symptomatic) myeloma or disease relapse after 6 months following primary induction therapy with the same regimen
- In combination with dexamethasone for patients who have received at least one prior therapy for previously treated myeloma for relapsed or progressive disease
- In combination with dexamethasone and pomalidomide for patients who have received at least two prior therapies including an immunomodulatory agent and a proteasome inhibitor and who have demonstrated disease progression on or within 60 days of completion of the last therapy for previously treated myeloma for relapsed or progressive disease

2. Systemic light chain amyloidosis

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Multiple Myeloma**

Authorization of 12 months may be granted for treatment of multiple myeloma when any of the following criteria is met:

- Ninlaro is prescribed in combination with lenalidomide and dexamethasone
- Ninlaro is prescribed in combination with dexamethasone for patients with relapsed or progressive disease
- Ninlaro is prescribed in combination with pomalidomide and dexamethasone for patients who have received at least two prior therapies.

B. **Systemic Light Chain Amyloidosis**

Authorization of 12 months may be granted for treatment of relapsed or refractory systemic light chain amyloidosis.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced unacceptable toxicity or disease progression while on the current regimen.

Reference number(s)
2372-A

IV. REFERENCES

1. Ninlaro [package insert]. Cambridge, MA: Takeda Pharmaceutical Company Limited; November 2016.
2. The NCCN Drugs & Biologics Compendium 2018 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed March 25, 2019.
3. The NCCN Clinical Practice Guidelines in Oncology Multiple Myeloma (Version 1.2019) 2018 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed March 25, 2019.

SPECIALTY GUIDELINE MANAGEMENT

NORTHERA (droxidopa)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Treatment of orthostatic dizziness, lightheadedness, or the “feeling that you are about to black out” in adult patients with symptomatic neurogenic orthostatic hypotension (NOH) caused by primary autonomic failure [Parkinson's disease (PD), multiple system atrophy, and pure autonomic failure], dopamine beta-hydroxylase deficiency, and non-diabetic autonomic neuropathy. Effectiveness beyond 2 weeks of treatment has not been established. The continued effectiveness of Northera should be assessed periodically.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: blood measure measurements demonstrating a persistent, consistent decrease in systolic blood pressure (SBP) of at least 20 mmHg or decrease in diastolic blood pressure (DBP) of at least 10 mmHg within 3 minutes of standing.

III. CRITERIA FOR INITIAL APPROVAL

Neurogenic orthostatic hypotension

Authorization of 3 months may be granted for treatment of neurogenic orthostatic hypotension when all of the following criteria are met:

- A. Member has a persistent, consistent decrease in SBP of at least 20 mmHg or decrease in DBP of at least 10 mmHg within 3 minutes of standing.
- B. Member has neurogenic orthostatic hypotension due to **ONE** of the following diagnoses:
 - 1. Primary autonomic failure due to Parkinson's disease, multiple system atrophy, and pure autonomic failure, OR
 - 2. Dopamine beta hydroxylase deficiency, OR
 - 3. Non-diabetic autonomic neuropathy

IV. CONTINUATION OF THERAPY

Neurogenic orthostatic hypotension

Authorization of 6 months may be granted for treatment of neurogenic orthostatic hypotension when all of the following criteria are met:

- A. Member has experienced a sustained decrease in dizziness
- B. Member has neurogenic orthostatic hypotension due to **ONE** of the following diagnoses:
 - 1. Primary autonomic failure due to Parkinson's disease, multiple system atrophy, and pure autonomic failure, OR
 - 2. Dopamine beta hydroxylase deficiency, OR
 - 3. Non-diabetic autonomic neuropathy

V. REFERENCES

- 1. Northera [package insert]. Deerfield, IL: Lundbeck Inc.; July 2019.

SPECIALTY GUIDELINE MANAGEMENT

NOVOSEVEN RT (coagulation factor VIIa [recombinant])

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Hemophilia A or hemophilia B with inhibitors
2. Congenital factor VII deficiency
3. Glanzmann's thrombasthenia
4. Acquired hemophilia

B. Compendial Uses

1. Acquired von Willebrand syndrome
2. Inhibitors to factor XI

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Congenital Factor VII Deficiency**

Indefinite authorization may be granted for treatment of congenital factor VII deficiency.

B. **Hemophilia A with Inhibitors**

Indefinite authorization may be granted for treatment of hemophilia A with inhibitors (see Appendix) when the inhibitor titer is ≥ 5 Bethesda units per milliliter (BU/mL) or the member has a history of an inhibitor titer ≥ 5 BU.

C. **Hemophilia B with Inhibitors**

Indefinite authorization may be granted for treatment of hemophilia B with inhibitors (see Appendix) when the inhibitor titer is ≥ 5 Bethesda units per milliliter (BU/mL) or the member has a history of an inhibitor titer ≥ 5 BU.

D. **Glanzmann's Thrombasthenia**

Indefinite authorization may be granted to members for treatment of Glanzmann's thrombasthenia.

E. **Acquired Hemophilia**

Indefinite authorization may be granted for treatment of acquired hemophilia.

F. Acquired von Willebrand Syndrome

Indefinite authorization may be granted for treatment of acquired von Willebrand syndrome when other therapies failed to control the member's condition (e.g., desmopressin or factor VIII/von Willebrand factor).

G. Inhibitors to Factor XI

Indefinite authorization may be granted for treatment of members with inhibitors to factor XI.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. APPENDIX

Appendix: Inhibitors - Bethesda Units (BU)

The presence of inhibitors is confirmed by a specific blood test called the Bethesda inhibitor assay.

- High-titer inhibitors:
 - ≥ 5 BU/mL
 - Inhibitors act strongly and quickly neutralize factor
- Low-titer inhibitors:
 - < 5 BU/mL
 - Inhibitors act weakly and slowly neutralize factor

V. REFERENCES

1. NovoSeven RT [package insert]. Princeton, NJ: Novo Nordisk Inc.; October 2018.
2. National Institutes of Health. The diagnosis, evaluation, and management of von Willebrand disease. Bethesda, MD: US Dept of Health and Human Services, National Institutes of Health; 2007. NIH publication No. 08-5832
3. Tiede A, Rand J, Budde U, et al. How I treat the acquired von Willebrand syndrome. *Blood*. 2011;117(25):6777-85.
4. Federici A, Budde U, Castaman G, Rand J, Tiede A. Current diagnostic and therapeutic approaches to patients with acquired von Willebrand syndrome: a 2013 update. *Semin Thromb Hemost*. 2013;39(2):191-201.
5. O'Connell NM. Factor XI deficiency – from molecular genetics to clinical management. *Blood Coagul Fibrinolysis*. 2003; 14(Suppl1):S59-S64.
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8. National Hemophilia Foundation. MASAC recommendations concerning products licensed for the treatment of hemophilia and other bleeding disorders. Revised April 2018. MASAC Document # 253. Accessed December 19, 2018.

Reference number(s)
1947-A

9. World Federation of Hemophilia. What are inherited platelet function disorders? <http://www1.wfh.org/publication/files/pdf-1336.pdf>. Accessed December 19, 2018.
10. World Federation of Hemophilia. Platelet function disorders. <http://www1.wfh.org/publication/files/pdf-1147.pdf>. Accessed December 11, 2017.
11. Rajpurkar M, Chitlur M, Recht M, Cooper DL. Use of recombinant activated factor VII in patients with Glanzmann's thrombasthenia: a review of the literature. *Haemophilia*. 2014;20(4):464-471.
12. Duga S, Salomon O. Congenital factor XI deficiency: an update. *Semin Thromb Hemost*. 2013;39(6):621-631.

SPECIALTY GUIDELINE MANAGEMENT

NOVOSEVEN RT (coagulation factor VIIa [recombinant])

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Hemophilia A or hemophilia B with inhibitors
2. Congenital factor VII deficiency
3. Glanzmann's thrombasthenia
4. Acquired hemophilia

B. Compendial Uses

1. Acquired von Willebrand syndrome
2. Inhibitors to factor XI

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Congenital Factor VII Deficiency**

Indefinite authorization may be granted for treatment of congenital factor VII deficiency.

B. **Hemophilia A with Inhibitors**

Indefinite authorization may be granted for treatment of hemophilia A with inhibitors (see Appendix) when the inhibitor titer is ≥ 5 Bethesda units per milliliter (BU/mL) or the member has a history of an inhibitor titer ≥ 5 BU.

C. **Hemophilia B with Inhibitors**

Indefinite authorization may be granted for treatment of hemophilia B with inhibitors (see Appendix) when the inhibitor titer is ≥ 5 Bethesda units per milliliter (BU/mL) or the member has a history of an inhibitor titer ≥ 5 BU.

D. **Glanzmann's Thrombasthenia**

Indefinite authorization may be granted for treatment of Glanzmann's thrombasthenia.

E. **Acquired Hemophilia**

Indefinite authorization may be granted for treatment of acquired hemophilia.

F. Acquired von Willebrand Syndrome

Indefinite authorization may be granted for treatment of acquired von Willebrand syndrome when other therapies failed to control the member's condition (e.g., desmopressin or factor VIII/von Willebrand factor).

G. Inhibitors to Factor XI

Indefinite authorization may be granted for treatment of inhibitors to factor XI.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. APPENDIX

Appendix: Inhibitors - Bethesda Units (BU)

The presence of inhibitors is confirmed by a specific blood test called the Bethesda inhibitor assay.

- High-titer inhibitors:
 - ≥ 5 BU/mL
 - Inhibitors act strongly and quickly neutralize factor
- Low-titer inhibitors:
 - < 5 BU/mL
 - Inhibitors act weakly and slowly neutralize factor

V. REFERENCES

1. NovoSeven RT [package insert]. Plainsboro, NJ: Novo Nordisk Inc.; January 2019.
2. National Institutes of Health. The diagnosis, evaluation, and management of von Willebrand disease. Bethesda, MD: US Dept of Health and Human Services, National Institutes of Health; 2007. NIH publication No. 08-5832
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6. Salomon O, Zivelin A, Livnat T, Seligsohn U. Inhibitors to factor XI in patients with severe factor XI deficiency. *Semin Hematol*. 2006;43(1 Suppl 1):S10-S12.
7. Srivastava A, Brewer AK, Mauser-Bunschoten EP, et al. Guidelines for the management of hemophilia. *Haemophilia*. 2013;19(1):e1-e47.
8. National Hemophilia Foundation. MASAC recommendations concerning products licensed for the treatment of hemophilia and other bleeding disorders. Revised April 2018. MASAC Document # 253. Accessed December 3, 2019.

Reference number(s)
1947-A

9. World Federation of Hemophilia. What are inherited platelet function disorders? <http://www1.wfh.org/publication/files/pdf-1336.pdf>. 2010. Accessed December 10, 2019.
10. World Federation of Hemophilia. Platelet function disorders. <http://www1.wfh.org/publication/files/pdf-1147.pdf>. 2008. Accessed December 10, 2019.
11. Rajpurkar M, Chitlur M, Recht M, Cooper DL. Use of recombinant activated factor VII in patients with Glanzmann's thrombasthenia: a review of the literature. *Haemophilia*. 2014;20(4):464-471.
12. Duga S, Salomon O. Congenital factor XI deficiency: an update. *Semin Thromb Hemost*. 2013;39(6):621-631.

SPECIALTY GUIDELINE MANAGEMENT

NPLATE (romiplostim)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Nplate is indicated for the treatment of thrombocytopenia in:

1. Adult patients with immune thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy.
2. Pediatric patients 1 year of age and older with ITP for at least 6 months who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy.

B. Compendial Uses

Myelodysplastic syndromes, for lower risk disease in patients with severe or refractory thrombocytopenia following disease progression or no response to hypomethylating agents or immunosuppressive therapy

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

Immune thrombocytopenia: pretreatment and current platelet counts

III. EXCLUSIONS

Coverage will not be provided for members with the following exclusion: concomitant use of Nplate with other thrombopoietin receptor agonists (e.g., Promacta, Doptelet, Muplesta) or with spleen tyrosine kinase inhibitors (e.g., Tavalisse)

IV. CRITERIA FOR INITIAL APPROVAL

A. **Immune thrombocytopenia (ITP)**

Authorization of 6 months may be granted for treatment of ITP when both of the following criteria are met:

1. Inadequate response or intolerance to prior therapy with corticosteroids, immunoglobulins, or splenectomy.
2. Untransfused platelet count at time of diagnosis is less than $30 \times 10^9/L$ OR $30 \times 10^9/L$ to $50 \times 10^9/L$ with symptomatic bleeding (e.g., significant mucous membrane bleeding, gastrointestinal bleeding or trauma) or risk factors for bleeding (see Section VI).

Reference number(s)
1927-A

B. Myelodysplastic Syndromes

Authorization of 12 months may be granted for treatment of myelodysplastic syndromes when both of the following criteria are met:

1. Member has lower risk disease defined as Revised International Prognostic Scoring System (IPSS-R) (Very Low, Low, Intermediate), International Prognostic Scoring System (IPSS) (Low/Intermediate-1), WHO classification-based Prognostic Scoring System (WPSS) (Very Low, Low, Intermediate).
2. Member has severe or refractory thrombocytopenia following disease progression or no response to hypomethylating agents (such as azacitidine and decitabine) or immunosuppressive therapy.

V. CONTINUATION OF THERAPY

A. Immune thrombocytopenia (ITP)

1. Authorization of 3 months may be granted to members with current platelet count less than $50 \times 10^9/L$ for whom the platelet count is not sufficient to prevent clinically important bleeding and who have not received a maximal Nplate dose for at least 4 weeks.
2. Authorization of 12 months may be granted to members with current platelet count less than $50 \times 10^9/L$ for whom the current platelet count is sufficient to prevent clinically important bleeding.
3. Authorization of 12 months may be granted to members with current platelet count of $50 \times 10^9/L$ to $200 \times 10^9/L$.
4. Authorization of 12 months may be granted to members with current platelet count greater than $200 \times 10^9/L$ to less than or equal to $400 \times 10^9/L$ for whom Nplate dosing will be adjusted to achieve a platelet count sufficient to avoid clinically important bleeding.

B. Myelodysplastic Syndromes

Authorization of 12 months may be granted for continued treatment of myelodysplastic syndromes in members who experience benefit from therapy (e.g., increased platelet counts, decreased bleeding events, reduced need for platelet transfusions).

VI. APPENDIX

Examples of risk factors for bleeding (not all inclusive)

- Undergoing a medical or dental procedure where blood loss is anticipated
- Comorbidity (e.g., peptic ulcer disease, hypertension)
- Mandated anticoagulation therapy
- Profession (e.g., construction worker) or lifestyle (e.g., plays contact sports) that predisposes patient to trauma

VII. REFERENCES

1. Nplate [package insert]. Thousand Oaks, CA: Amgen Inc.; October 2019.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed June 13, 2019.
3. The NCCN Clinical Practice Guidelines in Oncology® Myelodysplastic Syndrome (Version 2.2019). © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed June 13, 2019.
4. Bose P, Hussein KK, Terrell DR, et al. Successful treatment of cyclic thrombocytopenia with thrombopoietin-mimetic agents: a report of two patients. *Am J Hematol*. 2009;84:459-461.
5. Rice L, Nichol JL, McMillan R, et al. Cyclic immune thrombocytopenia responsive to thrombopoietic growth factor therapy. *Am J Hematol*. 2001;68:210-214.

Reference number(s)
1927-A

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8. Rodeghiero F, Stasi R, Gernsheimer T, et al. Standardization of terminology, definitions and outcome criteria in immune thrombocytopenic purpura of adults and children: report from an international working group. *Blood*. 2009;113(11):2386-2393.

SPECIALTY GUIDELINE MANAGEMENT

NUBEQA (darolutamide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication ^[1]

Nubeqa is indicated for the treatment of patients with non-metastatic castration-resistant prostate cancer.

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

Coverage will not be provided if the requested medication is used in combination with a second-generation oral anti-androgen (e.g., apalutamide [Erleada]) or an oral androgen metabolism inhibitor (e.g., abiraterone acetate [Zytiga]).

III. CRITERIA FOR INITIAL APPROVAL

Prostate Cancer ^[1]

Authorization of 12 months may be granted to members for the treatment of non-metastatic castration-resistant prostate cancer when the member has had a bilateral orchiectomy or will be using the requested medication in combination with a GnRH analog.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III if who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES

1. Nubeqa [package insert]. Whippany, NJ: Bayer Healthcare Pharmaceuticals Inc.; July 2019.

SPECIALTY GUIDELINE MANAGEMENT

NUCALA (mepolizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

- A. Nucala is indicated for add-on maintenance treatment of patients with severe asthma aged 6 years and older, and with an eosinophilic phenotype.
- B. Nucala is indicated for the treatment of adult patients with eosinophilic granulomatosis with polyangiitis (EGPA).

Limitations of Use: Not for relief of acute bronchospasm or status asthmaticus

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review (initial requests only):

- A. Asthma: Member's chart or medical record showing baseline blood eosinophil count
- B. EGPA: Member's chart or medical record showing blood eosinophil count or level as noted in section III.B.2. below

III. CRITERIA FOR INITIAL APPROVAL

A. Asthma

Authorization of 6 months may be granted for treatment of asthma when all of the following criteria are met:

1. Member is 6 years of age or older.
2. Member has a baseline blood eosinophil count of at least 150 cells per microliter.
3. Member has inadequate asthma control (e.g., hospitalization or emergency medical care visit within the past year) despite current treatment with both of the following medications at optimized doses:
 - a. Inhaled corticosteroid
 - b. Additional controller (long acting beta₂-agonist, leukotriene modifier, or sustained-release theophylline)
4. Member will not use Nucala as monotherapy.
5. Member will not use Nucala concomitantly with other biologics (e.g., Cinqair, Dupixent, Fasenra, Xolair).

B. Eosinophilic granulomatosis with polyangiitis

Authorization of 12 months may be granted for treatment of eosinophilic granulomatosis with polyangiitis when all of the following criteria are met:

1. Member is 18 years of age or older.
2. Member has a history or the presence of an eosinophil count of more than 1000 cells per microliter or a blood eosinophil level of greater than 10%
3. Member has at least two of the following disease characteristics of EGPA:
 - a. Biopsy showing histopathological evidence of eosinophilic vasculitis, perivascular eosinophilic infiltration, or eosinophil-rich granulomatous inflammation
 - b. Neuropathy, mono or poly (motor deficit or nerve conduction abnormality)
 - c. Pulmonary infiltrates, non-fixed; sino-nasal abnormality
 - d. Cardiomyopathy (established by echocardiography or magnetic resonance imaging)
 - e. Glomerulonephritis (hematuria, red cell casts, proteinuria)
 - f. Alveolar hemorrhage (by bronchoalveolar lavage)
 - g. Palpable purpura
 - h. Anti-neutrophil cytoplasmic anti-body (ANCA) positive (Myeloperoxidase or proteinase 3)
4. Member has had at least one relapse (requiring increase in oral corticosteroids dose, initiation/increased dose of immunosuppressive therapy or hospitalization) within 2 years prior to starting treatment with Nucala or has a refractory disease.

IV. CONTINUATION OF THERAPY**A. Asthma**

Authorization of 12 months may be granted for continuation of treatment of asthma when all of the following criteria are met:

1. Member is 6 years of age or older.
2. Asthma control has improved on Nucala treatment as demonstrated by at least one of the following:
 - a. A reduction in the frequency and/or severity of symptoms and exacerbations
 - b. A reduction in the daily maintenance oral corticosteroid dose⁷
3. Member will not use Nucala as monotherapy.
4. Member will not use Nucala concomitantly with other biologics (e.g., Cinqair, Dupixent, Fasenna, Xolair).

B. Eosinophilic granulomatosis with polyangiitis

Authorization of 12 months may be granted for continuation of treatment of eosinophilic granulomatosis with polyangiitis when all of the following criteria are met:

1. Member is 18 years of age or older.
2. Member has beneficial response to treatment with Nucala as demonstrated by any of the following:
 - a. A reduction in the frequency of relapses, or
 - b. A reduction in the daily oral corticosteroid dose, or
 - c. No active vasculitis

V. OTHER

Note: If the member is a current smoker, they should be counseled on the harmful effects of smoking on pulmonary conditions and available smoking cessation options.

VI. REFERENCES

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2. Ortega HG, Liu MC, Pavord ID, et al. Mepolizumab treatment in patients with severe eosinophilic asthma. *N Engl J Med*. 2014;371:1198-1207.
3. Bel EH, Wenzel SE, Thompson PJ, et al. Oral glucocorticoid-sparing effect of mepolizumab in eosinophilic asthma. *N Engl J Med*. 2014;371:1189-1197.
4. National Institutes of Health. *National Asthma Education and Prevention Program Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma - Full Report 2007*. Bethesda, MD: National Heart Lung and Blood Institute; August 2007. <http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf>. Accessed March 18, 2019.
5. Global Initiative for Asthma (GINA). Global Strategy for Asthma Management and Prevention. 2018 update. <http://ginasthma.org/2018-gina-report-global-strategy-for-asthma-management-and-prevention/>. Accessed March 18, 2019.
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8. GlaxoSmithKline. A Study to Investigate Mepolizumab in the Treatment of Eosinophilic Granulomatosis With Polyangiitis. Available from <https://clinicaltrials.gov/ct2/show/record/NCT02020889>. NLM identifier: NCT02020889. Accessed March 21, 2019.
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10. Yates M, Watts RA, Bajema M, et al. EULAR/ERA-EDTA recommendations for the management of ANCA-associated vasculitis. *Ann Rheum Dis* 2016;75:1583-1594.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

NUEDEXTA
(dextromethorphan hydrobromide/quinidine sulfate)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

Ref# 870-A
Ref# 599-A

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Nuedexta is indicated for the treatment of pseudobulbar affect (PBA). PBA occurs secondary to a variety of otherwise unrelated neurologic conditions, and is characterized by involuntary, sudden, and frequent episodes of laughing and/or crying. PBA episodes typically occur out of proportion or incongruent to the underlying emotional state. PBA is a specific condition, distinct from other types of emotional lability that may occur in patients with neurological disease or injury.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has a diagnosis of pseudobulbar affect (PBA)

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Nuedexta is indicated for the treatment of pseudobulbar affect (PBA). PBA occurs secondary to a variety of otherwise unrelated neurologic conditions, and is characterized by involuntary, sudden, and frequent episodes of laughing and/or crying. PBA episodes typically occur out of proportion or incongruent to the underlying emotional state. PBA is a specific condition, distinct from other types of emotional lability that may occur in patients with neurological disease or injury.

REFERENCES

1. Nuedexta [package insert]. Aliso Viejo, CA: Avanir Pharmaceuticals, Inc.; June 2019.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed July 2019.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed July 2019.

Written by: UM Development (TM)
Date Written: 12/2010
Revised: 870-A: (MS) 09/2011, 08/2012; (PL) 10/2012 (extended duration), (SE) 08/2013; (MS) 08/2014, 08/2015, 08/2016 (removed safety question), (SE/AJ) 08/2017
MDC-2 599-A: (MS) 09/2011, 08/2012, (SE) 04/2013, (SE) 07/2013 (removed quantity limits), 08/2013; (MS) 08/2014, (LN) 04/2015 (Added denial Reasons); (MS) 08/2015, (SE) 06/2016 (created separate Med D); (MS) 08/2016 (removed safety question), (SE/AJ) 08/2017
Reviewed: (SE/AH) 08/2018 (combined documents - no clinical changes); (DS) 08/2019 (no clinical changes)
Medical Affairs 870-A: (KP) 12/2010, 09/2011; (DC) 08/2012, (LMS) 08/2013; (SS) 08/2014; (LB) 08/2015; (ME) 08/2016, (JG) 08/2017
Medical Affairs MDC-2 599-A: (KP) 12/2010, 09/2011; (DC) 08/2012, (DR) 05/2013, (LMS) 07/2013, 08/2013; (SS) 08/2014; (LB) 08/2015; (ME) 08/2016, (JG) 08/2017; (CHART) 08/29/19
External Review: 02/2011, 12/2011, 02/2013, 02/2014, 12/2014, 12/2015, 12/2016, 12/2017, 12/2018, 12/2019

CRITERIA FOR APPROVAL (870-A and MDC-2 599-A)

1 Does the patient have a diagnosis of pseudobulbar affect (PBA)? Yes No

Mapping Instructions (870-A)

	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Approve, 36 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have pseudobulbar affect. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]

Guidelines for Approval (599-A)

Duration of Approval		12 Months
Set 1		
Yes to question(s)		No to question(s)
1		None

Mapping Instructions (599-A)

	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have pseudobulbar affect. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]

SPECIALTY GUIDELINE MANAGEMENT

NUPLAZID (pimavanserin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Nuplazid is indicated for the treatment of hallucinations and delusions associated with Parkinson's disease psychosis.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for initial treatment of hallucinations and delusions associated with Parkinson's disease psychosis when the member has mild or no cognitive impairment as determined by physician's clinical diagnosis and/or cognitive impairment screening tests (e.g. Mini-Mental Status Examination [MMSE], Montreal Cognitive Assessment [MOCA]).

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment of hallucinations and delusions associated with Parkinson's disease psychosis when the member has experienced improvement in psychotic symptoms (hallucinations and/or delusions) since starting therapy.

IV. REFERENCES

1. Nuplazid [package insert]. San Diego, CA: Acadia Pharmaceuticals, Inc.; May 2019.
2. Cummings J, Isaacson S, Mills R, et al. Pimavanserin for patients with Parkinson's disease psychosis: a randomized, placebo-controlled phase 3 trial. *Lancet*. 2014; 383:533-540.
3. Hoops S, Nazem S, et al. Validity of the MoCA and MMSE in the detection of MCI and dementia in Parkinson disease. *Neurology*. 2009; 73 (21): 1738-1745.

SPECIALTY GUIDELINE MANAGEMENT

OBIZUR (antihemophilic factor [recombinant], porcine sequence)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Obizur is indicated for the treatment of bleeding episodes in adults with acquired hemophilia A.

Limitations of Use:

- A. Safety and efficacy of Obizur has not been established in patients with a baseline anti-porcine factor VIII inhibitor titer of greater than 20 BU.
- B. Obizur is not indicated for the treatment of congenital hemophilia A or von Willebrand disease

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Acquired hemophilia A

Authorization of 1 month may be granted for treatment of acquired hemophilia A.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Obizur [package insert]. Westlake Village, CA: Baxter Healthcare Corporation; October 2015.
2. National Hemophilia Foundation. MASAC recommendations concerning products licensed for the treatment of hemophilia and other bleeding disorders. Revised April 2018. MASAC Document # 253. Accessed December 19, 2018.
3. Gomperts E. Recombinant B domain deleted porcine factor VIII for the treatment of bleeding episodes in adults with acquired hemophilia A. *Expert Review of Hematology*. 2015 Aug;8(4):427-32.

SPECIALTY GUIDELINE MANAGEMENT

OBIZUR (antihemophilic factor [recombinant], porcine sequence)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Obizur is indicated for the treatment of bleeding episodes in adults with acquired hemophilia A.

Limitations of Use:

- A. Safety and efficacy of Obizur has not been established in patients with a baseline anti-porcine factor VIII inhibitor titer of greater than 20 BU.
- B. Obizur is not indicated for the treatment of congenital hemophilia A or von Willebrand disease.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Acquired hemophilia A

Authorization of 1 month may be granted for treatment of acquired hemophilia A.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Obizur [package insert]. Lexington, MA: Baxalta US Inc.; September 2017.
2. National Hemophilia Foundation. MASAC recommendations concerning products licensed for the treatment of hemophilia and other bleeding disorders. Revised April 2018. MASAC Document # 253. Available at <https://www.wfh.org/en/resources/wfh-treatment-guidelines>. Accessed December 12, 2019.
3. Gomperts E. Recombinant B domain deleted porcine factor VIII for the treatment of bleeding episodes in adults with acquired hemophilia A. *Expert Review of Hematology*. 2015 Aug;8(4):427-32.

SPECIALTY GUIDELINE MANAGEMENT

OCALIVA (obeticholic acid)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Ocaliva is indicated for the treatment of primary biliary cholangitis (PBC) in combination with ursodeoxycholic acid (UDCA) in adults with an inadequate response to UDCA, or as monotherapy in adults unable to tolerate UDCA. This indication is approved under accelerated approval based on a reduction in alkaline phosphatase (ALP). An improvement in survival or disease-related symptoms has not been established. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

- A. For initial requests: Pretreatment serum alkaline phosphatase (ALP) level
- B. For continuation of therapy: Current serum alkaline phosphatase (ALP) and/or current total bilirubin level

III. CRITERIA FOR INITIAL APPROVAL

Primary biliary cholangitis (PBC) (previously known as primary biliary cirrhosis)

Authorization of 6 months may be granted for treatment of PBC in members 18 years of age or older when all of the following criteria are met:

- A. Diagnosis of PBC is confirmed by at least two of the following three criteria:
 1. Biochemical evidence of cholestasis with elevation of alkaline phosphatase (ALP) level for at least 6 months duration
 2. Presence of antimitochondrial antibodies (AMA) (titer >1:40 by immunofluorescence or immunoenzymatic reactivity) or PBC-specific antinuclear antibodies (ANA) (eg, anti-gp210, anti-sp100)
 3. Histologic evidence of PBC on liver biopsy (eg, non-suppurative inflammation and destruction of interlobular and septal bile ducts)
- B. Member has an elevated serum ALP level prior to initiation of therapy with obeticholic acid
- C. Member meets at least one of the following requirements:
 1. Inadequate response to at least 12 months of prior therapy with ursodeoxycholic acid (UDCA)/ursodiol and the member will continue concomitant therapy with UDCA/ursodiol, or
 2. Intolerance to UDCA/ursodiol

IV. CONTINUATION OF THERAPY

Reference number(s)
2029-A

Authorization of 12 months may be granted for members who have achieved or maintained a clinical benefit from Ocaliva therapy (i.e., at least a 15% reduction in ALP level, ALP level less than 1.67-times ULN, or total bilirubin less than or equal to ULN).

V. REFERENCES

1. Ocaliva [package insert]. New York, NY: Intercept Pharmaceuticals, Inc.; February 2018.
2. Lindor KD, Gershwin E, Poupon R, et al. Primary biliary cirrhosis. *Hepatology*. 2009;50:291-308.
3. European Association for the Study of the Liver. EASL Clinical Practice Guidelines: management of cholestatic liver diseases. *J Hepatol*. 2017;67:145-172.

SPECIALTY GUIDELINE MANAGEMENT

OCREVUS (ocrelizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications:

Ocrevus is indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults. Ocrevus is also indicated for the treatment of primary progressive MS, in adults.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Relapsing Forms of Multiple Sclerosis

Authorization of 12 months may be granted to members who have been diagnosed with a relapsing form of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse).

B. Clinically isolated syndrome

Authorization of 12 months may be granted to members for the treatment of clinically isolated syndrome of multiple sclerosis.

C. Primary Progressive Multiple Sclerosis

Authorization of 12 months may be granted to members for the treatment of primary progressive MS.

III. CONTINUATION OF THERAPY

For all indications: Authorization of 12 months may be granted for members who are experiencing disease stability or improvement while receiving Ocrevus.

IV. OTHER CRITERIA

Members will not use Ocrevus concomitantly with other medications used for the treatment of multiple sclerosis, excluding Ampyra.

V. REFERENCES

Reference number(s)
1707-A

1. Ocrevus [package insert]. South San Francisco, CA: Genentech, Inc.; July 2019.

SPECIALTY GUIDELINE MANAGEMENT

SANDOSTATIN (octreotide acetate injection) SANDOSTATIN LAR DEPOT (octreotide acetate for injectable suspension) octreotide acetate injection

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. octreotide acetate/Sandostatin:
 - a. Indicated to reduce blood levels of growth hormone and IGF-1 (somatomedin C) in acromegaly patients who have had inadequate response to or cannot be treated with surgical resection, pituitary irradiation, and bromocriptine mesylate at maximally tolerated doses.
 - b. Indicated for the symptomatic treatment of patients with metastatic carcinoid tumors where it suppresses or inhibits the severe diarrhea and flushing episodes associated with the disease.
 - c. Indicated for the treatment of the profuse watery diarrhea associated with vasoactive intestinal peptide (VIP)-secreting tumors.
2. Sandostatin LAR: Sandostatin LAR Depot is indicated in patients in whom initial treatment with Sandostatin injection has been shown to be effective and tolerated.
 - a. Indicated for long-term maintenance therapy in acromegalic patients who have had an inadequate response to surgery and/or radiotherapy, or for whom surgery and/or radiotherapy is not an option.
 - b. Indicated for long-term treatment of the severe diarrhea and flushing episodes associated with metastatic carcinoid tumors.
 - c. Indicated for long-term treatment of the profuse watery diarrhea associated with vasoactive intestinal peptide (VIP)-secreting tumors.

B. Compendial Uses

1. Neuroendocrine tumors (NETs):
 - a. Tumors of the gastrointestinal (GI) tract, lung, and thymus (carcinoid tumors)
 - b. Tumors of the pancreas
2. Pheochromocytoma and paraganglioma
3. Meningiomas
4. Thymomas and thymic carcinomas
5. Congenital hyperinsulinism (CHI)/persistent hyperinsulinemic hypoglycemia of infancy (PHHI) (octreotide and Sandostatin only)
6. Acquired immune deficiency syndrome (AIDS)-associated diarrhea
7. Inoperable bowel obstruction
8. Chemotherapy- and radiation-induced diarrhea
9. Enterocutaneous fistula
10. Gastroesophageal varices
11. Islet cell tumors
12. Pancreatic fistulas
13. Pituitary adenoma

14. Short bowel syndrome
15. Zollinger-Ellison syndrome

All other indications are considered experimental/investigational and are not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

- A. For acromegaly:
 1. For initial approval: Laboratory report indicating high pretreatment insulin-like growth factor-1 (IGF-1) level and chart notes indicating an inadequate or partial response to surgery or radiotherapy or a clinical reason for not having surgery or radiotherapy.
 2. For continuation: Laboratory report indicating normal current IGF-1 levels or chart notes indicating that the member's IGF-1 level has decreased or normalized since initiation of therapy
- B. Chemotherapy- and radiation-induced diarrhea: Chart notes indicating grade 3 or 4 diarrhea with current chemotherapy or radiation.

III. CRITERIA FOR INITIAL APPROVAL

A. Acromegaly

Authorization of 12 months may be granted for the treatment of acromegaly when all of the following criteria are met:

1. Member has a high pretreatment IGF-1 level for age and/or gender based on the laboratory reference range.
2. Member had an inadequate or partial response to surgery or radiotherapy OR there is a clinical reason why the member has not had surgery or radiotherapy.

B. Neuroendocrine tumors (NETs)

1. Tumors of the gastrointestinal (GI) tract (carcinoid tumor)
Authorization of 12 months may be granted for treatment of locoregional advanced or metastatic NETs of the GI tract or unresected primary gastrinoma.
2. Tumors of the thymus (carcinoid tumor)
Authorization of 12 months may be granted for treatment of unresectable or metastatic NETs of the thymus.
3. Tumors of the lung (carcinoid tumor)
Authorization of 12 months may be granted for treatment of unresectable or metastatic NETs of the lung.
4. Tumors of the pancreas
Authorization of 12 months may be granted for treatment of NETs of the pancreas.

C. Carcinoid syndrome

Authorization of 12 months may be granted for treatment of carcinoid syndrome when it is used in any of the following clinical settings:

1. As a single agent
2. In combination with telotristat for persistent diarrhea due to poorly controlled carcinoid syndrome
3. In combination with other systemic therapy options for persistent symptoms such as flushing or diarrhea, or for progressive disease

D. Vasoactive intestinal peptide tumors (VIPomas)

Authorization of 12 months may be granted for management of symptoms related to hormone hypersecretion of VIPomas.

E. Meningiomas

Authorization of 12 months may be granted for treatment of unresectable recurrent or progressive meningioma.

F. Pheochromocytoma and paraganglioma

Authorization of 12 months may be granted for treatment of locally unresectable or metastatic pheochromocytoma and paraganglioma.

G. Thymomas and thymic carcinomas

Authorization of 12 months may be granted for treatment of thymomas and thymic carcinomas when the requested drug is used as a second-line therapy with or without prednisone in any of the following clinical settings:

1. Unresectable disease following first-line chemotherapy for potentially resectable locally advanced disease, solitary metastasis, or ipsilateral pleural metastasis
2. Extrathoracic metastatic disease

H. Congenital hyperinsulinism (CHI)/persistent hyperinsulinemic hypoglycemia of infancy (octreotide and Sandostatin only)

Authorization of 6 months may be granted for treatment of CHI and persistent hyperinsulinemic hypoglycemia in an infant.

I. AIDS-associated diarrhea

Authorization of 12 months may be granted for treatment of AIDS-associated severe secretory diarrhea when anti-microbial (e.g., ciprofloxacin or metronidazole) or anti-motility agents (e.g., loperamide or diphenoxylate and atropine) have become ineffective.

J. Bowel obstruction in terminal cancer

Authorization of 12 months may be granted for management of GI symptoms (e.g., nausea, pain, vomiting) of inoperable bowel obstruction in members with terminal cancer.

K. Chemotherapy- and radiation-induced diarrhea

Authorization of 12 months may be granted for treatment of chemotherapy- or radiation-induced diarrhea when any of the following criteria are met:

1. Member is receiving treatment with chemotherapy or radiation
2. Member has grade 3 or greater diarrhea according to National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE).

L. Enterocutaneous fistula

Authorization of 12 months may be granted for management of volume depletion from enterocutaneous fistula.

M. Gastroesophageal varices

Authorization of 6 months may be granted for treatment of acute bleeding of gastroesophageal varices associated with cirrhosis.

N. Islet cell tumors

Authorization of 12 months may be granted for stabilization of blood glucose levels in patients with functioning islet cell tumors (e.g., insulinomas or glucagonomas).

O. Pancreatic fistulas

Authorization of 6 months may be granted for prevention and treatment of pancreatic fistulas following pancreatic surgery.

P. Pituitary adenoma

Authorization of 12 months may be granted for treatment of pituitary adenoma.

Q. Short bowel syndrome

Authorization of 12 months may be granted for treatment of short bowel syndrome when the daily intravenous fluid requirement is greater than 3 liters.

R. Zollinger-Ellison syndrome

Authorization of 12 months may be granted for treatment of Zollinger-Ellison syndrome.

IV. CONTINUATION OF THERAPY**A. Acromegaly**

Authorization of 12 months may be granted for continuation of therapy for acromegaly when the member's IGF-1 level has decreased or normalized since initiation of therapy.

B. Carcinoid syndrome, VIPomas, AIDS-associated diarrhea, bowel obstruction, chemotherapy/radiation-induced diarrhea, islet cell tumors, and Zollinger-Ellison syndrome

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization when the member is experiencing clinical benefit as evidenced by improvement or stabilization in clinical signs and symptoms since initiation of therapy.

C. All other indications

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. REFERENCES

1. Octreotide acetate [package insert]. Rockford, IL: Mylan Institutional LLC; September 2017.
2. Sandostatin [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; April 2019.
3. Sandostatin LAR Depot [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; April 2019.
4. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: <http://www.nccn.org>. Accessed June 11, 2019.
5. Katznelson L, Laws ER, Melmed S, et al. Acromegaly: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab*. 2014;99:3933-3951.
6. American Association of Clinical Endocrinologists Acromegaly Guidelines Task Force. Medical guidelines for clinical practice for the diagnosis and treatment of acromegaly – 2011 update. *Endocr Pract*. 2011;17(suppl 4):1-44.
7. The NCCN Clinical Practice Guidelines in Oncology® Neuroendocrine Tumors (Version 1.2019). © 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed June 11, 2019.
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11. The NCCN Clinical Practice Guidelines in Oncology® Palliative Care (Version 2.2019). © 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed June 11, 2019.
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Reference number
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35. Leandros E, Antonakis PT, Albanopoulos K, et al. Somatostatin versus octreotide in the treatment of patients with gastrointestinal and pancreatic fistulas. *Can J Gastroenterol*. 2004;18(5):303-306.
36. Allen PJ, Gonen M, Brennan MF, et al. Pasireotide for postoperative pancreatic fistula. *N Engl J Med*. 2014;370(21):2014-2022.

SPECIALTY GUIDELINE MANAGEMENT

ODOMZO (sonidegib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Odomzo is indicated for the treatment of adult patients with locally advanced basal cell carcinoma (BCC) that has recurred following surgery or radiation therapy, or those who are not candidates for surgery or radiation therapy.

Compendial Uses

Nodal or distant metastatic basal cell carcinoma

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Basal Cell Carcinoma

Authorization of 12 months may be granted for treatment of locally advanced or metastatic basal cell carcinoma.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy for an indication outlined in Section II when there is no evidence of unacceptable toxicity or disease progression on the current regimen.

IV. REFERENCES

1. Odomzo [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; September 2017.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at <http://www.nccn.org>. Accessed November 09, 2018.

SPECIALTY GUIDELINE MANAGEMENT

OFEV (nintedanib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

- A. **Idiopathic Pulmonary Fibrosis**
Ofev is indicated for the treatment of idiopathic pulmonary fibrosis (IPF).
- B. **Systemic Sclerosis-Associated Interstitial Lung Disease**
Ofev is indicated to slow the rate of decline in pulmonary function in patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD).

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review (where applicable):

- A. Result of a chest high-resolution computed tomography (HRCT) study.
- B. If a lung biopsy is conducted, submit the associated pathology report.

III. CRITERIA FOR INITIAL APPROVAL

A. Idiopathic Pulmonary Fibrosis (IPF)

Authorization of 12 months may be granted for treatment of idiopathic pulmonary fibrosis when the member has undergone a diagnostic work-up which includes the following:

1. Other known causes of interstitial lung disease (e.g., domestic and occupational environmental exposures, connective tissue disease, drug toxicity) have been excluded AND
2. The member has completed a high-resolution computed tomography (HRCT) study of the chest or a lung biopsy which reveals a result consistent with the usual interstitial pneumonia (UIP) pattern, OR has completed an HRCT study of the chest which reveals a result other than the UIP pattern (e.g., probable UIP, indeterminate for UIP) and the diagnosis is supported by a lung biopsy. If a lung biopsy has not been previously conducted, the diagnosis is supported by a multidisciplinary discussion between a radiologist and pulmonologist who are experienced in IPF.

B. Systemic Sclerosis-Associated Interstitial Lung Disease

Authorization of 12 months may be granted for treatment of systemic sclerosis-associated interstitial lung disease when the member has completed a high-resolution computed tomography (HRCT) study of the chest that shows fibrosis affecting at least 10 percent of the lungs.

Reference number(s)
1882-A

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy for an indication listed in section III may be granted an authorization of 12 months when the member is currently receiving treatment with Ofev, excluding when Ofev is obtained as samples or via manufacturer's patient assistance programs.

V. OTHER

Note: If the member is a current smoker, they should be counseled on the harmful effects of smoking on pulmonary conditions and available smoking cessation options.

VI. REFERENCES

1. Ofev [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc. September 2019.
2. Raghu G, Remy-Jardin M, Myers JL, et al. Diagnosis of Idiopathic Pulmonary Fibrosis. An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline. *Am J Respir Crit Care Med*. 2018 Sep 1;198(5):e44-e68.
3. Vancheri C, Kreuter M, Richeldi L, et al. Nintedanib with add-on pirfenidone in idiopathic pulmonary fibrosis: results of the Injourney trial. *Am J Respir Crit Care Med*. 2017 Sept 10. doi: 10.1164/rccm.201706-1301OC. [Epub ahead of print].
4. Distler O, Highland KB, Gahlemann M, et al. Nintedanib for systemic sclerosis-associated interstitial lung disease. *N Engl J Med*. 2019;380(26):2518-2528.
5. van den Hoogen F, Khanna D, Fransen J, et al. 2013 Classification criteria for systemic sclerosis: an American College of Rheumatology/European League against Rheumatism collaborative initiative. *Ann Rheum Dis*. 2013; 72: 1747-55.

SPECIALTY GUIDELINE MANAGEMENT

OLUMIANT (baricitinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Olumiant is indicated for the treatment of adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more TNF antagonist therapies.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Moderately to severely active rheumatoid arthritis (RA)

- A. Authorization of 12 months may be granted for members who have previously received a biologic or targeted synthetic DMARD (e.g., Rinvoq, Xeljanz) indicated for moderately to severely active rheumatoid arthritis.
- B. Authorization of 12 months may be granted for treatment of moderately to severely active RA for members who have experienced an inadequate response to at least one tumor necrosis factor (TNF) inhibitor.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who are using Olumiant for an indication outlined in section II and who achieve or maintain positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

For all indications: Member has had a documented negative TB test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic DMARDs or targeted synthetic DMARDs (e.g., Xeljanz), and repeated yearly for members with risk factors** for TB that are continuing therapy with biologics.

* If the screening testing for TB is positive, there must be documentation of further testing to confirm there is no active disease. Do not administer baricitinib to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of baricitinib.

** Risk factors for TB include: Persons with close contact to people with infectious TB disease; persons who have recently immigrated from areas of the world with high rates of TB (e.g., Africa, Asia, Eastern Europe, Latin America, Russia); children less than 5 years of age who have a positive TB test; groups with high rates

Reference number
2597-A

of TB transmission (e.g., homeless persons, injection drug users, persons with HIV infection); persons who work or reside with people who are at an increased risk for active TB (e.g., hospitals, long-term care facilities, correctional facilities, homeless shelters).

For all indications: Member cannot use Olumiant concomitantly with any other biologic DMARD or targeted synthetic DMARD.

V. REFERENCES

1. Olumiant [package insert]. Indianapolis, IN: Lilly USA, LLC; May 2018.
2. Tuberculosis (TB). TB risk factors. Centers for Disease Control and Prevention. Retrieved on 21 June 2019 from: <https://www.cdc.gov/tb/topic/basics/risk.htm>.

SPECIALTY GUIDELINE MANAGEMENT

OLYSIO (simeprevir)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Olysio is indicated for the treatment of adults with chronic hepatitis C virus (HCV) infection:

- A. in combination with sofosbuvir in patients with HCV genotype 1 without cirrhosis or with compensated cirrhosis
- B. in combination with peginterferon alfa (PEG-IFN) and ribavirin (RBV) in patients with HCV genotype 1 or 4 without cirrhosis or with compensated cirrhosis

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

Coverage will not be provided for members with decompensated cirrhosis/moderate or severe hepatic impairment (Child Turcotte Pugh Class B or C).

Note: When the requested drug is being used in a combination therapy regimen, exclusions to the other antiviral drugs also apply.

III. INITIAL CRITERIA FOR APPROVAL

A. Chronic hepatitis C virus infection, in combination with PEG-IFN and RBV

1. Genotype 1 or 4 infection

Authorization of up to 6 weeks total may be granted for initiation of therapy in members who are treatment-naïve or failed prior treatment with PEG-IFN and RBV AND meet one of the following criteria:

- a. Genotype 1a infection without the NS3 Q80K polymorphism
- b. Genotype 1b infection
- c. Genotype 4 infection

B. Chronic hepatitis C virus infection, in combination with Sovaldi

1. Genotype 1a infection

- a. Authorization of up to 12 weeks total may be granted for members without cirrhosis who are treatment-naïve or failed prior treatment with PEG-IFN and RBV.
- b. Authorization of up to 24 weeks total may be granted for members with compensated cirrhosis without the NS3 Q80K polymorphism who are treatment-naïve or failed prior treatment with PEG-IFN and RBV.

2. Genotype 1b infection

Reference number(s)
2138-A, 2679-A

- a. Authorization of up to 12 weeks total may be granted for members without cirrhosis who are treatment-naïve or failed prior treatment with PEG-IFN and RBV.
- b. Authorization of up to 24 weeks total may be granted for members with compensated cirrhosis who are treatment-naïve or failed prior treatment with PEG-IFN and RBV.

3. Recurrent HCV infection post liver transplantation

Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who have recurrent HCV genotype 1 or 4 infection post liver transplantation.

C. Chronic hepatitis C virus infection, in combination with Sovaldi and RBV

Recurrent HCV infection post liver transplantation

Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who have recurrent HCV genotype 1 or 4 infection post liver transplantation.

D. HCV and HIV Coinfection

Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in Section A, B or C above are met.

IV. CONTINUATION OF THERAPY

Chronic hepatitis C virus infection, in combination with PEG-IFN and RBV

Genotype 1 or 4 infection at week 4 assessment

Authorization of up to 12 weeks total for Olysio and up to 48 weeks total for PEG-IFN and RBV may be granted for members with HCV-RNA < 25 IU/mL at week 4 of treatment.

V. REFERENCES

1. Olysio [package insert]. Titusville, NJ: Janssen Products, LP; November 2017.
2. AASLD/IDSA/IAS–USA. Recommendations for testing, managing, and treating hepatitis C. <http://www.hcvguidelines.org>. Last changes made May 24, 2018. Accessed August 02, 2018.

SPECIALTY GUIDELINE MANAGEMENT

ONCASPAR (pegaspargase)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Acute lymphoblastic leukemia (ALL):

1. Oncaspar is indicated as a component of a multi-agent chemotherapeutic regimen for the first line treatment of pediatric and adult patients with ALL.
2. Oncaspar is indicated as a component of a multi-agent chemotherapeutic regimen for the treatment of pediatric and adult patients with ALL and hypersensitivity to native forms of L-asparaginase.

B. Compendial Uses

1. Extranodal natural killer/T-cell lymphoma, nasal type: as a component of multi-agent chemotherapeutic regimen
2. Lymphoblastic lymphoma (managed in the same manner as ALL)
3. Acute lymphoblastic leukemia (ALL) as a component of multi-agent chemotherapeutic regimen or central nervous system directed therapy as systemic therapy (IV/IM route)
4. Pediatric acute lymphoblastic leukemia (ALL) as a component of a multi-agent chemotherapeutic regimen^{2,4}

All other indications are considered experimental/investigational and are not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Acute Lymphoblastic Leukemia (ALL) and Lymphoblastic Lymphoma**

Authorization of 12 months may be granted for the treatment of ALL or lymphoblastic lymphoma when the requested medication is used in conjunction with multi-agent chemotherapy.

B. **Extranodal Natural Killer/T-cell Lymphoma, nasal type**

Authorization of 12 months may be granted for the treatment of extranodal natural killer/T-cell lymphoma, nasal type when the requested medication is used in conjunction with multi-agent chemotherapy.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced disease progression or an unacceptable toxicity while on the current regimen.

IV. REFERENCES

Reference number
2291-A

1. Oncaspar [package insert]. Westlake Village, CA: Baxalta US Inc.; January 2019.
2. National Comprehensive Cancer Network. The NCCN Drugs & Biologics Compendium. <http://www.nccn.org>. Accessed July 15, 2019.
3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Acute Lymphoblastic Leukemia. Version 2.2019. http://www.nccn.org/professionals/physician_gls/pdf/all.pdf. Accessed July 15, 2019.
4. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Pediatric Acute Lymphoblastic Leukemia. Version 1.2020. https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf. Accessed July 15, 2019.

SPECIALTY GUIDELINE MANAGEMENT

ONPATTRO (patisiran)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Onpattro is indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults.

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

- A. Testing or analysis confirming a mutation of the TTR gene
- B. Medical record documentation confirming the member demonstrates signs and symptoms of polyneuropathy and an improvement in these signs and symptoms since starting therapy for continuation

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a neurologist, geneticist, or physician specializing in the treatment of amyloidosis.

IV. CRITERIA FOR INITIAL APPROVAL

Polyneuropathy of Hereditary Transthyretin-mediated Amyloidosis

Authorization of 12 months may be granted for treatment of polyneuropathy of hereditary transthyretin-mediated amyloidosis (also called transthyretin-type familial amyloid polyneuropathy [ATTR-FAP]) when all of the following criteria are met:

- A. The diagnosis is confirmed by detection of a mutation of the TTR gene.
- B. Member exhibits clinical manifestations of ATTR-FAP (e.g., amyloid deposition in biopsy specimens, TTR protein variants in serum, progressive peripheral sensory-motor polyneuropathy).
- C. The member is not a liver transplant recipient.
- D. The requested medication will not be used in combination with inotersen (Tegsedi) or tafamidis.

V. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for the continued treatment of ATTR-FAP when all of the following criteria are met:

- A. The member must have met all initial authorization criteria.
- B. The member must have demonstrated a beneficial response to treatment with Onpattro therapy compared to baseline (e.g., improvement of neuropathy severity and rate of disease progression as demonstrated by the modified Neuropathy Impairment Scale+7 (mNIS+7) composite score, the Norfolk Quality of Life-Diabetic Neuropathy (QoL-DN) total score, polyneuropathy disability (PND) score, FAP disease stage, manual grip strength). Documentation from the medical record must be provided.

REFERENCES

1. Onpattro [package insert]. Cambridge, MA: Alnylam Pharmaceuticals, Inc.; August 2018.
2. Adams, et al. Patisiran, an RNAi Therapeutic, for Hereditary Transthyretin Amyloidosis. *N Engl J Med*. 2018 Jul 5; 379(1):11-21.
3. Ando Y, Coelho T, Berk JL, Cruz MW, Ericzon BG, Ikeda S, Lewis WD, Obici L, Planté-Bordeneuve V, Rapezzi C, et al. Guideline of transthyretin-related hereditary amyloidosis for clinicians. *Orphanet J Rare Dis*. 2013; 8:31.
4. Sekijima Y, Yoshida K, Tokuda T, Ikeda S. Familial transthyretin amyloidosis. In: GeneReviews. Seattle (WA): University of Washington, Seattle. 1993-2017. <https://www.ncbi.nlm.nih.gov/books/NBK1194/>. Accessed 16 Aug 2018.

SPECIALTY GUIDELINE MANAGEMENT

OPDIVO (nivolumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. **Unresectable or Metastatic Melanoma**
Opdivo (nivolumab), as a single agent or in combination with ipilimumab, is indicated for the treatment of patients with unresectable or metastatic melanoma.
2. **Adjuvant Treatment of Melanoma**
Opdivo is indicated for the adjuvant treatment of patients with melanoma with involvement of lymph nodes or metastatic disease who have undergone complete resection.
3. **Metastatic Non-Small Cell Lung Cancer**
Opdivo is indicated for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) with progression on or after platinum-based chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Opdivo.
4. **Small Cell Lung Cancer**
Opdivo is indicated for the treatment of patients with metastatic small cell lung cancer (SCLC) with progression after platinum-based chemotherapy and at least one other line of therapy.
5. **Advanced Renal Cell Carcinoma**
 - a. Opdivo as a single agent is indicated for the treatment of patients with advanced renal cell carcinoma (RCC) who have received prior anti-angiogenic therapy.
 - b. Opdivo, in combination with ipilimumab, is indicated for the treatment of patients with intermediate or poor risk, previously untreated advanced RCC.
6. **Classical Hodgkin Lymphoma**
Opdivo is indicated for the treatment of adult patients with classical Hodgkin lymphoma (cHL) that has relapsed or progressed after:
 - a. Autologous hematopoietic stem cell transplantation (HSCT) and brentuximab vedotin, or
 - b. 3 or more lines of systemic therapy that includes autologous HSCT.
7. **Squamous Cell Carcinoma of the Head and Neck**
Opdivo (nivolumab) is indicated for the treatment of patients with recurrent or metastatic squamous cell carcinoma of the head and neck (SCCHN) with disease progression on or after platinum-based therapy.
8. **Urothelial Carcinoma**

Opdivo is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma who:

- a. Have disease progression during or following platinum-containing chemotherapy
- b. Have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.

9. Microsatellite Instability-High or Mismatch Repair Deficient Metastatic Colorectal Cancer

Opdivo, as a single agent or in combination with ipilimumab, is indicated for the treatment of adult and pediatric patients 12 years and older with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer (CRC) that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan.

10. Hepatocellular Carcinoma

Opdivo is indicated for the treatment of patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib.

B. Compendial Uses

1. Cutaneous melanoma
2. Non-small cell lung cancer
3. Kidney cancer
4. Classical Hodgkin lymphoma
5. Squamous cell carcinoma of the head and neck
6. Urothelial carcinoma
 - a. Bladder cancer
 - b. Primary carcinoma of the urethra
 - c. Upper genitourinary tract tumors
 - d. Urothelial carcinoma of the prostate
7. Colorectal cancer
8. Small cell lung cancer
9. Hepatocellular carcinoma
10. Uveal Melanoma
11. Anal Carcinoma
12. Merkel Cell Carcinoma
13. Central Nervous System (CNS) brain metastases
14. Gestational trophoblastic neoplasia
15. Malignant pleural mesothelioma

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: documentation of laboratory report confirming MSI-H or mismatch repair deficient (dMMR) tumor status, where applicable.

III. EXCLUSIONS

Coverage will not be provided for members who have experienced disease progression while on programmed death receptor-1 (PD-1) or programmed death ligand 1 (PD-L1) inhibitor therapy (other than when used as second-line or subsequent therapy for metastatic or unresectable melanoma in combination with ipilimumab following progression on single agent checkpoint inhibitor therapy).

IV. CRITERIA FOR INITIAL APPROVAL

A. Cutaneous Melanoma

Authorization of 6 months may be granted for treatment of cutaneous melanoma in either of the following settings:

1. Opdivo will be used as a single agent or in combination with ipilimumab (4 doses of ipilimumab, followed by Opdivo as a single agent) for unresectable or metastatic disease.
2. Opdivo will be used as a single agent as adjuvant treatment following complete lymph node resection or complete resection of metastatic disease.

B. Non-Small Cell Lung Cancer (NSCLC)

Authorization of 6 months may be granted for treatment of NSCLC when either of the following conditions is met:

1. Opdivo will be used as a single agent as subsequent therapy for recurrent, advanced, or metastatic disease.
2. Opdivo will be used as a single agent or in combination with ipilimumab for treatment of disease with tumor mutational burden (TMB).

C. Kidney Cancer

Authorization of 6 months may be granted for treatment of relapsed, advanced, or stage IV kidney cancer, including renal cell carcinoma, in any of the following settings:

1. Opdivo will be used as a single agent for clear cell histology as subsequent therapy.
2. Opdivo will be used as a single agent for non-clear cell histology.
3. Opdivo will be used in combination with ipilimumab (4 doses of ipilimumab, followed by Opdivo as a single agent) for:
 - i. First-line therapy for poor or intermediate risk.
 - ii. First-line therapy for clear cell histology and favorable risk.
 - iii. Subsequent therapy for clear cell histology.

D. Classical Hodgkin Lymphoma (cHL)

Authorization of 6 months may be granted as a single agent for treatment of classical Hodgkin lymphoma when either of the following criteria is met:

1. Member has relapsed after 2 or more prior lines of therapy or following hematopoietic stem cell transplant.
2. Members has relapsed or refractory disease and is transplant-ineligible.

E. Squamous Cell Carcinoma of the Head and Neck (SCCHN)

Authorization of 6 months may be granted as a single agent for subsequent treatment of recurrent, unresectable, metastatic, or second primary SCCHN in members with disease progression on or after platinum-containing chemotherapy.

F. Urothelial Carcinoma – Bladder Cancer

Authorization of 6 months may be granted as a single agent as subsequent therapy for treatment of bladder cancer following platinum-containing chemotherapy when either of the following conditions is met:

1. Disease is locally advanced or metastatic.
2. Member has metastatic or local recurrence post-cystectomy.

G. Urothelial Carcinoma – Primary Carcinoma of the Urethra

Authorization of 6 months may be granted as a single agent as subsequent therapy for treatment of primary carcinoma of the urethra for recurrent, locally advanced, or metastatic disease following platinum-containing chemotherapy.

H. Urothelial Carcinoma – Upper Genitourinary Tract Tumors or Urothelial Carcinoma of the Prostate

Authorization of 6 months may be granted as a single agent as subsequent therapy for treatment of upper genitourinary (GU) tract tumors or urothelial carcinoma of the prostate following platinum-containing chemotherapy for locally advanced or metastatic disease.

I. Colorectal Cancer

Authorization of 6 months may be granted for treatment of colorectal cancer, including small bowel adenocarcinoma, appendiceal carcinoma, and anal adenocarcinoma for microsatellite-instability high or mismatch repair deficient tumors when any of the following criteria are met:

1. Opdivo will be used as a single agent or in combination with ipilimumab (4 doses of ipilimumab, followed by Opdivo as a single agent) as primary treatment for unresectable metachronous metastases and previous adjuvant FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin) within the past 12 months.
2. Opdivo will be used as a single agent as initial therapy for unresectable advanced or metastatic disease in members who are not appropriate for intensive therapy.
3. Opdivo will be used as a single agent or in combination with ipilimumab (4 doses of ipilimumab, followed by Opdivo as a single agent) as subsequent therapy for unresectable advanced or metastatic disease following previous oxaliplatin- irinotecan- and/or fluoropyrimidine-based therapy.

J. Small Cell Lung Cancer

Authorization of 6 months may be granted for subsequent treatment of small cell lung cancer in any of the following settings:

1. Opdivo will be used as a single agent or in combination with ipilimumab for relapse within 6 months following complete or partial response or stable disease with initial treatment.
2. Opdivo will be used as a single agent or in combination with ipilimumab for primary progressive disease.
3. Opdivo will be used for metastatic disease following progression after platinum-based chemotherapy and at least one other line of therapy.

K. Hepatocellular Carcinoma

Authorization of 6 months may be granted as a single agent for subsequent treatment of hepatocellular carcinoma.

L. Uveal Melanoma

Authorization of 6 months may be granted as a single agent or in combination with ipilimumab for treatment of uveal melanoma for distant metastatic disease.

M. Anal Carcinoma

Authorization of 6 months may be granted as a single agent for second-line or subsequent treatment of metastatic anal carcinoma.

N. Merkel Cell Carcinoma

Authorization of 6 months may be granted for treatment of Merkel cell carcinoma in members with disseminated, metastatic disease.

O. CNS Brain Metastases

Authorization of 6 months may be granted as a single agent or in combination with ipilimumab for treatment of CNS brain metastases in patients with melanoma.

P. Gestational Trophoblastic Neoplasia

Authorization of 6 months may be granted as a single agent for treatment of gestational trophoblastic neoplasia when either of the following criteria is met:

Reference number(s)
1894-A

1. Member has recurrent or progressive intermediate trophoblastic tumor (placental site trophoblastic tumor or epithelioid trophoblastic tumor) following treatment with a platinum/etoposide-containing regimen.
2. Member has methotrexate-resistant high-risk disease.

Q. Malignant Pleural Mesothelioma

Authorization of 6 months may be granted as a single agent or in combination with ipilimumab for subsequent treatment of malignant pleural mesothelioma.

V. CONTINUATION OF THERAPY

A. Adjuvant treatment of melanoma

Authorization of 6 months may be granted (up to 12 months total) for continued treatment in members requesting reauthorization for cutaneous melanoma who have not experienced disease recurrence or an unacceptable toxicity.

B. All other indications

Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section IV who have not experienced disease progression or an unacceptable toxicity.

VI. REFERENCES

1. Opdivo [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; May 2019.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed July 11, 2019.

SPECIALTY GUIDELINE MANAGEMENT

Opsumit (macitentan)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Opsumit is an endothelin receptor antagonist (ERA) indicated for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group 1) to delay disease progression. Disease progression included: death, initiation of intravenous or subcutaneous prostanoids, or clinical worsening of PAH (decreased 6-minute walk distance, worsened PAH symptoms and need for additional PAH treatment). Opsumit also reduced hospitalization for PAH.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Pulmonary Arterial Hypertension (PAH)

Authorization of 12 months may be granted for treatment of PAH when ALL of the following criteria are met:

- A. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
- B. PAH was confirmed by either criterion (1) or criterion (2) below:
 1. Pretreatment right heart catheterization with all of the following results:
 - i. mPAP \geq 25 mmHg
 - ii. PCWP \leq 15 mmHg
 - iii. PVR $>$ 3 Wood units
 2. For infants less than one year of age with any of the following conditions, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed:
 - i. Post cardiac surgery
 - ii. Chronic heart disease
 - iii. Chronic lung disease associated with prematurity
 - iv. Congenital diaphragmatic hernia

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with an indication listed in Section II who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

IV. APPENDIX

WHO Classification of Pulmonary Hypertension**1 PAH**

- 1.1 Idiopathic (PAH)
- 1.2 Heritable PAH
- 1.3 Drug- and toxin-induced PAH
- 1.4. PAH associated with:
 - 1.4.1 Connective tissue diseases
 - 1.4.2 HIV infection
 - 1.4.3 Portal hypertension
 - 1.4.4 Congenital heart diseases
 - 1.4.5 Schistosomiasis
- 1.5 PAH long-term responders to calcium channel blockers
- 1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement
- 1.7 Persistent PH of the newborn syndrome

2 PH due to left heart disease

- 2.1 PH due to heart failure with preserved LVEF
- 2.2 PH due to heart failure with reduced LVEF
- 2.3 Valvular heart disease
- 2.4 Congenital/acquired cardiovascular conditions leading to post-capillary PH

3 PH due to lung diseases and/or hypoxia

- 3.1 Obstructive lung disease
- 3.2 Restrictive lung disease
- 3.3 Other lung disease with mixed restrictive/obstructive pattern
- 3.4 Hypoxia without lung disease
- 3.5 Developmental lung disorders

4 PH due to pulmonary artery obstruction

- 4.1 Chronic thromboembolic PH
- 4.2 Other pulmonary artery obstructions
 - 4.2.1 Sarcoma (high or intermediate grade) or angiosarcoma
 - 4.2.2 Other malignant tumors
 - Renal carcinoma
 - Uterine carcinoma
 - Germ cell tumours of the testis
 - Other tumours
 - 4.2.3 Non-malignant tumours
 - Uterine leiomyoma
 - 4.2.4 Arteritis without connective tissue disease
 - 4.2.5 Congenital pulmonary artery stenosis
 - 4.2.6 Parasites
 - Hydatidosis

5 PH with unclear and/or multifactorial mechanisms

- 5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders
- 5.2 Systemic and metabolic disorders: Pulmonary Langerhans cell histiocytosis, Gaucher disease, glycogen storage disease, neurofibromatosis, sarcoidosis
- 5.3 Others: chronic renal failure with or without hemodialysis, fibrosing mediastinitis
- 5.4 Complex congenital heart disease

Reference number(s)
1647-A

V. REFERENCES

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2. Chin KM, Rubin LJ. Pulmonary arterial hypertension. *J Am Coll Cardiol*. 2008;51(16):1527-1538.
3. McLaughlin VV, Archer SL, Badesch DB, et al. ACCF/AHA 2009 expert consensus document on pulmonary hypertension a report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents and the American Heart Association developed in collaboration with the American College of Chest Physicians; American Thoracic Society, Inc.; and the Pulmonary Hypertension Association. *J Am Coll Cardiol*. 2009;53(17):1573-1619.
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5. Simonneau G, Robbins IM, Beghetti M, et al. Updated clinical classification of pulmonary hypertension. *J Am Coll Cardiol*. 2013;62:D34-S41.
6. Rubin LJ; American College of Chest Physicians. Diagnosis and management of pulmonary arterial hypertension: ACCP evidence-based clinical practice guidelines. *Chest*. 2004;126(1 Suppl):7S-10S.
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SPECIALTY GUIDELINE MANAGEMENT

ORENCIA (abatacept)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Moderately to severely active rheumatoid arthritis in adults
2. Moderately to severely active polyarticular juvenile idiopathic arthritis in patients 2 years of age or older
3. Active psoriatic arthritis in adults

B. Compendial Uses

Oligoarticular juvenile idiopathic arthritis

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Moderately to severely active rheumatoid arthritis (RA)**

1. Authorization of 12 months may be granted for members who have previously received a biologic or targeted synthetic DMARD (e.g., Rinvoq, Xeljanz) indicated for moderately to severely active rheumatoid arthritis.
2. Authorization of 12 months may be granted for treatment of moderately to severely active RA when any of the following criteria is met:
 - a. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to 20 mg/week).
 - b. Member has an intolerance or contraindication to methotrexate (see Appendix).

B. **Moderately to severely active articular juvenile idiopathic arthritis**

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for moderately to severely active articular juvenile idiopathic arthritis.
2. Authorization of 12 months may be granted for treatment of moderately to severely active articular juvenile idiopathic arthritis when any of the following criteria are met:
 - a. The member had an inadequate response to methotrexate or another non-biologic DMARD administered at an adequate dose and duration.
 - b. The member has risk factors (See Appendix B) and the member also meets one of the following:
 - i. High-risk joints are involved (e.g., cervical spine, wrist, or hip).
 - ii. High disease activity.

iii. Are judged to be at high risk for disabling joint disease.

C. Active psoriatic arthritis (PsA)

Authorization of 12 months may be granted for treatment of active psoriatic arthritis (PsA).

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who are using Orenzia for an indication outlined in section II and who achieve or maintain positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

For all indications: Member has had a documented negative TB test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic DMARDs or targeted synthetic DMARDs (e.g., Xeljanz), and repeated yearly for members with risk factors** for TB that are continuing therapy with biologics.

* If the screening testing for TB is positive, there must be documentation of further testing to confirm there is no active disease. Do not administer abatacept to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of abatacept.

** Risk factors for TB include: Persons with close contact to people with infectious TB disease; persons who have recently immigrated from areas of the world with high rates of TB (e.g., Africa, Asia, Eastern Europe, Latin America, Russia); children less than 5 years of age who have a positive TB test; groups with high rates of TB transmission (e.g., homeless persons, injection drug users, persons with HIV infection); persons who work or reside with people who are at an increased risk for active TB (e.g., hospitals, long-term care facilities, correctional facilities, homeless shelters).

For all indications: Member cannot use Orenzia concomitantly with any other biologic DMARD or targeted synthetic DMARD.

V. APPENDIX A: Examples of Contraindications to Methotrexate

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
4. Elevated liver transaminases
5. History of intolerance or adverse event
6. Hypersensitivity
7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
8. Myelodysplasia
9. Pregnancy or planning pregnancy
10. Renal impairment
11. Significant drug interaction

APPENDIX B: Risk factors for articular juvenile idiopathic arthritis

Reference number
2127-A

1. Positive rheumatoid factor
2. Positive anti-cyclic citrullinated peptide antibodies
3. Pre-existing joint damage

VI. REFERENCES

1. Orencia [package insert]. Princeton, NJ: Bristol-Myers Squibb; March 2019.
2. Smolen JS, Landewé R, Billsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. *Ann Rheum Dis.* 2017;0:1-18.
3. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. *Arthritis Rheumatol.* 2016;68(1)1-26.
4. Saag KG, Teng GG, Patkar NM, et al. American College of Rheumatology 2008 recommendations for the use of nonbiologic and biologic disease-modifying antirheumatic drugs in rheumatoid arthritis. *Arthritis Rheum.* 2008;59(6):762-784.
5. Ringold S, Angeles-Han S, Beukelman T, et al. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Treatment of Juvenile Idiopathic Arthritis: Therapeutic Approaches for Non-Systemic Polyarthritis, Sacroiliitis, and Enthesitis. American College of Rheumatology. 2019;1-18.
6. Singh JA, Guyatt G, Ogdie A, et al. 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the Treatment of Psoriatic Arthritis. *Arthritis Rheum.* 2018;71:5-32.
7. Tuberculosis (TB). TB risk factors. Centers for Disease Control and Prevention. Retrieved on 21 June 2019 from: <https://www.cdc.gov/tb/topic/basics/risk.htm>.

SPECIALTY GUIDELINE MANAGEMENT

Orenitram (treprostinil extended-release tablets)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Orenitram is indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to improve exercise capacity.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of PAH when ALL of the following criteria are met:

- A. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
- B. PAH was confirmed by either criterion (1) or criterion (2) below:
 1. Pretreatment right heart catheterization with all of the following results:
 - i. mPAP \geq 25 mmHg
 - ii. PCWP \leq 15 mmHg
 - iii. PVR $>$ 3 Wood units
 2. For infants less than one year of age with any of the following conditions, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed:
 - i. Post cardiac surgery
 - ii. Chronic heart disease
 - iii. Chronic lung disease associated with prematurity
 - iv. Congenital diaphragmatic hernia

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with an indication listed in Section II who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

IV. APPENDIX

WHO Classification of Pulmonary Hypertension

1 PAH

1.1 Idiopathic (PAH)

Reference number(s)
1643-A

- 1.2 Heritable PAH
- 1.3 Drug- and toxin-induced PAH
- 1.4. PAH associated with:
 - 1.4.1 Connective tissue diseases
 - 1.4.2 HIV infection
 - 1.4.3 Portal hypertension
 - 1.4.4 Congenital heart diseases
 - 1.4.5 Schistosomiasis
- 1.5 PAH long-term responders to calcium channel blockers
- 1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement
- 1.7 Persistent PH of the newborn syndrome

2 PH due to left heart disease

- 2.1 PH due to heart failure with preserved LVEF
- 2.2 PH due to heart failure with reduced LVEF
- 2.3 Valvular heart disease
- 2.4 Congenital/acquired cardiovascular conditions leading to post-capillary PH

3 PH due to lung diseases and/or hypoxia

- 3.1 Obstructive lung disease
- 3.2 Restrictive lung disease
- 3.3 Other lung disease with mixed restrictive/obstructive pattern
- 3.4 Hypoxia without lung disease
- 3.5 Developmental lung disorders

4 PH due to pulmonary artery obstruction

- 4.1 Chronic thromboembolic PH
- 4.2 Other pulmonary artery obstructions
 - 4.2.1 Sarcoma (high or intermediate grade) or angiosarcoma
 - 4.2.2 Other malignant tumors
 - Renal carcinoma
 - Uterine carcinoma
 - Germ cell tumours of the testis
 - Other tumours
 - 4.2.3 Non-malignant tumours
 - Uterine leiomyoma
 - 4.2.4 Arteritis without connective tissue disease
 - 4.2.5 Congenital pulmonary artery stenosis
 - 4.2.6 Parasites
 - Hydatidosis

5 PH with unclear and/or multifactorial mechanisms

- 5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders
- 5.2 Systemic and metabolic disorders: Pulmonary Langerhans cell histiocytosis, Gaucher disease, glycogen storage disease, neurofibromatosis, sarcoidosis
- 5.3 Others: chronic renal failure with or without hemodialysis, fibrosing mediastinitis
- 5.4 Complex congenital heart disease

V. REFERENCES

1. Orenitram [package insert]. Research Triangle Park, NC: United Therapeutics Corp.; January 2017.
2. Chin KM, Rubin LJ. Pulmonary arterial hypertension. *J Am Coll Cardiol*. 2008;51(16):1527-1538.
3. McLaughlin VV, Archer SL, Badesch DB, et al. ACCF/AHA 2009 expert consensus document on pulmonary hypertension a report of the American College of Cardiology Foundation Task Force on Expert

Reference number(s)
1643-A

- Consensus Documents and the American Heart Association developed in collaboration with the American College of Chest Physicians; American Thoracic Society, Inc.; and the Pulmonary Hypertension Association. *J Am Coll Cardiol.* 2009;53(17):1573-1619.
4. Badesch DB, Champion HC, Gomez-Sanchez MA, et al. Diagnosis and assessment of pulmonary arterial hypertension. *J Am Coll Cardiol.* 2009;54:S55-S66.
 5. Simonneau G, Robbins IM, Beghetti M, et al. Updated clinical classification of pulmonary hypertension. *J Am Coll Cardiol.* 2013;62:D34-S41.
 6. Rubin LJ; American College of Chest Physicians. Diagnosis and management of pulmonary arterial hypertension: ACCP evidence-based clinical practice guidelines. *Chest.* 2004;126(1 Suppl):7S-10S.
 7. Barst RJ, Gibbs SR, Ghofrani HA, et al. Updated evidence-based treatment algorithm in pulmonary arterial hypertension. *J Am Coll Cardiol.* 2009;54:S78-S84.
 8. Taichman DB, Ornelas J, Chung L, et al. Pharmacologic therapy for pulmonary arterial hypertension in adults. CHEST guideline and expert panel report. *Chest.* 2014;46(2):449-475.
 9. Abman, SH, Hansmann G, Archer SL, et al. Pediatric pulmonary hypertension: guidelines from the American Heart Association and American Thoracic Society. *Circulation.* 2015;132(21):2037-99.
 10. Klinger, JR., Elliott, CG, Levine, DJ, et al. Therapy for Pulmonary Arterial Hypertension in Adults: Update of the CHEST Guidelines and Expert Panel Report. *Chest.* 2019;155(3): 565-586.
 11. Galie, N., McLaughlin, VV, Rubin, LJ, Simonneau, G. An overview of the 6th World Symposium on Pulmonary Hypertension. *Eur Respir J* 2019; 53: 1802148; DOI: 10.1183/13993003.02148-2018. Published 24 January 2019.

SPECIALTY GUIDELINE MANAGEMENT

ORFADIN (nitisinone) NITYR (nitisinone)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Orfadin is indicated for the treatment of adult and pediatric patients with hereditary tyrosinemia type 1 (HT-1) in combination with dietary restriction of tyrosine and phenylalanine.

Nityr is indicated for the treatment of patients with hereditary tyrosinemia type 1 (HT-1) in combination with dietary restriction of tyrosine and phenylalanine.

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: enzyme assay or genetic testing results supporting diagnosis.

III. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of hereditary tyrosinemia type 1 (HT-1) when the diagnosis is confirmed by biochemical testing (e.g., detection of succinylacetone in urine) or DNA testing and the requested medication is being used as an adjunct to dietary restriction of tyrosine and phenylalanine.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for hereditary tyrosinemia type 1 (HT-1) who are experiencing benefit from therapy as evidenced by a reduction in tyrosine levels from baseline.

V. REFERENCE

1. Orfadin [package insert]. Ardmore, PA: Sobi, Inc; September 2017.
2. Nityr [package insert]. Cambridge, United Kingdom: Cycle Pharmaceuticals Ltd.; November 2018.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

ORILISSA
(elagolix)

Status: CVS Caremark Criteria

Type: Initial Prior Authorization

Ref # 2634-A

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Orilissa is indicated for the management of moderate to severe pain associated with endometriosis.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has the diagnosis of moderate to severe pain associated with endometriosis

AND

- The patient has not received the maximum recommended treatment course of 12 months of Lupron Depot or Lupaneta Pack or 6 months of Synarel or Zoladex

AND

- The patient will receive 150 mg once daily of the requested drug

AND

- The patient has not already received greater than or equal to 24 months of therapy of the requested drug

OR

- The patient will receive 200 mg twice daily of the requested drug

AND

- The patient has not already received greater than or equal to 6 months of therapy of the requested drug

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Orilissa is indicated for the management of moderate to severe pain associated with endometriosis.^{3, 6-7}

Nonsteroidal anti-inflammatory drugs (NSAIDs) are often the first-line treatment for endometriosis, followed by hormone therapy. If NSAIDs and hormonal contraceptives are ineffective, then the next step is treatment with a gonadotropin-releasing hormone (GnRH) analogue such as leuprolide, goserelin (Zoladex)⁸, or nafarelin (Synarel). GnRH analogues may have significant side effects, including hot flushes, vaginal dryness, and osteopenia. Osteopenia has been shown to be reversible with short-term use, but may not be with long-term use or use of multiple cycles.⁹ Due to risk of osteopenia and bone loss, Orilissa will not be approved if the patient has received a 12-month¹⁻² treatment course of Lupron Depot or Lupaneta Pack or a 6-month⁴⁻⁵ course of Zoladex or Synarel.

Danazol, an androgen, is effective in the treatment of pelvic pain associated with endometriosis. However, androgenic adverse effects, such as acne, hirsutism, and male pattern baldness often limit its use. The drug has several United States Food and Drug Administration boxed warnings, including the risk of thrombosis and teratogenicity.⁸ Due to significant adverse effects, a trial of Danazol is not required.

Orilissa causes a dose-dependent decrease in bone mineral density (BMD). BMD loss is greater with increasing duration of use and may not be completely reversible after stopping treatment. It is recommended to limit the duration of use to reduce the extent of bone loss. The use of higher doses increases exposures and risk for bone loss.^{3, 6-7} Therefore, the duration of approval is 24 months for patients taking a maximum of 150 mg once daily, and the duration of approval is 6 months for patients taking 200 mg twice daily.

REFERENCES

1. Lupaneta Pack [package insert]. North Chicago, IL: AbbVie Inc.; November 2018.
2. Lupron Depot [package insert]. North Chicago, IL: AbbVie Inc.; November 2018.
3. Orilissa [package insert]. North Chicago, IL: AbbVie Inc.; November 2018.
4. Synarel [package insert]. New York, NY: Pfizer Inc.; March 2018.
5. Zoladex [package insert]. Lake Forest, IL: TerSera Therapeutics LLC; March 2018.
6. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed December 2018.
7. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed December 2018.
8. Schrager S, Falleroni J, Edgoose J. Evaluation and treatment of endometriosis. Am Fam Physician. 2013 Jan 15;87(2):107-13.
9. Management of endometriosis. Practice Bulletin No. 114. American College of Obstetricians and Gynecologists. Obstet Gynecol 2010;116:223-36.

Written by: UM Development (DS/AH/NP)
Date Written: 08/2018
Revised: (CF) 12/2018 (no clinical changes)
Reviewed: Medical Affairs: (ME) 08/2018
External Review: 10/2018, 04/2019

CRITERIA FOR APPROVAL

1	Does the patient have the diagnosis of moderate to severe pain associated with endometriosis?	Yes	No
2	Has the patient received the maximum recommended treatment course of 12 months of Lupron Depot or Lupaneta Pack OR 6 months of Synarel or Zoladex?	Yes	No
3	Will the patient receive 150 mg once daily of the requested drug? [If no, then skip to question 5.]	Yes	No
4	Has the patient already received greater than or equal to 24 months of therapy of the requested drug? [No further questions.]	Yes	No
5	Will the patient receive 200 mg twice daily of the requested drug?	Yes	No
6	Has the patient already received greater than or equal to 6 months of therapy of the requested drug?	Yes	No

Mapping Instructions			
	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you have moderate to severe pain associated with endometriosis. Your request has been denied based on the information we have.</p> <p>[Short Description: No approvable diagnosis.]</p>
2.	Deny	Go to 3	<p>You do not meet the requirements of your plan. Your plan covers this drug when you have not taken full treatment courses of any of the following:</p> <ul style="list-style-type: none"> - Lupron Depot for 12 months - Lupaneta Pack for 12 months - Synarel for 6 months - Zoladex for 6 months <p>Your request has been denied based on the information we have.</p> <p>[Short Description: Prior therapy exclusion.]</p>
3.	Go to 4	Go to 5	
4.	Deny	Approve, 24 months	<p>You do not meet the requirements of your plan. Your plan covers this drug when the prescribed dose and duration falls within the manufacturer's published dosing guidelines. Your request has been denied based on the information we have.</p> <p>[Short Description: Unapproved dose and/or duration.]</p>
5.	Go to 6	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when the prescribed dose falls within the manufacturer's published dosing guidelines. Your request has been denied based on the information we have.</p> <p>[Short Description: Unapproved dose.]</p>
6.	Deny	Approve, 6 months	<p>You do not meet the requirements of your plan. Your plan covers this drug when the prescribed dose and duration falls within the manufacturer's published dosing guidelines. Your request has been denied based on the information we have.</p> <p>[Short Description: Unapproved dose and/or duration.]</p>

SPECIALTY GUIDELINE MANAGEMENT

ORKAMBI (lumacaftor/ivacaftor)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Orkambi is indicated for the treatment of cystic fibrosis (CF) in patients age 2 years and older who are homozygous for the *F508del* mutation in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene. If the patient's genotype is unknown, an FDA cleared CF mutation test should be used to detect the presence of the *F508del* mutation on both alleles of the *CFTR* gene.

Limitation of use: The efficacy and safety of Orkambi have not been established in patients with CF other than those homozygous for the *F508del* mutation.

All other indications are considered experimental/investigational and are not medically necessary.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review: genetic testing report confirming the presence of the appropriate *CFTR* gene mutation.

III. CRITERIA FOR INITIAL APPROVAL

Cystic Fibrosis

Authorization of 12 months may be granted for treatment of cystic fibrosis when all of the following criteria are met:

- A. Genetic testing was conducted to detect a mutation in the *CFTR* gene.
- B. The member is positive for the *F508del* mutation on both alleles of the *CFTR* gene.
- C. The member is at least 2 years of age.
- D. Orkambi will not be used in combination with Kalydeco or Symdeko.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who are experiencing benefit from therapy as evidenced by disease stability or disease improvement (e.g., improvement in FEV1 from baseline).

V. REFERENCES

1. Orkambi [package insert]. Boston, MA: Vertex Pharmaceuticals Inc.; July 2019.

SPECIALTY GUIDELINE MANAGEMENT

OTEZLA (apremilast)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Moderate to severe plaque psoriasis
2. Active psoriatic arthritis
3. Oral ulcers associated with Behçet's disease

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Moderate to severe plaque psoriasis**

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for the treatment of moderate to severe plaque psoriasis.
2. Authorization of 12 months may be granted for treatment of moderate to severe plaque psoriasis when all of the following criteria are met:
 - a. At least 3% of body surface area (BSA) is affected OR crucial body areas (i.e., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
 - b. Member meets any of the following criteria:
 - i. Member has had an inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) or pharmacologic treatment with methotrexate, cyclosporine or acitretin.
 - ii. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine and acitretin (see Appendix A).

B. **Active psoriatic arthritis (PsA)**

Authorization of 12 months may be granted for treatment of active psoriatic arthritis (PsA).

C. **Behçet's syndrome**

Authorization of 12 months may be granted for members who have previously received a biologic indicated for the treatment of Behçet's syndrome.

Authorization of 12 months may be granted for the treatment of oral ulcers associated with Behçet's syndrome when the member has had an inadequate response to at least one nonbiologic medication for Behçet's disease (e.g., colchicine, systemic glucocorticoids, azathioprine).

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who are using Otezla for an indication outlined in section II and who achieve or maintain positive clinical response with Otezla as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. Appendix A: Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine or Acitretin

1. Alcoholism, alcoholic liver disease, or other chronic liver disease
2. Breastfeeding
3. Drug interaction
4. Cannot be used due to risk of treatment-related toxicity
5. Pregnancy or planning pregnancy
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

V. REFERENCES

1. Otezla [package insert]. Summit, NJ: Celgene Corporation; July 2019.
2. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 4: Guidelines of care for the management and treatment of psoriasis with traditional systemic agents. *J Am Acad Dermatol*. 2009;61:451-485.
3. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 6: Guidelines of care for the treatment of psoriasis and psoriatic arthritis: case-based presentations and evidence-based conclusions. *J Am Acad Dermatol*. 2011;65(1):137-174.
4. Coates LC, Kavanaugh A, Mease PJ, et al. Group for research and assessment of psoriasis and psoriatic arthritis 2015 treatment recommendation for psoriatic arthritis. *Arthritis Rheumatol*. 2016 May;68(5):1060-71.

SPECIALTY GUIDELINE MANAGEMENT

OTREXUP (methotrexate injection)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

1. Rheumatoid Arthritis (RA) including Polyarticular Juvenile Idiopathic Arthritis (pJIA)
Otrexup is indicated in the management of selected adults with severe, active rheumatoid arthritis (RA) or children with active polyarticular juvenile idiopathic arthritis (pJIA), who have had an insufficient therapeutic response to, or are intolerant of, an adequate trial of first-line therapy including full dose non-steroidal anti-inflammatory agents (NSAIDs).
2. Psoriasis
Otrexup is indicated in adults for the symptomatic control of severe, recalcitrant, disabling psoriasis that is not adequately responsive to other forms of therapy, but only when the diagnosis has been established, as by biopsy and/or after dermatologic consultation. It is important to ensure that a psoriasis "flare" is not due to an undiagnosed concomitant disease affecting immune responses.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of RA, pJIA, or psoriasis when BOTH of the following criteria are met:

- A. Member has tried and had an inadequate response or intolerance to generic oral methotrexate.
- B. Member has inability to prepare and administer generic injectable methotrexate.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who meet ALL initial authorization criteria and achieve or maintain positive clinical response after at least 3 months of therapy with Otrexup as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. REFERENCES

1. Otrexup [package insert]. Ewing, NJ: Antares Pharma, Inc.; March 2018.
2. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. *Arthritis Rheumatol*. 2016;68(1):1-26.
3. Smolen JS, Landewé R, Billsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. *Ann Rheum Dis*. 2017;0:1-18.

4. Beukelman T, Patkar NM, Saag KG, et al. 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: initiation and safety monitoring of therapeutic agents for the treatment of arthritis and systemic features. *Arthritis Care Res.* 2011;63(4):465-482.
5. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 4: Guidelines of care for the management and treatment of psoriasis with traditional systemic agents. *J Am Acad Dermatol.* 2009;61:451-485.

SPECIALTY GUIDELINE MANAGEMENT

Eloxatin (oxaliplatin) oxaliplatin (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Oxaliplatin, used in combination with infusional 5-fluorouracil/leucovorin, is indicated for:

1. Adjuvant treatment of stage III colon cancer in patients who have undergone complete resection of the primary tumor.
2. Treatment of advanced colorectal cancer.

B. Compendial Uses

1. Colon cancer
2. Rectal cancer
3. Esophageal or esophagogastric junction cancers
4. Gastric cancer
5. Hepatobiliary cancers
 - Extrahepatic cholangiocarcinoma
 - Intrahepatic cholangiocarcinoma
 - Gallbladder cancer
6. Bladder cancer (including non-urothelial and urothelial cancer with variant histology)
7. Neuroendocrine and adrenal tumors
 - a. Neuroendocrine tumors of the pancreas
 - b. Poorly differentiated (high grade)/large or small cell disease
8. Occult primary tumors (cancer of unknown primary)
9. Ovarian cancer, fallopian tube cancer, and primary peritoneal cancer
 - a. Epithelial ovarian cancer, fallopian tube cancer, and primary peritoneal cancer
 - b. Mucinous carcinoma
11. Pancreatic adenocarcinoma
12. Testicular cancer
13. Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL)
14. Anal carcinoma
15. B-Cell lymphomas
 - a. Follicular lymphoma (grade 1-2)
 - b. Histologic Transformation of Marginal Zone Lymphoma to Diffuse Large B-Cell Lymphoma
 - c. Mantle Cell Lymphoma
 - d. Diffuse Large B-Cell Lymphoma
 - e. High-Grade B-Cell Lymphomas
 - f. AIDS-Related B-Cell Lymphomas
 - g. Post-Transplant Lymphoproliferative Disorders
16. Primary cutaneous lymphomas
 - a. Mycosis fungoides/Sezary syndrome
 - b. Primary cutaneous CD30+ T-Cell lymphoproliferative disorders
17. T-Cell lymphomas

- a. Peripheral T-Cell lymphomas
- b. Adult T-Cell leukemia/lymphoma
- c. Extranodal NK/T-Cell lymphoma, nasal type
- d. Hepatosplenic Gamma-Delta T-Cell lymphoma

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Colorectal Cancer

Authorization of 6 months may be granted for the treatment of colorectal cancer (including colon and rectal cancer).

B. Pancreatic Adenocarcinoma

Authorization of 6 months may be granted for the treatment of pancreatic adenocarcinoma.

C. Esophageal and Esophagogastric Junction Cancers

Authorization of 6 months may be granted for the treatment of esophageal and esophagogastric junction cancers.

D. Gastric Cancer

Authorization of 6 months may be granted for the treatment of gastric cancer.

E. Hepatobiliary Cancers

Authorization of 6 months may be granted for the treatment of hepatobiliary cancers (including intrahepatic and extrahepatic cholangiocarcinoma and gallbladder cancer).

F. Neuroendocrine and Adrenal Tumors

Authorization of 6 months may be granted for the treatment of neuroendocrine and adrenal tumors (including neuroendocrine tumors of the pancreas and poorly differentiated [high grade]/large or small cell disease).

G. Occult Primary Tumors (cancer of unknown primary)

Authorization for 6 months may be granted for the treatment of occult primary tumors.

H. Ovarian Cancer, Fallopian Tube Cancer, and Primary Peritoneal Cancer

1. Epithelial Ovarian Cancer, Fallopian Tube Cancer, and Primary Peritoneal Cancer

Authorization of 6 months may be granted for the treatment of persistent or recurrent epithelial ovarian cancer, fallopian tube cancer, and primary peritoneal cancer.

2. Mucinous Carcinoma

Authorization of 6 months may be granted for the treatment of mucinous carcinoma.

I. Testicular Cancer

Authorization of 6 months may be granted for the treatment of testicular cancer.

J. Bladder Cancer

Authorization of 6 months may be granted for the treatment of bladder cancer (including non-urothelial and urothelial cancer with variant histology).

Reference number(s)
2041-A

K. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL)

Authorization of 6 months may be granted for the treatment of CLL/SLL.

L. Anal Carcinoma

Authorization of 6 months may be granted for the treatment of metastatic anal cancer.

M. B-Cell Lymphomas

Authorization of 6 months may be granted for the treatment of B-Cell lymphomas (including follicular lymphoma [grade 1-2], histologic transformation of marginal zone lymphoma to diffuse large B-Cell lymphoma, mantle cell lymphoma, diffuse large B-Cell lymphoma, high-grade B-Cell lymphomas, AIDS-Related B-Cell lymphomas, and post-transplant lymphoproliferative disorders).

N. Primary Cutaneous Lymphomas

Authorization of 6 months may be granted for the treatment of primary cutaneous lymphomas (including mycosis fungoides/Sezary syndrome and primary cutaneous CD30+ T-Cell lymphoproliferative disorders).

O. T-Cell Lymphomas

Authorization of 6 months may be granted for the treatment of T-Cell lymphomas (including peripheral T-Cell lymphomas, adult T-Cell leukemia/lymphoma, hepatosplenic gamma-delta T-Cell lymphoma, and extranodal NKT/T-Cell lymphoma, nasal type).

III. CONTINUATION OF THERAPY

Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for an indication in Section II who have not experienced disease progression or an unacceptable toxicity.

IV. REFERENCES

1. Eloxatin [package insert]. Bridgewater, NJ: Sanofi-aventis U.S. LLC; October 2015.
2. Oxaliplatin [package insert]. Sunrise, FL: Cipla USA, Inc.; December 2018.
3. The NCCN Drugs & Biologics Compendium 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. July 25, 2019.

SPECIALTY GUIDELINE MANAGEMENT

OXBRYTA (voxelotor)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Oxbryta is indicated for the treatment of sickle cell disease (SCD) in adults and pediatric patients 12 years of age and older.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Sickle cell disease (SCD)

Authorization of 6 months may be granted for treatment of sickle cell disease in members 12 years of age or older with a pretreatment hemoglobin level of 10.5 g/dL or less.

Note: Requirements regarding pretreatment hemoglobin level exclude values due to a recent transfusion.

III. CONTINUATION OF THERAPY

Sickle cell disease (SCD)

Authorization of 12 months may be granted for continued treatment in members experiencing benefit from therapy demonstrated by increased hemoglobin levels or maintenance of increased hemoglobin levels since starting treatment.

IV. REFERENCES

1. Oxbryta [package insert]. South San Francisco, CA: Global Blood Therapeutics, Inc.; December 2019.
2. Vichinsky E, Hoppe CC, Ataga KI, et al. A phase 3 randomized trial of voxelotor in sickle cell disease. *N Engl J Med*. 2019 Aug 8;381(6):509-519.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME **OXBRYTA**
(generic) (voxelotor)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

MDC
Ref # 3465-A

FDA-APPROVED INDICATION

Oxbryta is indicated for the treatment of sickle cell disease (SCD) in adults and pediatric patients 12 years of age and older.¹

CRITERIA FOR APPROVAL

1	Does the patient have a diagnosis of sickle cell disease (SCD)? [If no, no further questions.]	Yes	No
2	Is the patient 12 years of age or older?	Yes	No

Guidelines for Approval	
Duration of Approval	12 months
Set 1: SCD	
Yes to question(s)	No to question(s)
1	None
2	

Mapping Instructions	
	Yes
1.	Go to 2
2.	Approve, 12 months
	No
	Deny
	Deny

RATIONALE

These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to ensure that patients follow selection elements noted in labeling and/or practice guidelines in order to decrease the potential for inappropriate utilization.

REFERENCES

1. Oxbryta [package insert]. South San Francisco, CA: Global Blood Therapeutics, Inc.; December 2019.

DOCUMENT HISTORY

Created: Specialty Clinical Development (IP) 12/2019
Revised:
Reviewed: CDPR / MMF 12/2019
External Review: 01/2020

SPECIALTY GUIDELINE MANAGEMENT

OXERVATE (cenegermin-bkbj)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Oxervate is a recombinant human nerve growth factor indicated for the treatment of neurotrophic keratitis.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Neurotrophic keratitis

Authorization of 8 weeks may be granted for treatment of neurotrophic keratitis when all of the following criteria are met:

- A. The patient must experience persistent epithelial defects (PED) or corneal ulceration of at least 2 weeks duration refractory to one or more conventional non-surgical treatments (e.g., preservative free artificial tears).
- B. Evidence of decreased corneal sensitivity (less than or equal to 4 cm using the Cochet-Bonnet aesthesiometer) within the area of the PED or corneal ulcer and outside of the area of the defect in at least one corneal quadrant.
- C. Performance of Schirmer test without anesthesia resulting in greater than 3 mm of moisture in 5 minutes
- D. The patient has not received a previous course of Oxervate in the affected eye.

REFERENCES

1. Oxervate [package insert]. Boston, MA: Dompe U.S. Inc.; August 2018.

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	GLUCAGON-LIKE PEPTIDE 1 (GLP-1) RECEPTOR AGONIST
BRAND NAME* (generic)	OZEMPIC (semaglutide)

Status: CVS Caremark Criteria

Type: Initial Prior Authorization with Quantity Limit

Ref #2439-C

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Ozempic is indicated:

- as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
- to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease.

Limitations of Use

- Ozempic has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis
- Ozempic is not a substitute for insulin. OZEMPIC is not indicated for use in patients with type 1 diabetes mellitus or for the treatment of patients with diabetic ketoacidosis, as it would not be effective in these settings.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has been receiving GLP-1 Agonist therapy for at least 3 months [Note: Examples of GLP-1 Agonists are Adlyxin, Bydureon, Byetta, Ozempic, Tanzeum, Trulicity, Victoza]

AND

- The patient has demonstrated a reduction in A1c (hemoglobin A1c) since starting GLP-1 Agonist therapy
- OR**
- The patient has established cardiovascular disease

OR

- The patient has a diagnosis of type 2 diabetes mellitus

AND

- The patient has experienced an inadequate treatment response, intolerance or contraindication to metformin
- OR**
- The patient requires combination therapy AND has an A1c (hemoglobin A1c) of 7.5 percent or greater
- OR**
- The patient has established cardiovascular disease

Quantity Limits apply.

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Ozempic is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Ozempic is also indicated to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease. Ozempic should be initiated 0.25mg administered

once weekly. The 0.25mg dose is intended for treatment initiation and is not effective for glycemic control. After 4 weeks, the dosage increases to 0.5mg once weekly. If additional glycemic control is needed after at least 4 weeks on the 0.5mg, the dosage may be increased to 1mg once weekly. The maximum recommended dosage is 1mg once weekly.

Clinical guidelines from the American Diabetes Association and the American Association of Clinical Endocrinologists and American College of Endocrinology for the management of hyperglycemia in type 2 diabetes indicate that metformin monotherapy should be started at diagnosis of type 2 diabetes unless there are contraindications. Metformin is effective and safe, is inexpensive, and may reduce risk of cardiovascular events and death. In patients with contraindications or intolerance of metformin, initial therapy should be based on patient factors; consider a drug from another class.⁴⁻⁵

The clinical guidelines also state that the A1c test is the major tool for assessing glycemic control and has strong predictive value for diabetes complications. Thus, A1c testing should be performed routinely in all patients with diabetes at initial assessment and as part of continuing care. The guidelines set goals for therapeutic effectiveness which must be evaluated frequently (e.g., every 3 months) until stable, using multiple criteria, including A1c. Less frequent monitoring is acceptable once targets are achieved.⁴⁻⁵ Therefore, continued use of any GLP-1 Agonist (e.g., Adlyxin, Byetta, Bydureon, Ozempic, Tanzeum, Trulicity, and Victoza) will be approved for patients who have demonstrated a reduction in A1c since starting GLP-1 Agonist therapy for at least three months.

If the A1c target is not achieved after approximately 3 months and patient does not have atherosclerotic cardiovascular disease (ASCVD) or chronic kidney disease (CKD), consider a combination of metformin and one of the preferred six treatment options: sulfonylurea, thiazolidinedione, dipeptidyl peptidase 4 (DPP-4) inhibitors, sodium-glucose cotransporter 2 (SGLT2) inhibitors, glucagon-like peptide 1 (GLP-1) receptor agonists, or basal insulin; the choice of which agent to add is based on drug-specific effects and patient factors. For patients in whom ASCVD, Heart Failure, or CKD predominates, the best choice for a second agent is a GLP-1 receptor agonist or SGLT2 inhibitor with demonstrated cardiovascular risk reduction, after consideration of drug-specific and patient factors.⁴⁻⁵

In patients with an initial A1c of 7.5% or greater, or in patients who are unable to achieve their glycemic goals with monotherapy, combination therapy is recommended.⁴⁻⁵

SUSTAIN 6 was a multi-national, multi-center, placebo-controlled, double-blind cardiovascular outcomes trial. Patients with inadequately controlled type 2 diabetes and atherosclerotic cardiovascular disease were randomized to Ozempic once weekly or placebo for two years. The trial compared the risk of Major Adverse Cardiovascular Event (MACE) between semaglutide and placebo when these were added to and used concomitantly with standard of care treatments for diabetes and cardiovascular disease.¹ The primary endpoint, MACE, was the time to first occurrence of a three-part composite outcome which included cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.¹ Ozempic significantly reduced the occurrence of MACE. Therefore, Ozempic (semaglutide) will be approved for initial therapy and continuation of therapy for patients have established cardiovascular disease.

Semaglutide slows gastric emptying, which reduces the rate at which meal-derived glucose appears in the circulation.¹⁻³ A quantity limit is in place to aid proper utilization of Ozempic. At maximum approved dosing for Ozempic, 2 pens will be allowed for a 28 day supply (6 pens per 84 day supply).

REFERENCES

1. Ozempic [package insert]. Plainsboro, NJ: Novo Nordisk Inc; January 2020.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed July 2019.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed July 2019.
4. American Diabetes Association (ADA) Standards of Medical Care in Diabetes-2019—*Diabetes Care*. 2019; 42(Supplement 1).
5. Garber AJ, et al. AACE/ACE Consensus Statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the Comprehensive Type 2 Diabetes Management Algorithm 2019, *Endocr Pract*. 2019; 25 (No 1); 69-100.

Written by: UM Development (SF)
 Date Written: 12/2017
 Revised: 07/2018 (no clinical changes), 07/2019 (no clinical changes), 01/2020
 Reviewed: Medical Affairs (AN) 12/2017, (CHART) 08/01/2019, (CHART) 01/2020
 External Review: 02/2018, 10/2018, 10/2019

CRITERIA FOR APPROVAL

1	Has the patient been receiving GLP-1 Agonist therapy for at least 3 months? [Note: Examples of GLP-1 Agonists are Adlyxin, Bydureon, Byetta, Ozempic, Tanzeum, Trulicity, Victoza] [If no, then skip to question 3.]	Yes	No
2	Has the patient demonstrated a reduction in A1c (hemoglobin A1c) since starting GLP-1 Agonist therapy? [If yes, then skip to question 7.] [If no, then skip to question 6.]	Yes	No
3	Is the requested drug being prescribed for type 2 diabetes mellitus?	Yes	No
4	Has the patient experienced an inadequate treatment response, intolerance, or contraindication to metformin? [If yes, then skip to question 7.]	Yes	No
5	Does the patient require combination therapy AND have an A1c (hemoglobin A1c) of 7.5 percent or greater?	Yes	No
6	Does the patient have established cardiovascular disease?	Yes	No
7	Does the patient require more than 2 prefilled pens per 28 days (or 6 prefilled pens per 84 days)? [RPh Note: If yes, then deny and enter a partial approval for 2 pens (3 mL) per 21 days (6 pens (9 mL) per 63 days)]	Yes	No

Mapping Instructions

DENIAL REASONS – DO NOT USE FOR MEDICARE PART D

	Yes	No	
1.	Go to 2	Go to 3	
2.	Go to 7	Go to 6	
3.	Go to 4	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have type 2 diabetes mellitus. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
4.	Go to 7	Go to 5	
5.	Go to 7	Go to 6	
6.	Go to 7	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet one of these conditions: - You have tried metformin it did not work for you, or you cannot use it - You require combination therapy and you have an A1c (hemoglobin A1c) of 7.5 percent or greater - You have established cardiovascular (heart) disease Your request has been denied based on the information we have. [Short description: No inadequate treatment response, intolerance or

			contraindication to metformin, No requirement for combination therapy or No established cardiovascular disease]
7.	Deny	Approve, 36 months, 2 prefilled pens (3mL) / 21 days* or 6 pens (9mL) / 63 days*	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 2 prefilled pen per 28 days of the requested drug and strength. You have been approved for the maximum quantity that your plan covers for a duration of 36 months. Your request for additional quantities of the requested drug and strength has been denied. [Short description: Over max quantity]

**The duration of 21 days is used for a 28-day fill period and 63 days is used for a 84-day fill period to allow time for refill processing.*

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS **GLUCAGON-LIKE PEPTIDE 1 (GLP-1) RECEPTOR AGONIST**

BRAND NAME*
(generic)

OZEMPIC
(semaglutide)

Status: CVS Caremark Criteria

Type: Initial Prior Authorization

Ref # 2440-A

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Ozempic is indicated:

- as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
- to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease.

Limitations of Use

- Ozempic has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis
- Ozempic is not a substitute for insulin. OZEMPIC is not indicated for use in patients with type 1 diabetes mellitus or for the treatment of patients with diabetic ketoacidosis, as it would not be effective in these settings.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has been receiving GLP-1 Agonist therapy for at least 3 months [Note: Examples of GLP-1 Agonists are Adlyxin, Bydureon, Byetta, Ozempic, Tanzeum, Trulicity, Victoza]

AND

- The patient has demonstrated a reduction in A1c (hemoglobin A1c) since starting GLP-1 Agonist therapy
- OR**
- The patient has established cardiovascular disease

OR

- The patient has a diagnosis of type 2 diabetes mellitus

AND

- The patient has experienced an inadequate treatment response, intolerance or contraindication to metformin
- OR**
- The patient requires combination therapy AND has an A1c (hemoglobin A1c) of 7.5 percent or greater
- OR**
- The patient has established cardiovascular disease

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Ozempic is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Ozempic is also indicated to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease.

Clinical guidelines from the American Diabetes Association and the American Association of Clinical Endocrinologists and American College of Endocrinology for the management of hyperglycemia in type 2 diabetes indicate that metformin monotherapy should be started at diagnosis of type 2 diabetes unless there are contraindications. Metformin is effective and safe, is inexpensive, and may reduce risk of cardiovascular events and death. In patients with contraindications or intolerance of metformin, initial therapy should be based on patient factors; consider a drug from another class.⁴⁻⁵

The clinical guidelines also state that the A1c test is the major tool for assessing glycemic control and has strong predictive value for diabetes complications. Thus, A1c testing should be performed routinely in all patients with diabetes at initial assessment and as part of continuing care. The guidelines set goals for therapeutic effectiveness which must be evaluated frequently (e.g., every 3 months) until stable, using multiple criteria, including A1c. Less frequent monitoring is acceptable once targets are achieved.⁴⁻⁵ Therefore; continued use of any GLP-1 Agonist (e.g., Adlyxin, Byetta, Bydureon, Ozempic, Tanzeum, Trulicity, and Victoza) will be approved for patients who have demonstrated a reduction in A1c since starting GLP-1 Agonist therapy for at least three months.

If the A1c target is not achieved after approximately 3 months and patient does not have atherosclerotic cardiovascular disease (ASCVD) or chronic kidney disease (CKD), consider a combination of metformin and one of the preferred six treatment options: sulfonylurea, thiazolidinedione, dipeptidyl peptidase 4 (DPP-4) inhibitors, sodium-glucose cotransporter 2 (SGLT2) inhibitors, glucagon-like peptide 1 (GLP-1) receptor agonists, or basal insulin; the choice of which agent to add is based on drug-specific effects and patient factors. For patients in whom ASCVD, Heart Failure, or CKD predominates, the best choice for a second agent is a GLP-1 receptor agonist or SGLT2 inhibitor with demonstrated cardiovascular risk reduction, after consideration of drug-specific and patient factors.⁴⁻⁵

In patients with an initial A1c of 7.5% or greater, or in patients who are unable to achieve their glycemic goals with monotherapy, combination therapy is recommended.⁴⁻⁵

SUSTAIN 6 was a multi-national, multi-center, placebo-controlled, double-blind cardiovascular outcomes trial. Patients with inadequately controlled type 2 diabetes and atherosclerotic cardiovascular disease were randomized to Ozempic once weekly or placebo for two years. The trial compared the risk of Major Adverse Cardiovascular Event (MACE) between semaglutide and placebo when these were added to and used concomitantly with standard of care treatments for diabetes and cardiovascular disease.¹ The primary endpoint, MACE, was the time to first occurrence of a three-part composite outcome which included cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.¹ Ozempic significantly reduced the occurrence of MACE. Therefore, Ozempic (semaglutide) will be approved for initial therapy and continuation of therapy for patients have established cardiovascular disease.

REFERENCES

1. Ozempic [package insert]. Plainsboro, NJ: Novo Nordisk Inc; January 2020.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed July 2019.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed July 2019.
4. American Diabetes Association (ADA) Standards of Medical Care in Diabetes-2019—*Diabetes Care*. 2019; 42(Supplement 1).
5. Garber AJ, et al. AACE/ACE Consensus Statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the Comprehensive Type 2 Diabetes Management Algorithm 2019, *Endocr Pract*. 2019; 25 (No 1); 69-100.

Written by: UM Development (SF)
Date Written: 12/2017
Revised: 07/2018 (no clinical changes), 07/2019 (no clinical changes, removed MDC designation), 01/2020
Reviewed: Medical Affairs (AN) 12/2017, (CHART) 08/01/2019, (CHART) 01/30/2020
External Review: 02/2018, 10/2018, 10/2019

CRITERIA FOR APPROVAL

1	Has the patient been receiving GLP-1 Agonist therapy for at least 3 months? [Note: Examples of GLP-1 Agonists are Adlyxin, Bydureon, Byetta, Ozempic, Tanzeum, Trulicity, Victoza] [If no, then skip to question 3.]	Yes	No
2	Has the patient demonstrated a reduction in A1c (hemoglobin A1c) since starting GLP-1 Agonist therapy? [If yes, then no further questions.] [If no, then skip to question 6.]	Yes	No
3	Does the patient have a diagnosis of type 2 diabetes mellitus?	Yes	No
4	Has the patient experienced an inadequate treatment response, intolerance, or contraindication to metformin? [If yes, then no further questions.]	Yes	No
5	Does the patient require combination therapy AND have an A1c (hemoglobin A1c) of 7.5 percent or greater? [If yes, then no further questions.]	Yes	No
6	Does the patient have established cardiovascular disease?	Yes	No

Guidelines for Approval

Duration of Approval 12 Months

Set 1		Set 2	
Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)
1	None	1	2
2		6	
Set 3		Set 4	
Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)
3	1	3	1
4		5	4
Set 5			
Yes to question(s)	No to question(s)		
3	1		
6	4		
	5		

Mapping Instructions

DENIAL REASONS – DO NOT USE FOR MEDICARE PART D

	Yes	No	
1.	Go to 2	Go to 3	
2.	Approve, 12 months	Go to 6	
3.	Go to 4	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have type 2 diabetes mellitus. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
4.	Approve, 12 months	Go to 5	
5.	Approve, 12 months	Go to 6	

6.	Approve, 12 months	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you meet one of these conditions:</p> <ul style="list-style-type: none"> - You have tried metformin and it did not work for you, or you cannot use it - You require combination therapy and you have an A1c (hemoglobin A1c) of 7.5 percent or greater - You have established cardiovascular (heart) disease <p>Your request has been denied based on the information we have. [Short description: No inadequate treatment response, intolerance or contraindication to metformin, No requirement for combination therapy or No established cardiovascular disease]</p>
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SPECIALTY GUIDELINE MANAGEMENT

PADCEV (enfortumab vedotin-ejfv)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Padcev (enfortumab vedotin-ejfv) is indicated for the treatment of adult patients with locally advanced or metastatic urothelial cancer who have previously received a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor, and a platinum-containing chemotherapy.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Urothelial Cancer

Authorization of 12 months may be granted for treatment of locally advanced or metastatic urothelial cancer (e.g., bladder cancer and cancers of the urinary tract) as a single agent when both of the following criteria are met:

1. Member has received prior treatment with a platinum-containing chemotherapy.
2. Member has received prior treatment with a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Padcev [package insert]. Northbrook, IL: Astellas Pharma; December 2019.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME (generic)	PADCEV (enfortumab vedotin-ejfv)
Status: CVS Caremark Criteria Type: Initial Prior Authorization	MDC Ref # 3472-A

FDA-APPROVED INDICATIONS¹

Urothelial Cancer

Padcev (enfortumab vedotin-ejfv) is indicated for the treatment of adult patients with locally advanced or metastatic urothelial cancer who have previously received a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor, and a platinum-containing chemotherapy.

CRITERIA FOR APPROVAL

1	Does the patient have a diagnosis of urothelial cancer? [If no, no further questions.]	Yes	No
2	Does the patient have locally advanced or metastatic disease? [If no, no further questions.]	Yes	No
3	Has the patient previously received treatment with a platinum-containing chemotherapy? [If no, no further questions.]	Yes	No
4	Has the patient previously received treatment with a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor?	Yes	No

Guidelines for Approval	
Duration of Approval	12 Months
Set 1	
Yes to question(s)	No to question(s)
1	None
2	
3	
4	

Mapping Instructions	
Yes	No
1. Go to 2	Deny
2. Go to 3	Deny
3. Go to 4	Deny
4. Approve, 12 months	Deny

RATIONALE

These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to ensure that patients follow selection elements noted in labeling and/or practice guidelines in order to decrease the potential for inappropriate utilization.

REFERENCES

1. Padcev [package insert]. Northbrook, IL: Astellas Pharma; December 2019.

DOCUMENT HISTORY

Created: Specialty Clinical Development (FS) 01/2020
Revised:
Reviewed: CDPR / MF 01/2020
External Review: 01/2020

SPECIALTY GUIDELINE MANAGEMENT

PALYNZIQ (pegvaliase-pqpz)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Palynziq is indicated to reduce blood phenylalanine concentrations in adult patients with phenylketonuria who have uncontrolled blood phenylalanine concentrations greater than 600 micromol/L on existing management.

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: enzyme assay or genetic testing results supporting diagnosis.

III. CRITERIA FOR INITIAL APPROVAL

Phenylketonuria (PKU)

Authorization of 6 months may be granted for members when baseline blood phenylalanine concentration, prior to initiation of the requested medication, is greater than 600 micromol/L.

IV. CONTINUATION OF THERAPY

Phenylketonuria (PKU)

A. Authorization of 12 months may be granted for members who have achieved a clinical response as evidenced by either of the following:

1. Member experienced a reduction in blood phenylalanine concentration of at least 20% from pre-treatment baseline.
2. Member achieved a blood phenylalanine concentration of less than or equal to 600 micromol/L.

Phenylketonuria (PKU)

B. Authorization of 6 months may be granted for members who have not achieved a clinical response to treatment with Palynziq (at least a 20% reduction in blood phenylalanine concentration from pre-treatment baseline or a blood phenylalanine concentration less than or equal to 600 micromol/L) and meets one of the following requirements:

1. Member has not been titrated to the maximum allowed dose of 40mg once daily.
2. Member has received less than 16 weeks of continuous treatment at the maximum allowed dose.

Reference number(s)
2585-A

V. REFERENCES

1. Palynziq [package insert]. Novato, CA: BioMarin Pharmaceutical Inc.; May 2018.

SPECIALTY GUIDELINE MANAGEMENT

PARSABIV (etelcalcetide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Secondary hyperparathyroidism in adult patients with chronic kidney disease (CKD) on hemodialysis

All other indications are considered experimental/investigational and not medically necessary.

II. INITIAL CRITERIA FOR APPROVAL

Secondary hyperparathyroidism with CKD on hemodialysis

Authorization of 12 months may be granted for treatment of secondary hyperparathyroidism in a member with chronic kidney disease on hemodialysis who has a serum calcium level (corrected for albumin) greater than or equal to 8.3 mg/dL (see Appendix).

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when the member is experiencing benefit from therapy as evidenced by a decrease in intact parathyroid hormone (iPTH) levels from pretreatment baseline.

IV. APPENDIX

Corrected calcium = measured total calcium + 0.8(4.0 – serum albumin)

V. REFERENCES

1. Parsabiv [package insert]. Thousand Oaks, CA: Amgen, Inc.; August 2018.
2. Micromedex Solutions [database online]. Truven Health Analytics, Inc. Ann Arbor, MI. Available at: www.micromedexsolutions.com. Accessed October 24, 2018.
3. AHFS DI (Adult and Pediatric) [database online]. Lexi-Comp, Inc. Hudson, OH. Available at: http://online.lexi.com/lco/action/index/dataset/complete_ashp [available with subscription]. Accessed October 24, 2018.
4. Clinical Pharmacology [Internet]. Elsevier. Tampa (FL). Available from: <http://www.clinicalpharmacology.com>. Accessed October 24, 2018.
5. Block GA, Bushinsky DA, Cunningham J, et al. Effect of etelcalcetide vs placebo on serum parathyroid hormone in patients receiving hemodialysis with secondary hyperparathyroidism: two randomized clinical trials. *JAMA*. 2017;317(2):146-155.
6. Shoback D. Hypoparathyroidism. *NEJM*. 2008;359: 391-403.

SPECIALTY GUIDELINE MANAGEMENT

PCSK9i PRALUENT (alirocumab), REPATHA (evolocumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

- A. Members with established atherosclerotic cardiovascular disease.
- B. Members with an untreated LDL-C of greater than, or equal to, 190 mg/dL.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Clinical atherosclerotic cardiovascular disease (ASCVD)

Authorization of 12 months may be granted when all of the following criteria are met:

- 1. The member has a history of clinical atherosclerotic cardiovascular disease or has experienced a cardiovascular event
- 2. The member has a current LDL-C level greater than, or equal to, 70 mg/dL
- 3. The member is receiving maximally tolerated statin therapy or is statin intolerant

B. Primary or familial hyperlipidemia

Authorization of 12 months may be granted when all of the following criteria are met:

- 1. The member had an untreated (before any lipid lowering therapy) LDL-C level greater than, or equal to, 190 mg/dL
- 2. The member has a current LDL-C level greater than, or equal to, 100 mg/dL
- 3. The member is receiving maximally tolerated statin therapy or is statin intolerant

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members who are continuing therapy with a PCSK9i.

IV. REFERENCES

1. Repatha [package insert]. Thousand Oaks, CA: Amgen, Inc.; December 2017.
2. Praluent [package insert]. Bridgewater, NJ: sanofi-aventis U.S. LLC; September 2017.
3. Stone NJ, Robinson JG, Lichtenstein AH, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;129:S1-S45.
4. Lloyd-Jones DM, Morris PB, Ballantyne CM, et al. 2017 Focused Update of the 2016 ACC expert consensus decision pathway on the role of non-statin therapies for LDL-cholesterol lowering in the

- management of atherosclerotic cardiovascular disease risk: a report of the American College of Cardiology Task Force on Clinical Expert Consensus Documents. *J Am Coll Cardiol*. 2017;70:1785-822.
5. Cannon CP, Blazing MA, Giugliano RP, et al. Ezetimibe added to statin therapy after acute coronary syndromes. *N Engl J Med*. 2015;372:2387-97.
 6. Jacobson TA, Ito MK, Maki KC, et al. National Lipid Association recommendations for patient-centered management of dyslipidemia: part 1 — full report. *J Clin Lipidol*. 2015;9:129–169.
 7. Nordestgaard BG, Chapman MJ, Humphries SE, et al. Familial hypercholesterolaemia is underdiagnosed and undertreated in the general population: guidance for clinicians to prevent coronary heart disease. Consensus Statement of the European Atherosclerosis Society. *Eur Heart J*. 2013;34:3478–3490.
 8. Cuchel M, Bruckert E, Ginsberg HN, et al. Homozygous familial hypercholesterolaemia: new insights and guidance for clinicians to improve detection and clinical management. A position paper from the Consensus Panel on Familial Hypercholesterolaemia of the European Atherosclerosis Society. *Eur Heart J*. 2014;35:2146-2157.
 9. Raal FJ, Honarpour N, Blom DJ, et al. Inhibition of PCSK9 with evolocumab in homozygous familial hypercholesterolaemia (TESLA Part B): a randomised, double-blind, placebo-controlled trial. *Lancet*. 2015;385:341-350.
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 11. Sabatine MC, Giugliano RP, Keech AC, et al. Evolocumab and clinical outcomes in patients with cardiovascular disease. *New England Journal of Medicine*. 2017; Published online before print.
 12. Hulten EA, Carbonaro S, Petrillo SP, et al. Prognostic value of cardiac computed tomography angiography. *Journal of the American College of Cardiology*. 2011;57(10):1237-1247.
 13. Min JK, Labounty TM, Gomez MJ, et al. Incremental prognostic value of coronary computed tomographic angiography over coronary artery calcium score for risk predication of major adverse cardiac events in asymptomatic diabetic individuals. *Atherosclerosis*. 2014;232(2):298-304.
 14. Robinson, J. G., Rogers, W. J., Nedergaard, B. S., Fialkow, J., Neutel, J. M., Ramstad, D., Somaratne, R., Legg, J. C., Nelson, P., Scott, R., Wasserman, S. M. and Weiss, R. (2014), Rationale and Design of LAPLACE-2: A Phase 3, Randomized, Double-Blind, Placebo- and Ezetimibe-Controlled Trial Evaluating the Efficacy and Safety of Evolocumab in Subjects With Hypercholesterolemia on Background Statin Therapy. *Clin Cardiol*, 37: 195–203.
 15. Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC guideline on the management of blood cholesterol: report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol* 2018.

SPECIALTY GUIDELINE MANAGEMENT

PEGASYS (peginterferon alfa-2a)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. **Chronic Hepatitis C**
Pegasys, as part of a combination regimen with other hepatitis C virus (HCV) antiviral drugs, is indicated for the treatment of adults with chronic hepatitis C (CHC) with compensated liver disease. Pegasys in combination with ribavirin is indicated for treatment of pediatric patients 5 years of age and older with CHC and compensated liver disease. Pegasys monotherapy is only indicated for the treatment of patients with CHC with compensated liver disease if there are contraindications or significant intolerance to other HCV antiviral drugs.
2. **Chronic Hepatitis B**
Pegasys is indicated for the treatment of adult patients with HBeAg-positive and HBeAg-negative chronic hepatitis B infection who have compensated liver disease and evidence of viral replication and liver inflammation. Pegasys is indicated for the treatment of HBeAg-positive CHB in non-cirrhotic pediatric patients 3 years of age and older with evidence of viral replication and elevations in serum alanine.

B. Compendial Uses

1. Myeloproliferative neoplasm (essential thrombocythemia, polycythemia vera, primary myelofibrosis and post-polycythemia vera or post-essential thrombocythemia myelofibrosis)
2. Systemic mastocytosis

All other indications are considered experimental/investigational and not medically necessary.

II. INITIAL CRITERIA FOR APPROVAL

A. **Chronic hepatitis C virus (HCV) infection**

Refer to the SGM of requested regimen for the specific criteria for approval and approval durations.

B. **Chronic hepatitis B virus (HBV) infection (including HDV coinfection)**

Authorization of up to 48 weeks total may be granted for the treatment of chronic HBV infection, including HDV coinfection.

C. **Myeloproliferative neoplasm**

Authorization of 12 months may be granted for the treatment of myeloproliferative neoplasm (essential thrombocythemia, polycythemia vera, primary myelofibrosis and post-polycythemia vera or post-essential thrombocythemia myelofibrosis).

D. **Systemic mastocytosis**

Authorization of 12 months may be granted for the treatment of systemic mastocytosis.

III. CONTINUATION OF THERAPY

Reference number(s)
2139-A

A. Myeloproliferative neoplasm

Authorization of 12 months may be granted if the patient is experiencing benefit from therapy as evidenced by improvement in symptoms and/or disease markers (e.g., morphological response, reduction or stabilization in spleen size, improvement of thrombocytosis/leucocytosis, etc.)

B. Systemic mastocytosis

Authorization of 12 months may be granted if the patient is experiencing benefit from therapy as evidenced by improvement in symptoms and/or disease markers (e.g., reduction in serum and urine metabolites of mast cell activation, improvement in cutaneous lesions, skeletal disease, bone marrow mast cell burden, etc.)

IV. REFERENCES

1. Pegasys [package insert]. South San Francisco, CA: Genentech, Inc; October 2017.
2. The NCCN Drugs & Biologics Compendium® © 2018 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed March 19, 2019.
3. Olysio [package insert]. Titusville, NJ: Janssen Products, LP; November 2017.
4. Sovaldi [package insert]. Foster City, CA: Gilead Sciences, Inc.; October 2018.
5. AASLD/IDSA/IAS–USA. Recommendations for testing, managing, and treating hepatitis C. <http://www.hcvguidelines.org>. Last changes made May 24, 2018. Accessed March 19, 2019.
6. Terrault NA, Bzowej NH, Chang KM, et al. AASLD guidelines for treatment of chronic hepatitis B. *Hepatology*. 2016;63(1):261-283.
7. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology™ Myeloproliferative Neoplasms (Version 2.2019). <http://www.nccn.org>. Accessed March 19, 2019.
8. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology™ Systemic Mastocytosis (Version 2.2019). <http://www.nccn.org>. Accessed March 19, 2019.

SPECIALTY GUIDELINE MANAGEMENT

PERJETA (pertuzumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Metastatic breast cancer
In combination with trastuzumab and docetaxel for the treatment of patients with human epidermal growth factor receptor 2 (HER2)-positive metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease.
2. Neoadjuvant treatment of breast cancer
In combination with trastuzumab and chemotherapy as neoadjuvant treatment of patients with HER2-positive, locally advanced, inflammatory, or early stage breast cancer (either greater than 2 cm in diameter or node positive) as part of a complete treatment regimen for early breast cancer.
3. Adjuvant treatment of breast cancer
In combination with trastuzumab and chemotherapy as adjuvant treatment of patients with HER2-positive early breast cancer at high risk of recurrence.

B. Compendial Uses

Treatment of recurrent or stage IV (M1) human epidermal growth factor receptor 2 (HER2)-positive breast cancer.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of human epidermal growth factor receptor 2 (HER2) status is necessary to initiate the prior authorization review.

III. CRITERIA FOR INITIAL APPROVAL

Breast cancer

- A. Authorization of 12 months may be granted for pre-operative (neoadjuvant) therapy of HER2-positive breast cancer in combination with trastuzumab and chemotherapy for locally advanced, inflammatory or early stage breast cancer (either greater than 2 cm in diameter or node positive).
- B. Authorization of 12 months may be granted for adjuvant therapy of HER2-positive breast cancer that is either node-positive or at high risk for recurrence in combination with trastuzumab and chemotherapy.

Reference number(s)
1899-A

- C. Authorizations of 12 months may be granted for the treatment of recurrent or metastatic HER2-positive breast cancer in combination with trastuzumab.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy for an indication outlined in section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen. Adjuvant and neoadjuvant treatment of breast cancer will be approved for a total of 12 months of therapy.

V. REFERENCES

1. Perjeta [package insert]. South San Francisco, CA: Genentech, Inc.; December 2018.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed August 12, 2019.
3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Breast Cancer. Version 2.2019. https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed August 12, 2019.

SPECIALTY GUIDELINE MANAGEMENT

BUPHENYL (sodium phenylbutyrate) sodium phenylbutyrate (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Buphenyl is indicated as adjunctive therapy in the chronic management of patients with urea cycle disorders involving deficiencies of carbamylphosphate synthetase (CPS), ornithine transcarbamylase (OTC), or argininosuccinic acid synthetase (AS). It is indicated in all patients with neonatal-onset deficiency (complete enzymatic deficiency, presenting within the first 28 days of life). It is also indicated in patients with late-onset disease (partial enzymatic deficiency, presenting after the first month of life) who have a history of hyperammonemic encephalopathy. It is important that the diagnosis be made early and treatment initiated immediately to improve survival. Any episode of acute hyperammonemia should be treated as a life-threatening emergency.

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: enzyme assay, biochemical, or genetic testing results supporting diagnosis.

III. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for chronic management of urea cycle disorder (UCD) when the diagnosis is confirmed by enzymatic, biochemical, or genetic testing.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for chronic management of a urea cycle disorder (UCD), who are experiencing benefit from therapy as evidenced by a reduction in plasma ammonia levels from baseline.

V. REFERENCES

1. Buphenyl [package insert]. Lake Forest, IL: Horizon Pharma USA, Inc.; April 2016.
2. Mew NA, Lanpher BC. Urea Cycle Disorders Overview. In: Pagon RA, Adam MP, Ardinger HH, et. al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2017 [updated April 9, 2015]. Available at: <https://www.ncbi.nlm.nih.gov/books/NBK1217/?report=printable>.
3. Häberle J, Boddaert N, Burlina A, et al. Suggested guidelines for the diagnosis and management of urea cycle disorders. *Orphanet J Rare Dis*. 2012;7:32.

SPECIALTY GUIDELINE MANAGEMENT

PIQRAY (alpelisib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Piqray is indicated in combination with fulvestrant for the treatment of postmenopausal women, and men, with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, PIK3CA-mutated, advanced or metastatic breast cancer as detected by an FDA-approved test following progression on or after an endocrine-based regimen.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Documentation of FDA-approved test confirming presence of PIK3CA mutation.

III. CRITERIA FOR INITIAL APPROVAL

Breast cancer

Authorization of 12 months may be granted for treatment of HR-positive, HER2-negative, PIK3CA-mutated advanced or metastatic breast cancer when all of the following criteria are met:

- A. Piqray is used in combination with fulvestrant
- B. Disease has progressed while on or after an endocrine-based regimen

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES

1. Piqray [package insert]. East Hanover, NJ: Novartis; May 2019.

Reference number(s)
1844-A

SPECIALTY GUIDELINE MANAGEMENT

PLEGRIDY (peginterferon beta-1a)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications are considered covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication:

Plegridy is indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Relapsing forms of multiple sclerosis

Authorization of 12 months may be granted to members who have been diagnosed with a relapsing form of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse).

B. Clinically isolated syndrome

Authorization of 12 months may be granted to members for the treatment of clinically isolated syndrome of multiple sclerosis.

III. CONTINUATION OF THERAPY

For all indications: Authorization of 12 months may be granted for members who are experiencing disease stability or improvement while receiving Plegridy.

IV. OTHER CRITERIA

Members will not use Plegridy concomitantly with other medications used for the treatment of multiple sclerosis, excluding Ampyra.

V. REFERENCE

1. Plegridy [package insert]. Cambridge, MA: Biogen, Inc.; July 2019.

SPECIALTY GUIDELINE MANAGEMENT

POLIVY (polatuzumab vedotin-piiq)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Polivy in combination with bendamustine and a rituximab product is indicated for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, after at least two prior therapies.

B. Compendial Uses

1. High-grade B-cell lymphomas (HGBLs) with translocations of MYC and BCL2 and/or BCL6 after 2 or more prior therapies
2. Partially responsive, nonresponsive, or progressive DLBCL

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review for coverage of high-grade B cell lymphomas (HGBLs): Documentation of MYC and BCL2 and/or BCL6 translocations as detected by fluorescence in situ hybridization (FISH) or standard cytogenetics.

III. CRITERIA FOR INITIAL APPROVAL

A. **Diffuse large B-cell lymphoma**

Authorization of 6 months may be granted for treatment of diffuse large B-cell lymphoma (DLBCL) when all of the following criteria are met:

1. Polivy is used in combination with bendamustine and a rituximab product
2. Disease is partially responsive, not responsive, relapsed, refractory, or progressive after prior therapies
3. Member has received at least two prior therapies
4. Member will not receive more than 6 cycles of therapy
5. Member is not a candidate for transplant

B. **High-grade B-cell lymphomas (HGBLs)**

Authorization of 6 months may be granted for treatment of high-grade B-cell lymphomas (HGBLs) (also referred to as “double-hit” or “triple-hit” lymphomas) when all of the following criteria are met:

1. Member has translocations of MYC and BCL2 and/or BCL6 as detected by FISH or standard cytogenetics
2. Polivy is used in combination with bendamustine and a rituximab product

3. Disease is partially responsive, not responsive, relapsed, refractory, or progressive after prior therapies
4. Member has received at least two prior therapies
5. Member will not receive more than 6 cycles of therapy
6. Member is not a candidate for transplant

IV. CONTINUATION OF THERAPY

Authorization up to 6 months (6 cycles total) may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced disease progression or an unacceptable toxicity and who have not received 6 or more cycles of Polivy.

V. REFERENCES

1. Polivy [package insert]. South San Francisco, CA: Genentech, Inc.; June 2019.
2. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: B-Cell Lymphomas. Version 4.2019. <https://www.nccn.org>. Accessed June 19, 2019.
3. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed June 19, 2019.

SPECIALTY GUIDELINE MANAGEMENT

POMALYST (pomalidomide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Treatment of multiple myeloma, in combination with dexamethasone, in patients who have received at least two prior therapies including lenalidomide and a proteasome inhibitor and have demonstrated disease progression on or within 60 days of completion of their last therapy

B. Compendial Uses

1. Systemic light chain amyloidosis
2. AIDS-related Kaposi sarcoma

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Multiple myeloma**

Authorization of 12 months may be granted for the treatment of multiple myeloma when all of the following criteria are met:

1. The member has previously received at least two prior therapies for multiple myeloma including an immunomodulatory agent and proteasome inhibitor.
2. The requested medication will be used in one of the following regimens:
 - a. In combination with daratumumab and dexamethasone
 - b. In combination with elotuzumab and dexamethasone
 - c. In combination with ixazomib and dexamethasone
 - d. In combination with bortezomib and dexamethasone
 - e. In combination with carfilzomib and dexamethasone
 - f. In combination with cyclophosphamide and dexamethasone
 - g. In combination with dexamethasone
 - h. As a single agent

B. **Systemic light chain amyloidosis**

Authorization of 12 months may be granted for the treatment of relapsed or refractory systemic light chain amyloidosis in combination with dexamethasone.

C. **AIDS-Related Kaposi Sarcoma**

Authorization of 12 months may be granted for the treatment of AIDS-related Kaposi sarcoma in combination with antiretroviral therapy.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Pomalyst [package insert]. Summit, NJ: Celgene Corporation; May 2018.
2. The NCCN Drugs & Biologics Compendium® © 2018 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 25, 2019.
3. The NCCN Clinical Practice Guidelines in Oncology® Multiple Myeloma (Version 1.2019) © 2018 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed March 25, 2019.
4. The NCCN Clinical Practice Guidelines in Oncology® Systemic Light Chain Amyloidosis (Version 1.2018) © 2018 National Comprehensive Cancer Network, Inc. Available at: www.nccn.org. Accessed March 25, 2019.
5. The NCCN Clinical Practice Guidelines in Oncology® AIDS-Related Kaposi Sarcoma (Version 1.2018) © 2018 National Comprehensive Cancer Network, Inc. Available at: www.nccn.org. Accessed March 25, 2019.

SPECIALTY GUIDELINE MANAGEMENT

PORTRAZZA (necitumumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication¹

Portrazza is indicated for the first-line treatment of patients with metastatic squamous non-small cell lung cancer (NSCLC) in combination with gemcitabine and cisplatin.

Limitation of Use: Portrazza is not indicated for the treatment of non-squamous non-small cell lung cancer.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Non-Small Cell Lung Cancer (NSCLC)¹

Authorization of 12 months may be granted for treatment of metastatic squamous NSCLC when the requested medication is used in combination with gemcitabine and cisplatin.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced disease progression or an unacceptable toxicity.

REFERENCES

1. Portrazza [package insert]. Indianapolis, DE: Eli Lilly and Company; November 2015.

SPECIALTY GUIDELINE MANAGEMENT

POTELIGEO (mogamulizumab-kpkc)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Poteligeo is indicated for the treatment of adult patients with relapsed or refractory mycosis fungoides (MF) or Sézary syndrome (SS) after at least one prior systemic therapy.

B. Compendial Uses

1. Mycosis fungoides (MF) or Sézary syndrome (SS) as primary treatment
2. Adult T-cell leukemia/lymphoma

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Mycosis fungoides (MF) or Sézary syndrome (SS)**

Authorization of 12 months may be granted for treatment of mycosis fungoides (MF) or Sézary syndrome (SS).

B. **Adult T-cell leukemia/lymphoma**

Authorization of 12 months may be granted for treatment of adult T-cell leukemia/lymphoma when used as a single-agent second line or subsequent therapy for acute or lymphoma subtypes.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced disease progression or an unacceptable toxicity.

IV. REFERENCES

1. Poteligeo [package insert]. Bedminster, NJ: Kyowa Kirin, Inc.; August 2018.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed September 12, 2019.

ENHANCED SPECIALTY GUIDELINE MANAGEMENT

PRALUENT (alirocumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

- A. Praluent is indicated to reduce the risk of myocardial infarction, stroke, and unstable angina in adults with established cardiovascular disease.
- B. Praluent is indicated as an adjunct to diet, alone or in combination with other lipid-lowering therapies (e.g., statins, ezetimibe) for the treatment of adults with primary hyperlipidemia (including heterozygous familial hypercholesterolemia) to reduce low density lipoprotein cholesterol (LDL-C).

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

The following is necessary to initiate the prior authorization review:

- A. Current LDL-C level for both initial requests and continuation requests. The level must be dated within the six months preceding the authorization request.
- B. Untreated (before any lipid lowering therapy) LDL-C level if requesting Praluent to treat primary hyperlipidemia or heterozygous familial hypercholesterolemia.
- C. Chart notes confirming clinical atherosclerotic cardiovascular disease (ASCVD) if requesting Praluent to treat clinical ASCVD.
- D. If patient has contraindication or intolerance to statins, chart notes confirming the contraindication or intolerance. (See Appendix B and C).

III. CRITERIA FOR INITIAL APPROVAL

A. Clinical atherosclerotic cardiovascular disease (ASCVD)

Authorization of 6 months may be granted for treatment of clinical atherosclerotic cardiovascular disease when all of the following criteria are met:

1. Member has a history of clinical ASCVD (See Appendix A).
2. Member meets at least one of the following requirements:
 - a. Member has a current LDL-C level ≥ 70 mg/dL after at least three months of treatment with a high-intensity statin dose in combination with ezetimibe. If the member is unable to tolerate a high-intensity statin dose, a moderate-intensity statin dose may be used.
 - b. Member has a current LDL-C level ≥ 70 mg/dL with contraindication or intolerance to statins (See Appendix B and C).

B. Primary hyperlipidemia including heterozygous familial hypercholesterolemia (HeFH)

Authorization of 6 months may be granted for treatment of primary hyperlipidemia including heterozygous familial hypercholesterolemia (HeFH) when both of the following criteria are met:

1. Member had an untreated (before any lipid lowering therapy) LDL-C level ≥ 190 mg/dL in the absence of a secondary cause.
2. Member meets at least one of the following requirements:
 - a. Member has a current LDL-C level ≥ 100 mg/dL after at least three months of treatment with a high-intensity statin dose in combination with ezetimibe. If the member is unable to tolerate a high-intensity statin dose, a moderate-intensity statin dose may be used.
 - b. Member has a current LDL-C level ≥ 100 mg/dL with contraindication or intolerance to statins (See Appendix B and C).

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members who achieve or maintain an LDL-C reduction (e.g., LDL-C is now at goal, robust lowering of LDL-C).

V. APPENDICESAPPENDIX A. Clinical ASCVD

- Acute coronary syndromes
- Myocardial infarction
- Stable or unstable angina
- Coronary or other arterial revascularization procedure (e.g., percutaneous coronary angioplasty [PTCA], coronary artery bypass graft [CABG] surgery)
- Stroke of presumed atherosclerotic origin
- Transient ischemic attack (TIA)
- Non-cardiac peripheral arterial disease of presumed atherosclerotic origin (e.g., carotid artery stenosis, lower extremity PAD)
- Obstructive coronary artery disease (defined as fifty percent or greater stenosis on cardiac computed tomography angiogram or catheterization)

APPENDIX B. Statin-associated muscle symptoms (SAMS) and statin re-challenge

- Score of 7 or higher on the Statin-Associated Muscle Symptom Clinical Index (SAMS-CI)
 - Statin-associated elevation in creatine kinase (CK) level ≥ 10 times upper limit of normal (ULN)
- NOTE:** Statin re-challenge is NOT required for members who have experienced an elevation of CK level ≥ 10 times ULN after receiving lipid-lowering therapy (LLT) with a statin.

APPENDIX C. Contraindications to statins

- Active liver disease, including unexplained persistent elevations in hepatic transaminase levels (e.g., alanine transaminase (ALT) level ≥ 3 times ULN)
- Pregnancy or planned pregnancy
- Breastfeeding

VI. REFERENCES

1. Praluent [package insert]. Bridgewater, NJ: sanofi-aventis U.S. LLC; April 2019.
2. Stone NJ, Robinson JG, Lichtenstein AH, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;129:S1-S45.

3. Lloyd-Jones DM, Morris PB, Ballantyne CM, et al. 2017 Focused Update of the 2016 ACC expert consensus decision pathway on the role of non-statin therapies for LDL-cholesterol lowering in the management of atherosclerotic cardiovascular disease risk: a report of the American College of Cardiology Task Force on Clinical Expert Consensus Documents. *J Am Coll Cardiol*. 2017;70:1785-822.
4. Cannon CP, Blazing MA, Giugliano RP, et al. Ezetimibe added to statin therapy after acute coronary syndromes. *N Engl J Med*. 2015;372:2387-97.
5. Jacobson TA, Ito MK, Maki KC, et al. National Lipid Association recommendations for patient-centered management of dyslipidemia: part 1 — full report. *J Clin Lipidol*. 2015;9:129–169.
6. Nordestgaard BG, Chapman MJ, Humphries SE, et al. Familial hypercholesterolaemia is underdiagnosed and undertreated in the general population: guidance for clinicians to prevent coronary heart disease. Consensus Statement of the European Atherosclerosis Society. *Eur Heart J*. 2013;34:3478–3490.
7. Cuchel M, Bruckert E, Ginsberg HN, et al. Homozygous familial hypercholesterolaemia: new insights and guidance for clinicians to improve detection and clinical management. A position paper from the Consensus Panel on Familial Hypercholesterolaemia of the European Atherosclerosis Society. *Eur Heart J*. 2014;35:2146-2157.
8. Banach M, Rizzo M, Toth PP, et al. Statin intolerance – an attempt at a unified definition. Position paper from an International Lipid Expert Panel. *Arch Med Sci*. 2015;11:1-23.
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12. Pandor A, Ara RM, Tumur I, et al. Ezetimibe monotherapy for cholesterol lowering in 2,722 people: systematic review and meta-analysis of randomized controlled trials. *J Intern Med*. 2009 May;265(5):568-80.
13. Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC guideline on the management of blood cholesterol: report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol* 2018.
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PRIOR AUTHORIZATION CRITERIA

BRAND NAME*

(generic)

(pretomanid)

Status: CVS Caremark Criteria

Type: Initial Prior Authorization

Ref # 3195-A

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Limited Population: Pretomanid Tablet is indicated, as part of a combination regimen with bedaquiline and linezolid for the treatment of adults with pulmonary extensively drug resistant (XDR) or treatment-intolerant or nonresponsive multidrug-resistant (MDR) tuberculosis (TB). Approval of this indication is based on limited clinical safety and efficacy data. This drug is indicated for use in a limited and specific population of patients.

Limitations of Use:

- Pretomanid Tablets are not indicated in patients with the following conditions:
 - Drug-sensitive (DS) tuberculosis
 - Latent infection due to *Mycobacterium tuberculosis*.
 - Extra-pulmonary infection due to *Mycobacterium tuberculosis*.
 - MDR-TB that is not treatment-intolerant or nonresponsive to standard therapy.
- Safety and effectiveness of Pretomanid Tablets have not been established for its use in combination with drugs other than bedaquiline and linezolid as part of the recommended dosing regimen

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for pulmonary extensively-drug resistant (XDR) or treatment-intolerant/nonresponsive multidrug-resistant (MDR) tuberculosis

AND

- The requested drug will be prescribed as part of a combination regimen with Sirturo (bedaquiline) and Zyvox (linezolid)

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Pretomanid Tablet is indicated, as part of a combination regimen with bedaquiline and linezolid for the treatment of adults with pulmonary extensively drug resistant (XDR) or treatment-intolerant or nonresponsive multidrug-resistant (MDR) tuberculosis (TB). This drug is indicated for use in a limited and specific population of patients.

Safety and effectiveness of Pretomanid Tablets have not been established for its use in combination with drugs other than bedaquiline and linezolid as part of the recommended dosing regimen. Pretomanid Tablets must be used only in combination with bedaquiline and linezolid as part of the recommended dosing regimen. The recommended dosage and duration for this combination regimen are as follows:

- Pretomanid Tablet 200 mg orally (1 tablet of 200 mg), once daily, for 26 weeks. Swallow Pretomanid Tablets whole with water
- Bedaquiline 400 mg orally once daily for 2 weeks followed by 200 mg 3 times per week, with at least 48 hours between doses, for 24 weeks for a total of 26 weeks

If either bedaquiline or Pretomanid Tablets are discontinued, the entire combination regimen should also be discontinued.

- Linezolid starting at 1,200 mg orally per day for 26 weeks, with dose adjustments to 600 mg daily and further reduction to 300 mg daily or interruption of dosing as necessary for known linezolid adverse reactions of myelosuppression, peripheral neuropathy, and optic neuropathy.

If linezolid is permanently discontinued during the initial four consecutive weeks of treatment, bedaquiline and Pretomanid Tablets should also be discontinued. If linezolid is discontinued after the initial four weeks of consecutive treatment, continue administering bedaquiline and Pretomanid Tablets.

The duration of approval is set at 12 months since the dosing of the combination regimen of Pretomanid, bedaquiline, and linezolid can be extended beyond 26 weeks, if necessary.¹⁻³

REFERENCES

1. Pretomanid [package insert]. Hyderabad, India: Mylan Laboratories Limited for The Global Alliance for TB Drug Development (TB Alliance); August 2019.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed December 2019.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed December 2019.

Written by: UM Development (RP)
 Date Written: 08/2019
 Revised: (ME) 12/2019 (no clinical changes)
 Reviewed: Medical Affairs (CHART) 10/03/2019, (CHART) 01/02/2020
 External Review: 10/2019, 04/2020

CRITERIA FOR APPROVAL

- | | | | |
|---|---|-----|----|
| 1 | Is the requested drug being prescribed for pulmonary extensively-drug resistant (XDR) or treatment-intolerant/nonresponsive multidrug-resistant (MDR) tuberculosis? | Yes | No |
| 2 | Is the requested drug being prescribed as part of a combination regimen with both Sirturo (bedaquiline) and Zyvox (linezolid)? | Yes | No |

Mapping Instructions

	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when it is used with other drugs for a certain infection in the lungs that is resistant to multiple drugs. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
2.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when it is used with Sirturo (bedaquiline) and Zyvox (linezolid) for the infection. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis/combination regimen]

SPECIALTY GUIDELINE MANAGEMENT

PROCYSBI (cysteamine bitartrate delayed-release)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Procysbi is indicated for the treatment of nephropathic cystinosis in adults and pediatric patients 1 year of age and older.

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: assay detecting increase cystine concentration in leukocytes or genetic testing results supporting diagnosis.

III. CRITERIA FOR INITIAL APPROVAL

Nephropathic cystinosis

Authorization of 12 months may be granted for treatment of nephropathic cystinosis when all of the following criteria are met:

- A. Diagnosis of cystinosis was confirmed by the presence of increased cystine concentration in leukocytes or by genetic testing; and
- B. Member is 1 year of age or older; and
- C. Member will not use Procysbi in combination with Cystagon.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for nephropathic cystinosis who are responding to therapy (e.g., improvement, stabilization, or slowing of disease progression for serum creatinine, calculated creatinine clearance, leukocyte cystine concentration, or maintained growth (height)).

V. REFERENCES

1. Procysbi [package insert]. Novato, CA: Raptor Pharmaceuticals Inc.; December 2017.
2. Ivanova E, De Leo MG, De Matteis MA, Levchenko E. Cystinosis: clinical presentation, pathogenesis, and treatment. *Pediatr Endocrinol Rev.* 2014;12(1):176-184.

SPECIALTY GUIDELINE MANAGEMENT

PROLEUKIN (aldesleukin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Proleukin is indicated for the treatment of adults with metastatic renal cell carcinoma (metastatic RCC).
2. Proleukin is indicated for the treatment of adults with metastatic melanoma.

B. Compendial Uses

1. Relapsed or stage IV kidney cancer with clear cell histology; as high-dose single-agent therapy as first-line or subsequent therapy
2. Metastatic or unresectable cutaneous melanoma; as high-dose single-agent therapy as second-line or subsequent therapy
3. Neuroblastoma

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Renal Cell Carcinoma**

Authorization of 12 months may be granted for treatment of relapsed or metastatic renal cell carcinoma with clear cell histology for high-dose single-agent therapy as first-line or subsequent therapy.

B. **Melanoma**

Authorization of 12 months may be granted for treatment of metastatic or unresectable cutaneous melanoma for high-dose single-agent therapy as second-line or subsequent therapy.

C. **Neuroblastoma**

Authorization of 12 months may be granted for the treatment of neuroblastoma.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when all of the following criteria are met:

1. The member must be evaluated for response approximately 4 weeks after completion of a course of therapy and again immediately prior to the scheduled start of the next treatment course,
2. Additional courses of treatment should be given only if there is some tumor shrinkage following the last course,
3. Retreatment is not contraindicated,

4. Each treatment course should be separated by a rest period of at least 7 weeks from the date of hospital discharge.

IV. REFERENCES

1. Proleukin [package insert]. San Diego, CA: Prometheus Laboratories Inc.; August 2018.
2. The NCCN Drugs & Biologic Compendium 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed May 31, 2019.
3. Pistoia V, Bianchi G, Borgonovo G, Raffaghello L. Cytokines in neuroblastoma: From pathogenesis to treatment. *Immunotherapy*. 2011;3(7):895-907.
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5. Levy G, Bonneville M, Rocourt N, et al. Necrotizing enterocolitis as an adverse effect of recombinant interleukin-2 and Ch14.18 in maintenance therapy for high-risk neuroblastoma. *J Pediatr Hematol Oncol*. 2015;37(4):e250-e252.

SPECIALTY GUIDELINE MANAGEMENT

PROLIA (denosumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Treatment of postmenopausal women with osteoporosis at high risk for fracture
2. Treatment to increase bone mass in men with osteoporosis at high risk for fracture
3. Treatment of men and women with glucocorticoid-induced osteoporosis at high risk for fracture
4. Treatment to increase bone mass in men at high risk for fracture receiving androgen deprivation therapy (ADT) for non-metastatic prostate cancer
5. Treatment to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer

B. Compendial Uses

Prevention or treatment of osteoporosis during androgen deprivation therapy for prostate cancer in patients with high fracture risk

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Supporting chart notes or medical record indicating a history of fractures, T-score, and FRAX fracture probability as applicable to Sections III.A, III.B, and III.C.

III. CRITERIA FOR INITIAL APPROVAL

A. **Postmenopausal osteoporosis**

Authorization of 12 months may be granted to postmenopausal members with osteoporosis when ANY of the following criteria are met:

1. Member has a history of fragility fractures
2. Member has a pre-treatment T-score less than or equal to -2.5 OR member has osteopenia (i.e., pre-treatment T-score greater than -2.5 and less than -1) with a high pre-treatment FRAX fracture probability (See Appendix B) and meets ANY of the following criteria:
 - a. Member has indicators of higher fracture risk (e.g., advanced age, frailty, glucocorticoid use, very low T-scores [less than or equal to -3.5], or increased fall risk)
 - b. Member has failed prior treatment with or is intolerant to previous injectable osteoporosis therapy (e.g., zoledronic acid [Reclast], teriparatide [Forteo])

- c. Member has had an oral bisphosphonate trial of at least 1-year duration or there is a clinical reason to avoid treatment with an oral bisphosphonate (See Appendix A)

B. Osteoporosis in men

Authorization of 12 months may be granted to male members with osteoporosis when ANY of the following criteria are met:

1. Member has a history of an osteoporotic vertebral or hip fracture
2. Member meets criteria BOTH of the following criteria:
 - a. Member has a pre-treatment T-score less than or equal to -2.5 OR member has osteopenia (i.e., pre-treatment T-score greater than -2.5 and less than -1) with a high pre-treatment FRAX fracture probability (See Appendix B)
 - b. Member has had an oral bisphosphonate trial of at least 1-year duration OR there is a clinical reason to avoid treatment with an oral bisphosphonate (See Appendix A)

C. Glucocorticoid-induced osteoporosis

Authorization of 12 months may be granted to members with glucocorticoid-induced osteoporosis when ALL of the following criteria are met:

1. Member is currently receiving or will be initiating glucocorticoid therapy
2. Member has had an oral bisphosphonate trial of at least 1-year duration OR there is a clinical reason to avoid treatment with an oral bisphosphonate (See Appendix A)
3. Member meets ANY of the following criteria:
 - a. Member has a history of a fragility fracture
 - b. Member has a pre-treatment T-score less than or equal to -2.5
 - c. Member has osteopenia (i.e., pre-treatment T-score greater than -2.5 and less than -1) with a high pre-treatment FRAX fracture probability (See Appendix B)

D. Breast cancer

Authorization of 12 months may be granted to members who are receiving adjuvant aromatase inhibitor therapy for breast cancer.

E. Prostate cancer

Authorization of 12 months may be granted to members who are receiving androgen deprivation therapy for prostate cancer.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who meet all initial authorization criteria and experiences clinical benefit after at least 24 months of therapy with Prolia as evidenced by improvement or stabilization in T-score.

V. APPENDIX

Appendix A. Clinical reasons to avoid oral bisphosphonate therapy

- Esophageal abnormality that delays emptying such as stricture of achalasia
- Active upper gastrointestinal problem (e.g., dysphagia, gastritis, duodenitis, erosive esophagitis, ulcers)
- Inability to stand or sit upright for at least 30 to 60 minutes
- Inability to take at least 30 to 60 minutes before first food, drink, or medication of the day
- Renal insufficiency (creatinine clearance <35 mL/min)

- History of intolerance to an oral bisphosphonate

Appendix B. WHO Fracture Risk Assessment Tool

- High FRAX fracture probability: 10 year major osteoporotic fracture risk \geq 20% or hip fracture risk \geq 3%.
- 10-year probability; calculation tool available at: <https://www.sheffield.ac.uk/FRAX/>
- The estimated risk score generated with FRAX should be multiplied by 1.15 for major osteoporotic fracture and 1.2 for hip fracture if glucocorticoid treatment is greater than 7.5 mg per day.

VI. REFERENCES

1. Prolia [package insert]. Thousand Oaks, CA: Amgen Inc.; April 2019.
2. The NCCN Drugs & Biologics Compendium™ © 2018 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed October 25, 2018.
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SPECIALTY GUIDELINE MANAGEMENT

PROMACTA (eltrombopag)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Treatment of thrombocytopenia in adult and pediatric patients 1 year and older with chronic immune thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy
2. Treatment of thrombocytopenia in patients with chronic hepatitis C to allow the initiation and maintenance of interferon-based therapy
3. First-line treatment of severe aplastic anemia in adult and pediatric patients 2 years and older in combination with standard immunosuppressive therapy
4. Treatment of patients with severe aplastic anemia who have had an insufficient response to immunosuppressive therapy

B. Compendial Uses

1. MYH9-related disease with thrombocytopenia
2. Myelodysplastic syndromes, for lower risk disease in patients with severe or refractory thrombocytopenia following disease progression or no response to hypomethylating agents or immunosuppressive therapy

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

- A. Chronic or persistent primary immune thrombocytopenia: pretreatment and current platelet counts
- B. Aplastic anemia continuation of therapy: current platelet counts

III. EXCLUSIONS

Coverage will not be provided for members with the following exclusion: concomitant use of Promacta with other thrombopoietin receptor agonists (e.g., Nplate, Doptelet, Mulpleta) or with spleen tyrosine kinase inhibitors (e.g., Tavalisse)

IV. CRITERIA FOR INITIAL APPROVAL

A. Chronic or persistent primary immune thrombocytopenia (ITP)

Reference number(s)
1928-A

Authorization of 6 months may be granted for treatment of chronic or persistent ITP when both of the following criteria are met:

1. Inadequate response or intolerance to prior therapy with corticosteroids, immunoglobulins, or splenectomy
2. Untransfused platelet count at time of diagnosis is less than $30 \times 10^9/L$ OR $30 \times 10^9/L$ to $50 \times 10^9/L$ with symptomatic bleeding (e.g., significant mucous membrane bleeding, gastrointestinal bleeding or trauma) or risk factors for bleeding (see Section VI).

B. Thrombocytopenia associated with chronic hepatitis C

Authorization of 6 months may be granted to members who are prescribed Promacta for the initiation and maintenance of interferon-based therapy for the treatment of thrombocytopenia associated with chronic hepatitis C.

C. Aplastic anemia

1. Authorization of 6 months may be granted for first-line treatment of severe aplastic anemia when Promacta will be used in combination with standard immunosuppressive therapy (e.g., horse antithymocyte globulin (h-ATG) and cyclosporine).
2. Authorization of 6 months may be granted for treatment of aplastic anemia which has been previously treated with immunosuppressive therapy.

D. MYH9-related disease with thrombocytopenia

Authorization of 12 months may be granted to members with thrombocytopenia associated with MYH9-related disease.

E. Myelodysplastic Syndromes

Authorization of 12 months may be granted for treatment of myelodysplastic syndromes when both of the following criteria are met:

1. Member has lower risk disease defined as Revised International Prognostic Scoring System (IPSS-R) (Very Low, Low, Intermediate), International Prognostic Scoring System (IPSS) (Low/Intermediate-1), WHO classification-based Prognostic Scoring System (WPSS) (Very Low, Low, Intermediate).
2. Member has severe or refractory thrombocytopenia following disease progression or no response to hypomethylating agents (such as azacitidine and decitabine) or immunosuppressive therapy.

V. CONTINUATION OF THERAPY

A. Chronic or persistent ITP

1. Authorization of 3 months may be granted to members with current platelet count less than $50 \times 10^9/L$ for whom the platelet count is not sufficient to prevent clinically important bleeding and who have not received a maximal Promacta dose for at least 4 weeks.
2. Authorization of 12 months may be granted to members with current platelet count less than $50 \times 10^9/L$ for whom the current platelet count is sufficient to prevent clinically important bleeding.
3. Authorization of 12 months may be granted to members with current platelet count of $50 \times 10^9/L$ to $200 \times 10^9/L$.
4. Authorization of 12 months may be granted to members with current platelet count greater than $200 \times 10^9/L$ to less than or equal to $400 \times 10^9/L$ for whom Promacta dosing will be adjusted to achieve a platelet count sufficient to avoid clinically important bleeding.

B. Thrombocytopenia associated with chronic hepatitis C

Authorization of 6 months may be granted to members who are continuing to receive interferon-based therapy.

C. Aplastic anemia

1. Authorization of up to 16 weeks total may be granted to members with current platelet count less than $50 \times 10^9/L$ who have not received appropriately titrated therapy with Promacta for at least 16 weeks.
2. Authorization of up to 16 weeks total may be granted to members with current platelet count less than $50 \times 10^9/L$ who are transfusion-independent.
3. Authorization of 12 months may be granted to members with current platelet count of $50 \times 10^9/L$ to $200 \times 10^9/L$.
4. Authorization of 12 months may be granted to members with current platelet count greater than $200 \times 10^9/L$ to less than or equal to $400 \times 10^9/L$ for whom Promacta dosing will be adjusted to achieve and maintain an appropriate target platelet count.

D. MYH9-related disease with thrombocytopenia

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

E. Myelodysplastic Syndromes

Authorization of 12 months may be granted for continued treatment of myelodysplastic syndromes in members who experience benefit from therapy (e.g., increased platelet counts, decreased bleeding events, reduced need for platelet transfusions).

VI. APPENDIX

Examples of risk factors for bleeding (not all inclusive)

- Undergoing a medical or dental procedure where blood loss is anticipated
- Comorbidity (e.g., peptic ulcer disease, hypertension)
- Mandated anticoagulation therapy
- Profession (e.g., construction worker) or lifestyle (e.g., plays contact sports) that predisposes patient to trauma

VII. REFERENCES

1. Promacta [package insert]. Research Triangle Park, NC: GlaxoSmithKline; April 2019.
2. Pecci A, Gresele P, Klersy C, et al. Eltrombopag for the treatment of the inherited thrombocytopenia deriving from MYH9 mutations. *Blood*. 2010;116(26):5832-7.
3. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed June 13, 2019.
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5. Neunert C, Lim W, Crowther M, et al. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. *Blood*. 2011;117(16):4190-4207.
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8. Olnes MJ, Scheinberg P, Calvo KR, et al. Eltrombopag and improved hematopoiesis in refractory aplastic anemia. *N Engl J Med*. 2012;367(1):11-19.
9. Townsley DM, Scheinberg P, Winkler T, et al. Eltrombopag added to standard immunosuppression for aplastic anemia. *N Engl J Med* 2017;376:1540-1550.

Reference number(s)
1886-A

SPECIALTY GUIDELINE MANAGEMENT

PULMOZYME (dornase alfa)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Pulmozyme is indicated in conjunction with standard therapies for the management of cystic fibrosis (CF) patients to improve pulmonary function.

All other indications are considered experimental/investigational and are not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Cystic Fibrosis

Authorization of 12 months may be granted for treatment of cystic fibrosis when Pulmozyme will be used in conjunction with standard therapies for cystic fibrosis.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

IV. REFERENCES

1. Pulmozyme [package insert]. South San Francisco, CA: Genentech, Inc.; January 2018.
2. Mogayzel PJ, Naureckas ET, Robinson KA, et al. Cystic fibrosis pulmonary guidelines. Chronic medications for maintenance of lung health. *Am J Respir Crit Care Med*. 2013;187:680-689.
3. Cohen-Cymbberknoh M, Shoseyov D, Kerem E. Managing cystic fibrosis: strategies that increase life expectancy and improve quality of life. *Am J Respir Crit Care Med*. 2011;183:1463-1471.

SPECIALTY GUIDELINE MANAGEMENT

PURIXAN (mercaptopurine) mercaptopurine

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Purixan is indicated for the treatment of patients with acute lymphoblastic leukemia (ALL) as a component of a combination maintenance therapy regimen

B. Compendial Uses

1. For ALL as part of a regimen for induction, maintenance, or consolidation therapy
2. For acute promyelocytic leukemia (APL) as post-consolidation maintenance therapy, if included in the initial treatment protocol

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Documentation supporting an intolerable adverse event with the generic alternative mercaptopurine (the adverse event was not an expected adverse event attributed to the active ingredient as described in the prescribing information).

III. CRITERIA FOR INITIAL APPROVAL

A. **Acute lymphoblastic leukemia (ALL)**

Authorization of 12 months may be granted for treatment of ALL when either of the following criteria is met:

1. Member has a documented intolerable adverse event with the generic alternative mercaptopurine and the adverse event was not an expected adverse event attributed to the active ingredient as described in the prescribing information, OR
2. Member is unable to swallow the tablet formulation.

B. **Acute promyelocytic leukemia (APL)**

Authorization of 12 months may be granted for treatment of APL when either of the following criteria is met:

1. Member has a documented intolerable adverse event with the generic alternative mercaptopurine and the adverse event was not an expected adverse event attributed to the active ingredient as described in the prescribing information, OR
2. Member is unable to swallow the tablet formulation

Reference number(s)
2982-A

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for ALL or APL and who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES

1. Purixan [package insert]. Franklin, TN: Rare Disease Therapeutics, Inc.; February 2018.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed June 24, 2019.

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS

WEIGHT LOSS MANAGEMENT

BRAND NAME* (generic)

QSYMIA
(phentermine and topiramate extended-release)

Status: CVS Caremark Criteria

Type: Initial Prior Authorization

Ref # 794-A

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Qsymia is indicated as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adult patients with an initial body mass index (BMI) of

- 30 kg/m² or greater (obese), or
- 27 kg/m² or greater (overweight) in the presence of at least one weight related comorbidity such as hypertension, type 2 diabetes mellitus, or dyslipidemia

Limitations of Use

- The effect of Qsymia on cardiovascular morbidity and mortality has not been established.
- The safety and effectiveness of Qsymia in combination with other products intended for weight loss, including prescription and over-the-counter drugs and herbal preparations have not been established.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has completed at least 12 weeks of Qsymia 15 mg/92 mg therapy AND
 - The patient lost at least 5 percent of baseline body weight OR the patient has continued to maintain their initial 5 percent weight loss
- OR
- The patient has completed at least 12 weeks of Qsymia 7.5 mg/46 mg therapy AND
 - The patient lost at least 3 percent of baseline body weight or the patient's dose will be escalated
- OR
- The requested drug will be used with a reduced calorie diet and increased physical activity AND
 - The patient has a body mass index (BMI) greater than or equal to 30 kg per square meter
- OR
- The patient has a body mass index (BMI) greater than or equal to 27 kg per square meter AND has additional risk factors

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Qsymia is indicated as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adult patients with an initial body mass index (BMI) of 30 kg/m² or greater (obese), or 27 kg/m² or greater (overweight) in the presence of at least one weight related comorbidity such as hypertension, type 2 diabetes mellitus, or dyslipidemia.¹⁻³ The effect of Qsymia on cardiovascular morbidity and mortality has not been established. The safety and effectiveness of Qsymia in combination with other products intended for weight loss, including prescription and over-the-counter drugs and herbal preparations have not been established.¹⁻³

The guidelines state that the purpose of weight loss and weight maintenance is to reduce health risk. Weight loss programs should begin with a basic weight loss regimen consisting of a reduced-calorie diet and increased physical activity. The major role of medications is to help with patient compliance to a weight loss plan. Therefore, drugs should be used as part of a comprehensive weight loss program and should never be used without concomitant lifestyle modification. Drugs may be used as an adjunct to diet and physical activity for patients with a BMI that is greater than or equal to 30 kg/m² or greater than or equal to 27 kg/m² if other risk factors are present (e.g., hypertension, diabetes, dyslipidemia, sleep apnea, cardiovascular disease).⁴⁻⁶

Qsymia is to be taken once daily in the morning. Treatment should begin with Qsymia 3.75 mg/23 mg daily for 14 days. After 14 days, it is recommended to increase the dose to Qsymia 7.5 mg/46 mg. The patient should be evaluated at 12 weeks. If the patient has not lost 3% of baseline body weight on 7.5 mg/46 mg, Qsymia should be discontinued or the dose should be escalated, as it is unlikely that the patient will achieve and sustain clinically meaningful weight loss at the Qsymia 7.5 mg/46 mg dose. The dose should be escalated to Qsymia 11.25 mg/69 mg daily for 14 days, followed by Qsymia 15 mg/92 mg daily. The patient should then be evaluated after 12 weeks. If the patient has not lost at least 5% of baseline body weight, Qsymia treatment should be discontinued.

For renewal after 12 weeks of therapy, the patient must have lost at least 5% of their baseline body weight or has continued to maintain their initial 5 percent weight loss. It is recommended that therapy be discontinued after 12 weeks if the patient does not meet this goal, as it is unlikely that the patient will be able to achieve and sustain clinically meaningful weight loss with continued treatment.¹

The optimal duration of treatment is unclear. Considering that drug discontinuation invariably leads to weight regain, if clinically significant weight loss is achieved, longer courses of treatment are reasonable to consider after the benefits and risks of treatment are reviewed with the patient and lack of long-term data is acknowledged.⁴⁻⁶

REFERENCES

1. Qsymia [package insert]. Campbell, CA: Vivus, Inc.; March 2018.
2. Lexicomp Online, Lexi-Drugs (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed July 2019.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed July 2019.
4. Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents. National Heart, Lung, and Blood Institute. NIH Publication No. 12-7486. October 2012. http://www.nhlbi.nih.gov/guidelines/cvd_ped/peds_guidelines_full.pdf. 141-159. Accessed July 2019.
5. Pharmacological Management of Obesity: An Endocrine Society Clinical Practice Guideline. The Journal of Clinical Endocrinology & Metabolism, Volume 100, Issue 2, 1 February 2015, Pages 342–362. <https://academic.oup.com/jcem/article/100/2/342/2813109>. Accessed July 2019.
6. Jensen MD, et al. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society. *Circulation*. 2013; 129:S102–S138.

Written by: UM Development (CY)
 Date Written: 07/2012
 Revised: (TM/PL) 06/2013, 10/2013, (PL) 06/2014; (MS) 07/2015, 12/2015 (updated Q8 to make trade compatible); (SE) 01/2016 (Added guidelines for approval grid); (MS) 07/2016 (removed safety question); (JG) 07/2017 (no clinical changes), (ME) 07/2018, 07/2019 (no clinical changes)
 Reviewed: Medical Affairs (KP) 07/2012, (SS) 06/2013, (LS) 11/2013; (SES) 06/2014; (LB) 07/2015, (AM) 07/2018, (CHART) 8/1/19
 External Review: 08/2012, 10/2013, 10/2014, 10/2015, 12/2015, 10/2016, 09/2017, 10/2018, 10/2019

CRITERIA FOR APPROVAL

1	Has the patient completed at least 12 weeks of Qsymia 15 mg/92 mg therapy? [If yes, then skip to question 4.]	Yes	No
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2	Has the patient completed at least 12 weeks of Qsymia 7.5 mg/46 mg therapy? [If no, then skip to question 5.]	Yes	No
3	Did the patient lose at least 3 percent of baseline body weight or will the patient's dose be escalated? [No further questions.]	Yes	No
4	Did the patient lose at least 5 percent of baseline body weight OR has the patient continued to maintain their initial 5 percent weight loss? [No further questions.]	Yes	No
5	Does the patient have a body mass index (BMI) greater than or equal to 30 kg per square meter? [If yes, then skip to question 7.]	Yes	No
6	Does the patient have a body mass index (BMI) greater than or equal to 27 kg per square meter AND has additional risk factors?	Yes	No
7	Will the requested medication be used with a reduced calorie diet and increased physical activity?	Yes	No

Guidelines for Approval			
Duration of Approval 3 Months		Duration of Approval 3 Months	
Set 1		Set 2	
Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)
5	1	6	1
7	2	7	2
			5
Duration of Approval 12 Months		Duration of Approval 12 Months	
Set 3		Set 4	
Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)
1	None	2	1
4		3	

Mapping Instructions			
	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 4	Go to 2	
2.	Go to 3	Go to 5	
3.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet one of these conditions: - You have lost at least 3 percent of your body weight - If you did not lose at least 3 percent of your body weight, then you will take a higher dose Your request has been denied based on the information we have. [Short Description: No weight loss or move to higher dose]
4.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have met any of these conditions: - You lost at least 5 percent of your body weight - You have continued to keep your initial 5 percent weight loss off Your request has been denied based on the information we have. [Short Description: No confirmation of required weight loss]

5.	Go to 7	Go to 6	
6.	Go to 7	Deny	<p>You do not meet the requirements of your plan.</p> <p>Your plan covers this drug when you meet one of these conditions:</p> <ul style="list-style-type: none"> - You have a body mass index (BMI) of 30 kg per square meter or more - You have a body mass index (BMI) of 27 kg per square meter or more and you have risk factors <p>Your request has been denied based on the information we have.</p> <p>[Short Description: Not at BMI requirement]</p>
7.	Approve, 3 months	Deny	<p>You do not meet the requirements of your plan.</p> <p>Your plan covers this drug when you will diet and exercise.</p> <p>Your request has been denied based on the information we have.</p> <p>[Short Description: Diet and exercise requirement not met]</p>

SPECIALTY GUIDELINE MANAGEMENT

RADICAVA (edaravone)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Radicava is indicated for the treatment of amyotrophic lateral sclerosis (ALS).

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of ALS when all of the following criteria are met:

- A. Diagnosis of definite or probable ALS
- B. Member has scores of at least 2 points on all 12 areas of the revised ALS Functional Rating Scale (ALSFRS-R)
- C. Continuous use of ventilatory support during the day and night is not required (noninvasive or invasive)

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members continuing with Radicava therapy for the treatment of ALS when the following criteria are met:

- A. Diagnosis of definite or probable ALS
- B. There is a clinical benefit from Radicava therapy
- C. Invasive ventilation is not required

IV. REFERENCES

1. Radicava [package insert]. Jersey City, NJ: MT Pharma America, Inc.; August 2018.
2. EFNS Task Force on Diagnosis and Management of Amyotrophic Lateral Sclerosis; Andersen PM, et al. EFNS guidelines on the Clinical Management of Amyotrophic Lateral Sclerosis (MALS) – revised report of an EFNS task force. *Eur J Neurol.* 2012;19(3):360-75.
3. Writing Group, Edaravone (MCI-186) ALS 19 Study Group. Safety and efficacy of edaravone in well defined patients with amyotrophic lateral sclerosis: a randomised, double-blind, placebo-controlled trial. *Lancet Neurol.* 2017; 16:505-512.

SPECIALTY GUIDELINE MANAGEMENT

RASUVO (methotrexate injection)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

1. Rheumatoid Arthritis including Polyarticular Juvenile Idiopathic Arthritis
Rasuvo is indicated in the management of selected adults with severe, active rheumatoid arthritis (RA) or children with active polyarticular juvenile idiopathic arthritis, who have had an insufficient therapeutic response to, or are intolerant of, an adequate trial of first-line therapy including full dose non-steroidal anti-inflammatory agents (NSAIDs).
2. Psoriasis
Rasuvo is indicated in adults for the symptomatic control of severe, recalcitrant, disabling psoriasis that is not adequately responsive to other forms of therapy, but only when the diagnosis has been established, as by biopsy and/or after dermatologic consultation. It is important to ensure that a psoriasis "flare" is not due to an undiagnosed concomitant disease affecting immune responses.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of RA, pJIA, or psoriasis when BOTH of the following criteria are met:

- A. Member has tried and had an inadequate response or intolerance to generic oral methotrexate.
- B. Member has inability to prepare and administer generic injectable methotrexate.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who meet ALL initial authorization criteria and achieve or maintain positive clinical response after at least 3 months of therapy with Rasuvo as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. REFERENCES

1. Rasuvo [package insert]. Chicago, IL: Medac Pharma Inc.; March 2018.
2. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. *Arthritis Rheumatol*. 2016;68(1):1-26.
3. Smolen JS, Landewé R, Billsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. *Ann Rheum Dis*. 2017;0:1-18.

4. Beukelman T, Patkar NM, Saag KG, et al. 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: initiation and safety monitoring of therapeutic agents for the treatment of arthritis and systemic features. *Arthritis Care Res.* 2011;63(4):465-482.
5. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 4: Guidelines of care for the management and treatment of psoriasis with traditional systemic agents. *J Am Acad Dermatol.* 2009;61:451-485.

SPECIALTY GUIDELINE MANAGEMENT

RAVICTI (glycerol phenylbutyrate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Ravicti is indicated for the chronic management of patients with urea cycle disorders (UCDs) who cannot be managed by dietary protein restriction and/or amino acid supplementation alone. Ravicti must be used with dietary protein restriction and, in some cases, dietary supplements.

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: enzyme assay, biochemical, or genetic testing results supporting diagnosis.

III. CRITERIA FOR INITIAL APPROVAL

Authorizations of 12 months may be granted for chronic management of a urea cycle disorder (UCD) when the diagnosis is confirmed by enzymatic, biochemical, or genetic testing.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for chronic management of a urea cycle disorder (UCD), who are experiencing benefit from therapy as evidenced by a reduction in plasma ammonia levels from baseline.

V. REFERENCES

1. Ravicti [package insert]. Lake Forest, IL: Horizon Pharma USA, Inc.; December 2018.
2. Mew NA, Lanpher BC. Urea Cycle Disorders Overview. In: Pagon RA, Adam MP, Ardinger HH, et. al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2017 [updated April 9, 2015]. Available at: <https://www.ncbi.nlm.nih.gov/books/NBK1217/?report=printable>.
3. Häberle J, Boddaert N, Burlina A, et al. Suggested guidelines for the diagnosis and management of urea cycle disorders. *Orphanet J Rare Dis*. 2012;7:32.
4. Diaz GA, Krivitky LS, Mokhtarani M, et al. Ammonia control and neurocognitive outcome among urea cycle disorder patients treated with glycerol phenylbutyrate. *Hepatology*. 2013;57(6):2171-2179.
5. Smith W, Diaz GA, Lichter-Konecki U, et al. Ammonia control in children ages 2 months through 5 years with urea cycle disorders: comparison of sodium phenylbutyrate and glycerol phenylbutyrate. *J Pediatr*. 2013;162(6):1228-1234.

Reference number(s)
1839-A

SPECIALTY GUIDELINE MANAGEMENT

REBIF (interferon beta-1a)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Rebif is indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

Compendial Use

First clinical episode of multiple sclerosis with magnetic resonance imaging features consistent with multiple sclerosis

All other indications are considered experimental/investigational and are not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Relapsing forms of multiple sclerosis

Authorization of 12 months may be granted to members who have been diagnosed with a relapsing form of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse).

B. Clinically isolated syndrome

Authorization of 12 months may be granted to members for the treatment of clinically isolated syndrome of multiple sclerosis.

III. CONTINUATION OF THERAPY

For all indications: Authorization of 12 months may be granted for members who are experiencing disease stability or improvement while receiving Rebif.

IV. OTHER CRITERIA

Members will not use Rebif concomitantly with other medications used for the treatment of multiple sclerosis, excluding Ampyra.

V. REFERENCES

1. Rebif [package insert]. Rockland, MA; EMD Serono Inc.; July 2019.

Reference number(s)
1839-A

2. AHFS DI (Adult and Pediatric) [database online]. Hudson, OH: Lexi-Comp, Inc.; http://online.lexi.com/lco/action/index/dataset/complete_ashp [available with subscription]. Accessed April 19, 2019.
3. Clinical Pharmacology. [database online.] Tampa, FL: Gold Standard, Inc.; <http://www.clinicalpharmacology-ip.com/default.aspx> [available with subscription]. Accessed April 19, 2019.

SPECIALTY GUIDELINE MANAGEMENT

REBLOZYL (luspatercept-aamt)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Treatment of anemia in adult patients with beta thalassemia who require regular red blood cell (RBC) transfusions.

Limitations of Use: Reblozyl is not indicated for use as a substitute for red blood cell (RBC) transfusions in patients who require immediate correction of anemia.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

- A. Initial therapy requests
 - 1. Pretreatment or pretransfusion hemoglobin (Hgb) level
 - 2. Hemoglobin electrophoresis or high-performance liquid chromatography (HPLC) results
- B. Continuation of therapy requests: Current or current pretransfusion Hgb level

III. EXCLUSIONS

Coverage will not be provided for members with any of the following exclusions:

- A. Members with hemoglobin S/ β -thalassemia or alpha-thalassemia
- B. Members with recent (defined as less than or equal to 24 weeks prior to initiation of Reblozyl therapy) deep vein thrombosis or stroke
- C. Members with platelet count greater than 1000×10^9 per liter

IV. CRITERIA FOR INITIAL APPROVAL

Note: If a red blood cell (RBC) transfusion occurred prior to dosing, the pretransfusion hemoglobin (Hgb) level must be considered for dosing purposes.

Anemia with beta thalassemia

Authorization of 16 weeks may be granted for treatment of anemia with beta thalassemia when all of the following criteria are met:

- A. The member has a diagnosis of anemia evidenced by a pretreatment or pretransfusion Hgb level less than or equal to 11 grams per deciliter.

- B. The member has a diagnosis of beta thalassemia (β -thalassemia) or hemoglobin E/ β -thalassemia (β -thalassemia with mutation and/or multiplication of alpha globin is allowed) confirmed by hemoglobin electrophoresis or high performance liquid chromatography (HPLC).
- C. The member required at least 6 red blood cell (RBC) units to be transfused in the previous 24 weeks.

V. CONTINUATION OF THERAPY

Note: If a red blood cell (RBC) transfusion occurred prior to dosing, the pretransfusion hemoglobin (Hgb) level must be considered for dosing purposes.

Authorization of 6 months may be granted for continued treatment in members requesting authorization for anemia with beta thalassemia when the all of the following criteria are met:

- A. The member must achieve or maintain red blood cell transfusion burden reduction.
- B. The member must not experience an unacceptable toxicity from Reblozyl.
- C. The member must have a pre-dose Hgb level less than or equal to 11 grams per deciliter. If the Hgb level is greater than 11 grams per deciliter, the prescriber agrees to hold the dose until the level falls to 11 grams per deciliter.

VI. REFERENCES

1. Reblozyl [package insert]. Summit, NJ: Celgene Corporation; November 2019.
2. U.S. National Library of Medicine. ClinicalTrials.gov. An Efficacy and Safety Study of Luspatercept (ACE-536) Versus Placebo in Adults Who Require Regular Red Blood Cell Transfusions Due to Beta (β) Thalassemia (BELIEVE). <https://clinicaltrials.gov/ct2/show/NCT02604433>. Accessed 11/14/2019.
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SPECIALTY GUIDELINE MANAGEMENT

REBLOZYL (luspatercept-aamt)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

1. Treatment of anemia in adult patients with beta thalassemia who require regular red blood cell (RBC) transfusions
2. Treatment of anemia failing an erythropoiesis stimulating agent and requiring 2 or more red blood cell units over 8 weeks in adult patients with very low- to intermediate- risk myelodysplastic syndromes with ring sideroblasts (MDS-RS) or with myelodysplastic/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis (MDS/MPN-RS-T)

Limitations of Use: Reblozyl is not indicated for use as a substitute for red blood cell (RBC) transfusions in patients who require immediate correction of anemia.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

A. Anemia with Beta Thalassemia

Submission of the following information is necessary to initiate the prior authorization review:

1. Initial therapy requests
 - a. Pretreatment or pretransfusion hemoglobin (Hgb) level
 - b. Hemoglobin electrophoresis or high-performance liquid chromatography (HPLC) results
2. Continuation of therapy requests: Current or current pretransfusion Hgb level

B. Anemia of Myelodysplastic Syndrome or Myelodysplastic/Myeloproliferative Neoplasm

Submission of the following information is necessary to initiate the prior authorization review:

1. Initial therapy requests
 - a. Pretreatment or pretransfusion hemoglobin (Hgb) level
 - b. Pretreatment ring sideroblasts level
 - c. *SF3B1* mutation status (if pretreatment ring sideroblasts are greater than or equal to 5% and less than 15%)
 - d. Pretreatment serum erythropoietin levels
2. Continuation of therapy requests: Current or current pretransfusion Hgb level

III. EXCLUSIONS

Anemia with Beta Thalassemia

Coverage will not be provided for members with any of the following exclusions:

- A. Members with hemoglobin S/ β -thalassemia or alpha-thalassemia

- B. Members with recent (defined as less than or equal to 24 weeks prior to initiation of Reblozyl therapy) deep vein thrombosis or stroke
- C. Members with platelet count greater than 1000×10^9 per liter

IV. CRITERIA FOR INITIAL APPROVAL

A. Anemia with Beta Thalassemia

Authorization of 16 weeks may be granted for treatment of anemia with beta thalassemia when all of the following criteria are met:

1. The member has symptomatic anemia evidenced by a pretreatment or pretransfusion Hgb level less than or equal to 11 grams per deciliter
2. The member has a diagnosis of beta thalassemia (β -thalassemia) or hemoglobin E/ β -thalassemia (β -thalassemia with mutation and/or multiplication of alpha globin is allowed) confirmed by hemoglobin electrophoresis or high performance liquid chromatography (HPLC)
3. The member required at least 6 red blood cell (RBC) units to be transfused in the previous 24 weeks

Note: If a red blood cell (RBC) transfusion occurred prior to dosing, the pretransfusion hemoglobin (Hgb) level must be considered for dosing purposes.

B. Anemia of Myelodysplastic Syndrome or Myelodysplastic/Myeloproliferative Neoplasm

Authorization of 24 weeks may be granted for the treatment of very low- to intermediate-risk myelodysplastic syndrome or myelodysplastic/myeloproliferative neoplasm when all of the following criteria are met:

1. The member has symptomatic anemia evidenced by a pretreatment or pretransfusion Hgb level less than or equal to 11 grams per deciliter
2. The member has been receiving regular red blood cell (RBC) transfusions
3. The member meets either of the following:
 - a. Ring sideroblasts are greater than or equal to 15%
 - b. Ring sideroblasts are greater than or equal to 5% and less than 15% and the patient has an *SF3B1* mutation
4. The member meets either of the following:
 - a. Pretreatment serum erythropoietin levels greater than 500 mU/mL
 - b. Pretreatment serum erythropoietin levels less than or equal to 500mU/mL following no response to the combination of an erythropoiesis-stimulating agent (ESA) and granulocyte-colony stimulating factor (G-CSF)

V. CONTINUATION OF THERAPY

Authorization of 6 months may be granted for continued treatment in members requesting authorization for an indication listed in section IV when all of the following criteria are met:

- A. The member must achieve or maintain red blood cell transfusion burden reduction
- B. The member must not experience an unacceptable toxicity from Reblozyl
- C. The member must have a pre-dose Hgb level less than or equal to 11 grams per deciliter. If the Hgb level is greater than 11 grams per deciliter, the prescriber agrees to hold the dose until the level falls to 11 grams per deciliter

VI. REFERENCES

1. Reblozyl [package insert]. Summit, NJ: Celgene Corporation; April 2020.

2. U.S. National Library of Medicine. ClinicalTrials.gov. An Efficacy and Safety Study of Luspatercept (ACE-536) Versus Placebo in Adults Who Require Regular Red Blood Cell Transfusions Due to Beta (β) Thalassemia (BELIEVE). <https://clinicaltrials.gov/ct2/show/NCT02604433>. Accessed 11/14/2019.
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PRIOR AUTHORIZATION CRITERIA

BRAND NAME (generic)	REBLOZYL (luspatercept-aamt)
Status: CVS Caremark Criteria Type: Initial Prior Authorization	MDC Ref # 3417-A

FDA-APPROVED INDICATION¹

Reblozyl is indicated for the treatment of anemia in adult patients with beta thalassemia who require regular red blood cell (RBC) transfusions.

Limitations of use: Reblozyl is not indicated for use as a substitute for red blood cell (RBC) transfusions in patients who require immediate correction of anemia.

CRITERIA FOR APPROVAL

1	Does the patient have a diagnosis of anemia related to beta thalassemia? [If no, no further questions.]	Yes	No
2	Before starting therapy with the requested drug, did the patient require regular red blood cell (RBC) transfusions?	Yes	No

Guidelines for Approval	
Duration of Approval	12 Months
Set 1: Anemia with beta thalassemia	
Yes to question(s)	No to question(s)
1	None
2	

Mapping Instructions	
	No
1. Go to 2	Deny
2. Approve, 12 months	Deny

RATIONALE

These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to ensure that patients follow selection elements noted in labeling and/or practice guidelines in order to decrease the potential for inappropriate utilization.

REFERENCES

1. Reblozyl [package insert]. Summit, NJ: Celgene Corporation; November 2019.

DOCUMENT HISTORY

Created: Specialty Clinical Development (CM) 12/2019
Revised:
Reviewed: CDPR/MR 11/2019

Reblozyl 3417-A MDC 2020.docx

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PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

REGRANEX (all topical)
(becaplermin)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

MDC-1
Ref # 186-A

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Regranex gel is indicated for the treatment of lower extremity diabetic neuropathic ulcers that extend into the subcutaneous tissue or beyond and have an adequate blood supply, when used as an adjunct to, and not a substitute for, good ulcer care practices including initial sharp debridement, pressure relief and infection control.

Limitations of Use:

The efficacy of Regranex gel has not been established for the treatment of pressure ulcers and venous stasis ulcers and has not been evaluated for the treatment of diabetic neuropathic ulcers that do not extend through the dermis into subcutaneous tissue (Stage I or II, International Association of Enterostomal Therapy (IAET) staging classification) or ischemic diabetic ulcers.

The effects of becaplermin on exposed joints, tendons, ligaments, and bone have not been established in humans.

Regranex Gel is a non-sterile, low bioburden preserved product. Therefore, it should not be used in wounds that close by primary intention.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed as treatment of lower extremity diabetic neuropathic ulcers that extend into the subcutaneous tissue or beyond and have an adequate blood supply
- AND**
- The patient will have good ulcer care practices including initial sharp debridement, pressure relief, and infection control performed

RATIONALE

These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Regranex gel is indicated for the treatment of lower extremity diabetic neuropathic ulcers that extend into the subcutaneous tissue or beyond and have an adequate blood supply. Regranex is not a substitute for good ulcer care practices which includes initial sharp debridement, pressure relief and infection control.

In clinical studies, the effects of Regranex Gel on the incidence of and time to complete healing in lower extremity diabetic ulcers were assessed in four randomized controlled studies. All study participants had lower extremity diabetic neuropathic ulcers that extended into the subcutaneous tissue or beyond (Stages III and IV of the International Association of Enterostomal Therapy (IAET) guide to chronic wound staging) with an adequate blood supply. Patients were treated until complete healing, or for a period of up to 20 weeks. Patients were considered a treatment failure if their ulcer did not show an approximately 30% reduction in initial ulcer area after eight to ten weeks of Regranex Gel therapy.

The efficacy of Regranex gel for the treatment of non-diabetic ulcers has not been established.

REFERENCES

1. Regranex [package insert]. Fort Worth, TX: Smith & Nephew Inc.; December 2018.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed March 2019.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed March 2019.

Written by: UM Development (SE)
 Date written: 12/2009
 Revised: (CT/SE) 05/2010 (CAS adapted); (CT) 08/2011, 08/2012, 07/2013; (MS) 07/2014 (SF) 07/2015, (SE) 06/2016 (created separate Med D); (CT) 07/2016; (DS) 07/2017 (no clinical changes), 03/2018 (no clinical changes), 03/2019 (no clinical changes)
 Reviewed: Medical Affairs (KP) 12/2009, 08/2010, 08/2011; (LB) 08/2012; (LMS) 07/2013, (DC) 07/2014 (KRU) 07/2015; (ME) 07/2016
 External Review: 03/2010, 12/2010, 12/2011, 10/2012, 10/2013, 10/2014, 10/2015, 10/2016, 10/2017, 06/2018, 06/2019

CRITERIA FOR APPROVAL

- | | | | |
|---|---|-----|----|
| 1 | Is the requested drug being prescribed for the treatment of lower extremity diabetic neuropathic ulcers that extend into the subcutaneous tissue or beyond and have an adequate blood supply? | Yes | No |
| 2 | Will good ulcer care practices including initial sharp debridement, pressure relief, and infection control be performed? | Yes | No |

Guidelines for Approval	
Duration of Approval	20 Weeks
Set 1	
Yes to question(s)	No to question(s)
1	None
2	

Mapping Instructions			
	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions:</p> <ul style="list-style-type: none"> - You have lower extremity diabetic neuropathic ulcers that extend into the subcutaneous tissue and beyond - You have adequate blood supply to the tissue <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No approvable diagnosis]</p>
2.	Approve, 20 weeks	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions:</p> <ul style="list-style-type: none"> -You have good ulcer care practices including sharp debridement -You have good ulcer care including pressure relief -You have good ulcer care including infection control <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No approvable diagnosis]</p>

SPECIALTY GUIDELINE MANAGEMENT

REMICADE (infliximab) AVSOLA (infliximab-axxq) INFLECTRA (infliximab-dyyb) RENFLEXIS (infliximab-abda)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Moderately to severely active Crohn's disease (CD)
2. Moderately to severely active ulcerative colitis (UC)
3. Moderately to severely active rheumatoid arthritis (RA) in combination with methotrexate
4. Active ankylosing spondylitis (AS)
5. Active psoriatic arthritis (PsA)
6. Chronic severe plaque psoriasis (PsO)

B. Compendial Uses

1. Axial spondyloarthritis
2. Behçet's syndrome
3. Granulomatosis with polyangiitis (Wegener's granulomatosis)
4. Hidradenitis suppurativa
5. Juvenile idiopathic arthritis
6. Pyoderma gangrenosum
7. Sarcoidosis
8. Takayasu's arteritis
9. Uveitis
10. Reactive arthritis
11. Immune checkpoint inhibitor toxicity

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Moderately to severely active Crohn's disease (CD)**

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for the treatment of moderately to severely active Crohn's disease.

2. Authorization of 12 months may be granted for the treatment of moderately to severely active Crohn's disease in members who had an inadequate response, intolerance or contraindication to at least one conventional therapy option (See Appendix A).
3. Authorization of 12 months may be granted for the treatment of fistulizing CD.

B. Moderately to severely active ulcerative colitis (UC)

1. Authorization of 12 months may be granted for members who have previously received a biologic or targeted synthetic drug (e.g., Xeljanz) indicated for moderately to severely active ulcerative colitis.
2. Authorization of 12 months may be granted for the treatment of moderately to severely active UC for members who had an inadequate response, intolerance or contraindication to at least one conventional therapy option (See Appendix B).
3. Authorization of 12 months may be granted for members who have been hospitalized for acute severe UC (e.g., continuous bleeding, severe toxic symptoms, including fever and anorexia).

C. Moderately to severely active rheumatoid arthritis (RA)

1. Authorization of 12 months may be granted for members who have previously received a biologic or targeted synthetic DMARD (e.g., Rinvoq, Xeljanz) indicated for moderately to severely active rheumatoid arthritis. Remicade, Avsola, Inflectra, or Renflexis must be prescribed in combination with methotrexate or leflunomide unless the member has a clinical reason not to use methotrexate or leflunomide.
2. Authorization of 12 months may be granted for treatment of moderately to severely active RA when all of the following criteria are met:
 - a. Member is prescribed Remicade, Avsola, Inflectra, or Renflexis in combination with methotrexate or leflunomide, or has a clinical reason not to use methotrexate or leflunomide.
 - b. Member meets any of the following criteria:
 - i. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to 20 mg/week).
 - ii. Member has an intolerance or contraindication to methotrexate (see Appendix C).

D. Active ankylosing spondylitis (AS) and axial spondyloarthritis

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for active ankylosing spondylitis or axial spondyloarthritis.
2. Authorization of 12 months may be granted for treatment of active ankylosing spondylitis or axial spondyloarthritis when any of the following criteria is met:
 - a. Member has experienced an inadequate response to at least two non-steroidal anti-inflammatory drugs (NSAIDs).
 - b. Member has an intolerance or contraindication to two or more NSAIDs.

E. Active psoriatic arthritis (PsA)

Authorization of 12 months may be granted for treatment of active psoriatic arthritis (PsA).

F. Chronic severe plaque psoriasis

1. Authorization of 12 months may be granted for members who have previously received Otezla or a biologic indicated for the treatment of chronic severe plaque psoriasis.

2. Authorization of 12 months may be granted for treatment of chronic severe plaque psoriasis when all of the following criteria are met:
 - a. At least 3% of body surface area (BSA) is affected OR crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
 - b. Member meets any of the following criteria:
 - i. Member has had an inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) or pharmacologic treatment with methotrexate, cyclosporine or acitretin.
 - ii. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine and acitretin (see Appendix D).
 - iii. Member has severe psoriasis that warrants a biologic DMARD as first-line therapy (i.e. at least 10% of the body surface area (BSA) or crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected).

G. Behçet's disease

1. Authorization of 12 months may be granted for members who have previously received Otezla or a biologic indicated for the treatment of Behçet's disease.
2. Authorization of 12 months may be granted for the treatment of Behçet's disease when the member has had an inadequate response to at least one nonbiologic medication for Behçet's disease (e.g., apremilast, colchicine, systemic glucocorticoids, azathioprine).

H. Granulomatosis with polyangiitis (Wegener's granulomatosis)

Authorization of 12 months may be granted for treatment of granulomatosis with polyangiitis when either of the following criteria is met:

1. Member has experienced an inadequate response to corticosteroids or immunosuppressants (e.g., cyclophosphamide, azathioprine, methotrexate, or mycophenolate mofetil).
2. Member has an intolerance or contraindication to corticosteroids and immunosuppressive therapy.

I. Hidradenitis suppurativa

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for the treatment of severe, refractory hidradenitis suppurativa.
2. Authorization of 12 months may be granted for treatment of severe, refractory hidradenitis suppurativa when either of the following is met:
 - a. Member has experienced an inadequate response to oral antibiotics for at least 90 days.
 - b. Member has an intolerance or contraindication to oral antibiotics.

J. Juvenile Idiopathic arthritis (JIA)

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for juvenile idiopathic arthritis.
2. Authorization of 12 months may be granted for the treatment of JIA when any of the following criteria is met:
 - a. Member has an inadequate response to at least a 1-month trial of NSAIDs.
 - b. Member has an inadequate response to at least a 2-week trial of corticosteroids.
 - c. Member has an inadequate response to at least a 3-month trial of methotrexate or leflunomide.

K. Pyoderma gangrenosum

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for pyoderma gangrenosum.

2. Authorization of 12 months may be granted for treatment of pyoderma gangrenosum when either of the following is met:
 - a. Member has experienced an inadequate response to corticosteroids or immunosuppressive therapy (e.g., cyclosporine or mycophenolate mofetil).
 - b. Member has an intolerance or contraindication to corticosteroids and immunosuppressive therapy (e.g. cyclosporine, mycophenolate mofetil).

L. Sarcoidosis

Authorization of 12 months may be granted for treatment of sarcoidosis in members when any of the following criteria is met:

1. Member has experienced an inadequate response to corticosteroids or immunosuppressants.
2. Member has an intolerance or contraindication to corticosteroids and immunosuppressive therapy.

M. Takayasu's arteritis

Authorization of 12 months may be granted for treatment of refractory Takayasu's arteritis when any of the follow criteria is met:

1. Member has experienced an inadequate response to corticosteroids or immunosuppressive therapy (e.g., methotrexate, azathioprine, or mycophenolate mofetil).
2. Member has an intolerance or contraindication to corticosteroids and immunosuppressive therapy (e.g., methotrexate, azathioprine, or mycophenolate mofetil).

N. Uveitis

1. Authorization of 12 months may be granted for members who have previous received a biologic indicated for uveitis.
2. Authorization of 12 months may be granted for treatment of uveitis when any of the follow criteria is met:
 - a. Member has experienced an inadequate response to corticosteroids or immunosuppressive therapy (e.g., methotrexate, azathioprine, or mycophenolate mofetil).
 - b. Member has an intolerance or contraindication to corticosteroids and immunosuppressive therapy (e.g., methotrexate, azathioprine, or mycophenolate mofetil).

O. Reactive arthritis

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for reactive arthritis.
2. Authorization of 12 months may be granted for treatment of reactive arthritis when any of the following criteria is met:
 - a. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to 20 mg/week).
 - b. Member has an intolerance or contraindication to methotrexate (see Appendix C).

P. Immune Checkpoint Inhibitor Toxicity

Authorization of 1 month may be granted for the treatment of immune checkpoint inhibitor (e.g., CTLA-4, PD-L1 inhibitor) toxicity when either of the following is met:

1. Member has had an inadequate response to corticosteroids.
2. Member has cardiac toxicity.

III. CONTINUATION OF THERAPY

A. Immune Checkpoint Inhibitor Toxicity

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

B. All other indications

Authorization of 12 months may be granted for all members (including new members) who are using Remicade, Avsola, Inflectra, or Renflexis for an indication outlined in section II and who achieve or maintain positive clinical response with Remicade, Avsola, Inflectra, or Renflexis as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

For all indications: Member has had a documented negative TB test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic DMARDs or targeted synthetic DMARDs (e.g., Xeljanz), and repeated yearly for members with risk factors** for TB that are continuing therapy with biologics.

* If the screening testing for TB is positive, there must be further testing to confirm there is no active disease. Do not administer infliximab to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of infliximab.

** Risk factors for TB include: Persons with close contact to people with infectious TB disease; persons who have recently immigrated from areas of the world with high rates of TB (e.g., Africa, Asia, Eastern Europe, Latin America, Russia); children less than 5 years of age who have a positive TB test; groups with high rates of TB transmission (e.g., homeless persons, injection drug users, persons with HIV infection); persons who work or reside with people who are at an increased risk for active TB (e.g., hospitals, long-term care facilities, correctional facilities, homeless shelters).

For all indications: Member cannot use infliximab concomitantly with any other biologic DMARD or targeted synthetic DMARD.

V. APPENDICES**Appendix A: Examples of Conventional Therapy Options for CD**

1. Mild to moderate disease – induction of remission:
 - a. Oral budesonide
 - b. Alternatives: metronidazole, ciprofloxacin, rifaximin
2. Mild to moderate disease – maintenance of remission:
 - a. Azathioprine, mercaptopurine
 - b. Alternatives: oral budesonide, methotrexate intramuscular (IM) or subcutaneous (SC), sulfasalazine
3. Moderate to severe disease – induction of remission:
 - a. Prednisone, methylprednisolone intravenously (IV)
 - b. Alternatives: methotrexate IM or SC
4. Moderate to severe disease – maintenance of remission:
 - a. Azathioprine, mercaptopurine
 - b. Alternative: methotrexate IM or SC
5. Perianal and fistulizing disease – induction of remission

- a. Metronidazole ± ciprofloxacin, tacrolimus
- 6. Perianal and fistulizing disease – maintenance of remission
 - a. Azathioprine, mercaptopurine
 - b. Alternative: methotrexate IM or SC

Appendix B: Examples of Conventional Therapy Options for UC

1. Mild to moderate disease – induction of remission:
 - a. Oral mesalamine (e.g., Apriso, Asacol, Asacol HD, Lialda, Pentasa), balsalazide, olsalazine
 - b. Rectal mesalamine (e.g., Canasa, Rowasa)
 - c. Rectal hydrocortisone (e.g., Colocort, Cortifoam)
 - d. Alternatives: prednisone, azathioprine, mercaptopurine, sulfasalazine
2. Mild to moderate disease – maintenance of remission:
 - a. Oral mesalamine, balsalazide, olsalazine, rectal mesalamine
 - b. Alternatives: azathioprine, mercaptopurine, sulfasalazine
3. Severe disease – induction of remission:
 - a. Prednisone, hydrocortisone IV, methylprednisolone IV
 - b. Alternatives: cyclosporine IV, tacrolimus, sulfasalazine
4. Severe disease – maintenance of remission:
 - a. Azathioprine, mercaptopurine
 - b. Alternative: sulfasalazine
5. Pouchitis: Metronidazole, ciprofloxacin
 - a. Alternative: rectal mesalamine

Appendix C: Examples of Contraindications to Methotrexate

1. Clinical diagnosis of alcohol use disorder, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
4. Elevated liver transaminases
5. History of intolerance or adverse event
6. Hypersensitivity
7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
8. Myelodysplasia
9. Pregnancy or currently planning pregnancy
10. Renal impairment
11. Significant drug interaction

Appendix D: Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine or Acitretin

1. Clinical diagnosis of alcohol use disorder, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Drug interaction
4. Cannot be used due to risk of treatment-related toxicity
5. Pregnancy or currently planning pregnancy
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

VI. REFERENCES

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ENHANCED SPECIALTY GUIDELINE MANAGEMENT

REPATHA (evolocumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

- A. Repatha is indicated to reduce the risk of myocardial infarction, stroke, and coronary revascularization in adults with established cardiovascular disease.
- B. Repatha is indicated as an adjunct to diet, alone or in combination with other lipid-lowering therapies (e.g., statins, ezetimibe), for the treatment of adults with primary hyperlipidemia (including heterozygous familial hypercholesterolemia) to reduce low-density lipoprotein cholesterol.
- C. Repatha is indicated as an adjunct to diet and other LDL-lowering therapies (e.g., statins, ezetimibe, LDL apheresis) for the treatment of patients with homozygous familial hypercholesterolemia (HoFH) who require additional lowering of LDL-C.

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review:

- A. Current LDL-C level for both initial requests and continuation requests. The level must be dated within the six months preceding the authorization request.
- B. Untreated (before any lipid lowering therapy) LDL-C level if requesting Repatha to treat primary hyperlipidemia, heterozygous or homozygous familial hypercholesterolemia.
- C. Chart notes confirming clinical atherosclerotic cardiovascular disease (ASCVD) if requesting Repatha to treat clinical ASCVD.
- D. If patient has contraindication or intolerance to statins, chart notes confirming the contraindication or intolerance. (See Appendix B and C).

III. CRITERIA FOR INITIAL APPROVAL

A. Clinical atherosclerotic cardiovascular disease (ASCVD)

Authorization of 6 months may be granted for treatment of clinical atherosclerotic cardiovascular disease when all of the following criteria are met:

1. Member has a history of clinical ASCVD (See Appendix A).
2. Member meets at least one of the following requirements:
 - a. Member has a current LDL-C level ≥ 70 mg/dL after at least three months of treatment with a high-intensity statin dose in combination with ezetimibe. If the member is unable to tolerate a high-intensity statin dose, a moderate-intensity statin dose may be used.
 - b. Member has a current LDL-C level ≥ 70 mg/dL with contraindication or intolerance to statins (See Appendix B and C).

B. Primary hyperlipidemia including heterozygous familial hypercholesterolemia (HeFH)

Authorization of 6 months may be granted for treatment of primary hyperlipidemia including heterozygous familial hypercholesterolemia (HeFH) when both of the following criteria are met:

1. Member had an untreated (before any lipid lowering therapy) LDL-C level \geq 190 mg/dL in the absence of a secondary cause.
2. Member meets one of the following criteria:
 - a. Member has current LDL-C level \geq 100 mg/dL after at least three months of treatment with a high-intensity statin dose in combination with ezetimibe. If the member is unable to tolerate a high-intensity statin dose, a moderate-intensity statin dose may be used.
 - b. Member has current LDL-C level \geq 100 mg/dL with a contraindication or intolerance to statins (See Appendix B and C).

C. Homozygous familial hypercholesterolemia (HoFH)

Authorization of 6 months may be granted for treatment of homozygous familial hypercholesterolemia when both of the following criteria are met:

1. Member had an untreated (before any lipid lowering therapy) LDL-C level \geq 190 mg/dL in the absence of a secondary cause.
2. Member meets one of the following criteria:
 - a. Member has a current LDL-C level \geq 100 mg/dL after at least three months of treatment with a high-intensity statin dose in combination with ezetimibe. If the member is unable to tolerate a high-intensity statin dose, a moderate-intensity statin dose may be used.
 - b. Member has a current LDL-C level \geq 100 mg/dL with a contraindication or intolerance to statins (See Appendix B and C).
 - c. Member has received Juxtapid or Kynamro.
 - d. Member has been treated regularly with lipid apheresis.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members who achieve or maintain an LDL-C reduction (e.g., LDL-C is now at goal, robust lowering of LDL-C).

V. APPENDICES**APPENDIX A. Clinical ASCVD**

- Acute coronary syndromes
- Myocardial infarction
- Stable or unstable angina
- Coronary or other arterial revascularization procedure (e.g., percutaneous coronary angioplasty [PTCA], coronary artery bypass graft [CABG] surgery)
- Stroke of presumed atherosclerotic origin
- Transient ischemic attack (TIA)
- Non-cardiac peripheral arterial disease of presumed atherosclerotic origin (e.g., carotid artery stenosis)
- Obstructive coronary artery disease (defined as fifty percent or greater stenosis on cardiac computed tomography angiogram or catheterization)

APPENDIX B. Statin-associated muscle symptoms (SAMS) and statin re-challenge

- Score of 7 or higher on the Statin-Associated Muscle Symptom Clinical Index (SAMS-CI)
- Statin-associated elevation in creatine kinase (CK) level \geq 10 times upper limit of normal (ULN)

NOTE: Statin re-challenge is NOT required for members who have experienced an elevation of CK level ≥ 10 times ULN after receiving lipid-lowering therapy (LLT) with a statin.

APPENDIX C. Contraindications to statins

- Active liver disease, including unexplained persistent elevations in hepatic transaminase levels (e.g., alanine transaminase (ALT) level ≥ 3 times ULN)
- Pregnancy or planned pregnancy
- Breastfeeding

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SPECIALTY GUIDELINE MANAGEMENT

REVLIMID (lenalidomide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Multiple myeloma in combination with dexamethasone.
2. Multiple myeloma, as maintenance following autologous hematopoietic stem cell transplantation (auto-HSCT).
3. Transfusion-dependent anemia due to low- or intermediate-1-risk myelodysplastic syndromes associated with a deletion 5q cytogenetic abnormality with or without additional cytogenetic abnormalities.
4. Mantle cell lymphoma whose disease has relapsed or progressed after two prior therapies, one of which included bortezomib.
5. Previously treated follicular lymphoma, in combination with a rituximab product
6. Previously treated marginal zone lymphoma, in combination with a rituximab product

B. Compendial Uses

1. Multiple myeloma
2. Systemic light chain amyloidosis
3. Classical Hodgkin lymphoma
4. Myelodysplastic syndrome without the 5q deletion cytogenetic abnormality
5. Myelofibrosis-associated anemia
6. POEMS Syndrome
7. Non-Hodgkin lymphoma (NHL) with any of the following subtypes:
 - a. AIDS-related diffuse large B-cell lymphoma
 - b. Primary central nervous system (CNS) lymphoma
 - c. Post-transplant lymphoproliferative disorder
 - d. Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL)
 - e. Diffuse large B-cell lymphoma
 - f. Follicular lymphoma
 - g. Nongastric/Gastric mucosa associated lymphoid tissue (MALT) lymphoma
 - h. Primary cutaneous B-cell lymphoma
 - i. Nodal/splenic marginal zone lymphoma
 - j. Multicentric Castleman's disease
 - k. Adult T-cell leukemia/lymphoma
 - l. Mycosis fungoides (MF)/Sezary syndrome (SS)
 - m. Angioimmunoblastic T-cell lymphoma (AITL)
 - n. Peripheral T-cell lymphoma not otherwise specified (PTCL NOS)
 - o. Enteropathy-associated T-cell lymphoma
 - p. Monomorphic epithelotropic intestinal T-cell lymphoma
 - q. Nodal peripheral T-cell lymphoma
 - r. Follicular T-cell lymphoma
 - s. Primary cutaneous anaplastic large cell lymphoma (ALCL)

- t. Hepatosplenic gamma-delta T-cell lymphoma
- u. High-grade B-cell lymphomas

All other indications are considered experimental/investigational and are not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Multiple myeloma

Authorization of 12 months may be granted for treatment of multiple myeloma.

B. Non-Hodgkin lymphoma (NHL)

Authorization of 12 months may be granted for treatment of NHL with any of the following subtypes:

1. Second-line or subsequent therapy for relapse of AIDS-related diffuse large B-cell lymphoma
2. Relapsed or refractory primary central nervous system (CNS) lymphoma as a single agent or in combination with rituximab
3. Second-line or subsequent therapy of post-transplant lymphoproliferative disorder (non-germinal center B-cell type)
4. Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL)
5. Histologic transformation of marginal zone lymphoma to diffuse large B-cell lymphoma after multiple lines of chemoimmunotherapy
6. Second-line or subsequent therapy for non-germinal center diffuse large B-cell lymphoma in non-candidates for transplant
7. Follicular lymphoma
8. Mantle cell lymphoma
9. Refractory or progressive nongastric MALT lymphoma as a single agent or in combination with rituximab
10. Second-line or subsequent therapy for recurrent or progressive gastric MALT lymphoma
11. Primary cutaneous B-cell lymphoma
12. Second-line or subsequent therapy for refractory or progressive nodal marginal zone lymphoma
13. Second-line or subsequent therapy for splenic marginal zone lymphoma
14. Relapsed, refractory or progressive multicentric Castleman's disease
15. Relapsed or refractory primary cutaneous anaplastic large cell lymphoma (ALCL) or cutaneous ALCL as a single agent
16. Second-line or subsequent therapy for adult T-cell leukemia/lymphoma (acute or lymphoma subtypes)
17. Mycosis fungoides (MF)/Sezary syndrome (SS)
18. Second line or subsequent therapy for relapsed or refractory angioimmunoblastic T-cell lymphoma (AITL)
19. Second-line or subsequent therapy for relapsed or refractory peripheral T-cell lymphoma not otherwise specified (PTCL NOS)
20. Second-line or subsequent therapy for relapsed or refractory enteropathy-associated T-cell lymphoma
21. Second-line or subsequent therapy for relapsed or refractory monomorphic epitheliotropic intestinal T-cell lymphoma
22. Second-line or subsequent therapy for relapsed or refractory nodal peripheral T-cell lymphoma with TFH phenotype
23. Second-line or subsequent therapy for relapsed or refractory follicular T-cell lymphoma
24. Second-line or subsequent therapy for refractory hepatosplenic gamma-delta T-cell lymphoma
25. Second line or subsequent therapy for high-grade B-cell lymphomas

C. Myelodysplastic syndrome

Authorization of 12 months may be granted for treatment of low- to intermediate-1 risk myelodysplastic syndrome (IPSS scale) for those with symptomatic anemia.

D. Myelofibrosis-associated anemia

Authorization of 12 months may be granted for treatment of myelofibrosis-associated anemia when all of the following criteria are met:

1. The requested medication will be given as a single agent or in combination with prednisone.
2. The member has serum erythropoietin levels of either of the following:
 - a. 500 mU/mL or greater
 - b. Less than 500 mU/mL and no response or loss of response to erythropoietin stimulating agents

E. Systemic light chain amyloidosis

Authorization of 12 months may be granted for treatment of systemic light chain amyloidosis in combination with dexamethasone.

F. Classical Hodgkin lymphoma

Authorization of 12 months may be granted for treatment of relapsed or refractory classical Hodgkin lymphoma as a single agent.

G. POEMS Syndrome

Authorization of 12 months may be granted for treatment of POEMS syndrome in combination with dexamethasone.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced unacceptable toxicity or disease progression while on the current regimen.

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STEP THERAPY CRITERIA

BRAND NAME*
(generic)

REYVOW
(lasmiditan)

Status: CVS Caremark Criteria

Type: Initial Step Therapy with Quantity Limit;

Post Step Therapy Prior Authorization with Quantity Limit

Ref # 3373-E

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Reyvow is indicated for the acute treatment of migraine with or without aura in adults.

Limitations of Use

Reyvow is not indicated for the preventive treatment of migraine.

INITIAL STEP THERAPY with QUANTITY LIMIT*

**Include Rx and OTC products unless otherwise stated.*

If the patient has filled a prescription for at least a 30 day supply of TWO triptan medications within the past 180 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.** If the patient does not meet the initial step therapy criteria, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

****If the patient meets the initial step therapy criteria, then the initial limit criteria will apply. If the patient is requesting more than the initial quantity limit the claim will reject with a message indicating that a PA is required.**

****INITIAL LIMIT CRITERIA**

Limits should accumulate across all drugs and strengths up to highest quantity listed depending on the order the claims are processed. Accumulation does not apply if limit is coded for daily dose.

Drug	1 Month Limit*	3 Month Limit*
Reyvow 50 mg	4 tablets / 25 days	12 tablets / 75 days
Reyvow 100 mg	8 tablets / 25 days	24 tablets / 75 days

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has a diagnosis of migraine headache
- AND**
- The patient has experienced an inadequate treatment response to TWO triptan medications
- OR**

- The patient has experienced an intolerance to TWO triptan medications
OR
- The patient has a contraindication that would prohibit a trial of triptan medications
AND
- If additional quantities are being requested, medication overuse headache has been considered and ruled out
AND
- The patient is currently using migraine prophylactic therapy
OR
- The patient is unable to take migraine prophylactic therapy due to an inadequate treatment response, intolerance, or contraindication

Quantity Limits apply.

RATIONALE

If the patient has filled a prescription for at least a 30 day supply of TWO triptan medications within the past 180 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.

If the patient meets the initial step therapy criteria, then the initial limit criteria will apply. The initial limit will be 4 tablets of Reyvow 50 mg or 8 tablets of Reyvow 100 mg per month to allow for the treatment of 4 headaches per month at the maximum recommended dose.

If the patient does not meet the initial step therapy criteria, then prior authorization (PA) is required. If the patient is requesting more than the initial quantity limit the claim will reject with a message indicating that a PA is required.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Reyvow is indicated for the acute treatment of migraine with or without aura in adults.

All patients with migraine should be offered a trial of acute treatment.⁴ Effective and early acute treatment of migraine can reduce the pain, associated symptoms, and disability associated with attacks.^{4,5} Headaches should be categorized according to peak severity, duration of symptoms, and time to peak impairment. Treatment should be selected based on headache severity, although other features may influence choice in treatment (for example, parenteral administration should be considered for patients with time to peak disability less than one hour, who awaken with headache, and for those with severe nausea and vomiting).⁵ Mild migraine headaches may be managed by nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen, nonopioid analgesics, and caffeinated analgesic combinations; however, only 2-12% of initially mild migraine episodes remain mild, and not all mild migraine headaches respond to these therapies. Migraine-specific agents such as triptans are effective for mild, moderate, and severe migraine headache treatment.^{4,5} Several different triptans are available on the market with different dosage forms and routes of administration.^{2,3} Patients respond differently to the same medication; failure to respond to one triptan does not preclude a response to an alternate triptan.⁷ Due to the high evidence of triptan efficacy in the acute treatment of migraine headaches, patients will be required to experience an inadequate treatment response or intolerance to at least two different triptan medications unless the patient has a contraindication that would prohibit a trial of these drugs.

Patients with migraine should be considered for preventive treatment in any of the following situations: attacks significantly interfere with patients' daily routines despite acute treatment; frequent attacks (≥ 4 migraine headache days); a contraindication to, failure, or overuse of acute treatments; adverse events with acute treatments; or patient preference.⁴ Based on these recommendations, patients requiring treatment for more than 4 migraine headache days per month should be evaluated further for preventive treatment. Approved criteria will approve for a quantity sufficient to treat 4 headaches per month. The recommended dose for Reyvow for the treatment of acute migraine is either 50 mg, 100 mg, or 200 mg taken as needed. No more than one dose should be taken within 24 hours. Reyvow is available as 50 mg tablets and 100 mg tablets in cartons of 8 tablets.

If patients require treatment for more than 4 headaches per month, additional criteria will apply.

For prevention of migraine headache, the American Academy of Neurology and the American Headache Society 2012 guideline update recommendations state that the following medications are established as effective and should be offered for migraine prevention: β -adrenergic blocking agents, metoprolol, propranolol, timolol; and antiepileptic drugs (AEDs), divalproex sodium, topiramate, sodium valproate. Additionally the following medications are probably effective: antidepressants, amitriptyline, venlafaxine; and β -adrenergic blocking agents, atenolol, nadolol and should be considered for migraine prevention. Efficacy and safety of individual agents, even within the same class of drugs, may vary among patients therefore, if the patient fails one preventive medication, others should be tried as failure of one agent does not rule out success with another one.^{2,3,5,6,8} The Institute for Clinical Systems Improvement (ICSI) headache guidelines state that preventive therapy should be considered for all patients, and the American Academy of Neurology (AAN) guidelines recommend preventive medications when there is either an impact on life and acute therapy is not working or where headache frequency can lead to medication overuse headache.^{5,6} Therefore, patients with migraine headache requesting additional quantities of Reyvow must be currently taking prophylactic therapy or are unable to take prophylactic therapy due to an inadequate response, intolerance, or contraindication.

Frequent use of acute migraine drugs (e.g. ergotamine, triptans, opioids, or combination of these drugs for 10 or more days per month) may lead to exacerbation of headache (medication overuse headache).¹⁻³ To decrease the risk of medication-overuse headache ("rebound headache" or "drug-induced headache") many experts limit acute therapy to two headache days per week on a regular basis.⁵ More frequent treatment other than this may result in medication-overuse chronic daily headaches.^{4,5} Therefore, the prescriber must have considered and ruled out the diagnosis of medication overuse headache.

Since drug treatment of acute migraine headache should not exceed more than two days per week on a regular basis, limits are set at a quantity to treat 8 headaches per month at the maximum recommended dosing of Reyvow. The post limit for approval will be 8 tablets of Reyvow 50 mg and 16 tablets of Reyvow 100 mg per month to allow for the treatment of 8 headaches per month at the maximum recommended dose.

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Written by: UM Development (KC)
Date Written: 10/2019
Revised:
Reviewed: Medical Affairs (CHART) 10/31/19
External Review: 12/2019

CRITERIA FOR APPROVAL

1	Does the patient have a diagnosis of migraine headache?	Yes	No
2	Has the patient experienced an inadequate treatment response to TWO triptan medications? [If yes, then skip to question 5.]	Yes	No
3	Has the patient experienced an intolerance to TWO triptan medications? [If yes, then skip to question 5.]	Yes	No
4	Does the patient have a contraindication that would prohibit a trial of triptan medications?	Yes	No
5	Does the patient require more than the plan allowance of 4 tablets per month of Reyvow 50 mg OR 8 tablets per month of Reyvow 100 mg? [Note: If higher quantities are needed, additional questions are required.] [If no, then no further questions.]	Yes	No
6	Has medication overuse headache been considered and ruled out? [RPh Note: If no, then deny and enter a partial approval according to Columns A and B of the Quantity Limit Chart.]	Yes	No
7	Is the patient currently using migraine prophylactic therapy? [Note: Examples of prophylactic therapy are divalproex sodium, topiramate, valproate sodium, metoprolol, propranolol, timolol, atenolol, nadolol, amitriptyline, venlafaxine.] [If yes, then skip to question 9.]	Yes	No
8	Is the patient unable to take migraine prophylactic therapy due to an inadequate response, intolerance, or contraindication? [Note: Examples of prophylactic therapy are divalproex sodium, topiramate, valproate sodium, metoprolol, propranolol, timolol, atenolol, nadolol, amitriptyline, venlafaxine.] [RPh Note: If no, then deny and enter a partial approval according to Columns A and B of the Quantity Limit Chart.]	Yes	No
9	Does the patient require more than the plan allowance of 8 tablets per month of Reyvow 50 mg OR 16 tablets per month of Reyvow 100 mg? [Note: Coverage is provided up to an amount sufficient for treating up to eight headaches per month at the maximum recommended dose.] [RPh Note: If yes, then deny and enter a partial approval according to Columns C and D of the Quantity Limit Chart.]	Yes	No

Mapping Instructions

	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have migraine headaches. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis.]

2.	Go to 5	Go to 3	
3.	Go to 5	Go to 4	
4.	Go to 5	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have tried a triptan medication and it either did not work for you, or you cannot take these drugs. Your request has been denied based on the information we have. [Short Description: No inadequate response, intolerance, or contraindication to triptans]
5.	Go to 6	Approve, 12 months See Quantity Limits Chart (Column A for 1 month supply or Column B for 3 month supply)	
6.	Go to 7	Deny RPh Note: For the denial verbiage, only include the drug and strength the PA is for. Remove all the other drugs from the verbiage.	You do not meet the requirements of your plan. Your plan covers additional quantities of this drug when all of these conditions apply: - Headache from medication overuse has been considered - Headache from medication overuse has been ruled out Current plan approved criteria cover up to: - 4 tablets per month of Reyvow 50 mg - 8 tablets per month of Reyvow 100 mg You have been approved for the quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied based on the information we have. [Short Description: Medication overuse headache not ruled out]
7.	Go to 9	Go to 8	
8.	Go to 9	Deny RPh Note: For the denial verbiage, only include the drug and strength the PA is for. Remove all the other drugs from the verbiage.	You do not meet the requirements of your plan. Your plan covers additional quantities of this drug when you meet one of these conditions: - You currently take a preventive migraine drug (e.g., divalproex sodium, topiramate, valproate sodium, metoprolol, propranolol, timolol, atenolol, nadolol, amitriptyline, venlafaxine) - You tried a preventive migraine drug (e.g., divalproex sodium, topiramate, valproate sodium, metoprolol, propranolol, timolol, atenolol, nadolol, amitriptyline, venlafaxine) and it either did not work for you, or you cannot use these drugs Current plan approved criteria cover up to: - 4 tablets per month of Reyvow 50 mg - 8 tablets per month of Reyvow 100 mg You have been approved for the quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied based on the information we have. [Short Description: No use or trial of migraine prophylaxis drugs]
9.	Deny RPh Note: For the denial verbiage, only include the drug and strength the PA is for. Remove all the	Approve, 12 months See Quantity Limits Chart (Column C for 1 month supply or Column D for 3 month supply)	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 8 tablets per month of Reyvow 50 mg - 16 tablets per month of Reyvow 100 mg You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength have been denied. [Short Description: Over max quantity]

	other drugs from the verbiage.		
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QUANTITY LIMIT

Limits should accumulate across all drugs and strengths up to highest quantity listed depending on the order the claims are processed. Accumulation does not apply if limit is coded for daily dose.

	COLUMN A	COLUMN B	COLUMN C	COLUMN D
Drug	Initial 1 Month Limit*	Initial 3 Month Limit*	Post 1 Month Limit*	Post 3 Month Limit*
Reyvow 50 mg	4 tablets / 25 days	12 tablets / 75 days	8 tablets / 25 days	24 tablets / 75 days
Reyvow 100 mg	8 tablets / 25 days	24 tablets / 75 days	16 tablets / 25 days	48 tablets / 75 days

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

ENHANCED SPECIALTY GUIDELINE MANAGEMENT

DMARD Combination for the Treatment of Rheumatoid Arthritis

Actemra, Avsola, Cimzia, Enbrel, Humira, Inflectra, Kevzara, Kineret, Olumiant, Oencia, Remicade, Renflexis, Rinvoq, Simponi, Simponi Aria, Xeljanz, Xeljanz XR

PROGRAM RATIONALE: The intent of the criteria is to provide coverage for branded biologic disease modifying antirheumatic drugs (DMARDs) for members who have maximized the use of non-biologic generic DMARDs for the treatment of rheumatoid arthritis. For this program, all branded specialty medications approved for the treatment of rheumatoid arthritis (Actemra, Avsola, Cimzia, Enbrel, Humira, Inflectra, Kevzara, Kineret, Olumiant, Oencia, Remicade, Renflexis, Rinvoq, Simponi, Simponi Aria, Xeljanz, Xeljanz XR) are targeted.

STEP THERAPY CRITERIA

If the member has inadequate response, intolerance or contraindication to treatment with generic DMARD medications, the requested branded medication will be approved, provided that the member has met all criteria for approval on all programs implemented for the client. **These step therapy criteria only apply to adult members who have not received treatment with any branded biologic or targeted synthetic DMARD for the treatment of rheumatoid arthritis.**

Coverage for a requested branded biologic or targeted synthetic disease modifying antirheumatic drug (DMARD) is provided when the member meets one of the following (criteria set A or B):

- A. Member has previously received a branded biologic or targeted synthetic DMARD for rheumatoid arthritis (RA)
- B. Member has not previously received a branded biologic or targeted synthetic DMARD for RA and meets one of the following (criteria set 1 or 2):
 1. Member has failed to achieve a low disease activity after a 3-month trial of a treatment regimen of methotrexate (MTX) at a maximum titrated dose of 20 mg per week and meets any of the following conditions:
 - a. Member has had a documented inadequate response with methotrexate in combination with at least one other non-biologic DMARD (i.e., leflunomide, hydroxychloroquine, and/or sulfasalazine) after a 3-month trial at a maximum tolerated dose
 - b. Member has experienced a documented intolerable adverse event or has a documented contraindication to leflunomide, hydroxychloroquine, and/or sulfasalazine (see Appendix B)
 - c. Member has moderate to high disease activity
 2. Member has experienced a documented intolerable adverse event or has a documented contraindication to MTX (see Appendix A) and meets any of the following conditions:
 - a. Member has had a documented inadequate response with another non-biologic DMARD (i.e., leflunomide, hydroxychloroquine, and/or sulfasalazine) alone or in combination after a 3-month trial at a maximum tolerated dose(s)
 - b. Member has experienced an intolerable adverse event or has a contraindication to leflunomide, hydroxychloroquine, and/or sulfasalazine (see Appendix B)
 - c. Member has moderate to high disease activity

APPENDICES

Appendix A: Examples of contraindications to methotrexate

- Clinical diagnosis of alcohol use disorder, alcoholic liver disease or other chronic liver disease
- Blood dyscrasias (e.g. bone marrow hypoplasia, leukopenia, thrombocytopenia, or significant anemia)
- Breastfeeding
- Elevated liver transaminases
- History of intolerance or intolerable adverse event
- Hypersensitivity
- Interstitial pneumonitis or clinically significant pulmonary fibrosis
- Myelodysplasia
- Pregnancy or currently planning pregnancy
- Renal impairment
- Significant drug interaction

Appendix B: Examples of contraindications to leflunomide, hydroxychloroquine, and/or sulfasalazine

- Clinical diagnosis of alcohol use disorder, alcoholic liver disease or other chronic liver disease
- Blood dyscrasias (e.g. bone marrow hypoplasia, leukopenia, thrombocytopenia, or significant anemia)
- Breastfeeding
- Chronic liver disease
- Elevated liver transaminases
- Hypersensitivity
- Intestinal or urinary obstruction
- History of intolerance or intolerable adverse event
- Porphyria
- Pregnancy or currently planning pregnancy
- Presence of retinal or visual field changes attributable to any 4-aminoquinoline compound

Note: Submission of chart notes detailing the outcomes of treatment, intolerable adverse event(s) experienced, contraindication(s), or exclusion(s) to treatment with prerequisite product(s) is required (where applicable).

REFERENCES

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2. Goekoop-Ruiterman YP, de Vries-Bouwstra JK, Allaart CF, et al. Clinical and radiographic outcomes of four different treatment strategies in patients with early rheumatoid arthritis (the BeSt study): a randomized, controlled trial. *Arthritis Rheum.* 2005;52:3381–90.
3. Graudal N, Jurgens G. Similar effects of disease-modifying antirheumatic drugs, glucocorticoids, and biologic agents on radiographic progression in rheumatoid arthritis: meta-analysis of 70 randomized placebo-controlled or drug-controlled studies, including 112 comparisons. *Arthritis Rheum.* 2010;62:2852–63.
4. Ma MH, Kingsley GH, Scott DL. A systematic comparison of combination DMARD therapy and tumour necrosis inhibitor therapy with methotrexate in patients with early rheumatoid arthritis. *Rheumatology (Oxford).* 2010;49:91–8.
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6. Moreland LW, O'Dell JR, Paulus HE, et al. A randomized comparative effectiveness study of oral triple therapy versus etanercept plus methotrexate in early aggressive rheumatoid arthritis: the Treatment of Early Aggressive Rheumatoid Arthritis trial. *Arthritis Rheum.* 2012;64:2824–35.
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Reference number
1987-D

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SPECIALTY GUIDELINE MANAGEMENT

RIASTAP (fibrinogen concentrate [human])

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

RiaSTAP is indicated in patients with congenital fibrinogen deficiency, including afibrinogenemia and hypofibrinogenemia, for the treatment of acute bleeding episodes.

All other indications are considered experimental/investigational and are not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Fibrinogen Deficiency

Authorization of 1 month may be granted for treatment of acute bleeding episodes in members with a diagnosis of congenital fibrinogen deficiency, including afibrinogenemia and hypofibrinogenemia.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. RiaSTAP [package insert]. Kankakee, IL: CSL Behring LLC; April 2019.
2. National Hemophilia Foundation. MASAC recommendations concerning products licensed for the treatment of hemophilia and other bleeding disorders. Revised April 2018. MASAC Document # 253. Accessed December 3, 2019.

SPECIALTY GUIDELINE MANAGEMENT

RIBAVIRIN PRODUCTS (COPEGUS, MODERIBA, REBETOL, RIBASPHERE, RIBASPHERE RIBAPAK, RIBATAB, ribavirin capsules and tablets)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Copegus

Copegus is indicated for the treatment of chronic hepatitis C (CHC) virus infection in combination with Pegasys in patients 5 years of age and older with compensated liver disease not previously treated with interferon alpha, and in adult CHC patients coinfecting with HIV.

Moderiba

Moderiba is indicated for the treatment of chronic hepatitis C (CHC) virus infection in combination with peginterferon alfa-2a in patients 5 years of age and older with compensated liver disease not previously treated with interferon alpha, and in adult CHC patients coinfecting with HIV.

Rebetol

Rebetol is indicated in combination with interferon alfa-2b (pegylated and nonpegylated) for the treatment of chronic hepatitis C (CHC) in patients 3 years of age and older with compensated liver disease.

Ribasphere/RibaPak

Ribasphere is indicated for the treatment of chronic hepatitis C (CHC) virus infection in combination with peginterferon alfa-2a in patients 5 years of age and older with compensated liver disease not previously treated with interferon alpha, and in adult CHC patients coinfecting with HIV.

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

Exclusions to other antiviral drugs being used in combination with the requested drug apply. Refer to the SGM policy for each drug in the treatment regimen for applicable exclusions.

III. CRITERIA FOR APPROVAL

Chronic hepatitis C virus (HCV) infection

Refer to the SGM of requested regimen for the specific criteria for approval and approval durations.

IV. REFERENCES

Reference number(s)
2140-A

1. Copegus [package insert]. South San Francisco, CA: Genentech USA, Inc.; August 2015.
2. Moderiba [package insert]. North Chicago, IL: AbbVie Inc.; December 2017.
3. Rebetol [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; October 2017.
4. Ribasphere/Ribapak [package insert]. Warrendale, PA: Kadmon Pharmaceuticals, LLC; September 2017.
5. AASLD/IDSA/IAS–USA. Recommendations for testing, managing, and treating hepatitis C. <http://www.hcvguidelines.org>. Last changes made on May 24, 2018. Accessed August 02, 2018.
6. Olysio [package insert]. Titusville, NJ: Janssen Products, LP; November 2017.
7. Sovaldi [package insert]. Foster City, CA: Gilead Sciences, Inc.; November 2017.
8. Viekira Pak [package insert]. North Chicago, IL: AbbVie Inc.; July 2018.
9. Technivie [package insert]. North Chicago, IL: AbbVie Inc.; July 2018.
10. Zepatier [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; June 2018.
11. Epclusa [package insert]. Foster City, CA: Gilead Sciences, Inc.; November 2017.
12. Viekira XR [package insert]. North Chicago, IL: AbbVie Inc.; July 2018.
13. Vosevi [package insert]. Foster City, CA: Gilead Sciences, Inc.; November 2017.

SPECIALTY GUIDELINE MANAGEMENT

RINVOQ (upadacitinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response or intolerance to methotrexate.

All other indications are considered experimental/investigational and are not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Moderately to severely active rheumatoid arthritis (RA)

- A. Authorization of 12 months may be granted for members who have previously received a biologic or targeted synthetic DMARD (e.g., Xeljanz, Olumiant) indicated for moderately to severely active rheumatoid arthritis.
- B. Authorization of 12 months may be granted for treatment of moderately to severely active RA when any of the following criteria is met:
 1. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to 20 mg/week).
 2. Member has an intolerance or contraindication to methotrexate (See Appendix A).

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who are using Rinvoq for an indication outlined in section II and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

For all indications: Member has had a documented negative TB test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic DMARDs or targeted synthetic DMARDs (e.g., Xeljanz), and repeated yearly for members with risk factors** for TB that are continuing therapy with biologics.

* If the screening testing for TB is positive, there must be documentation of further testing to confirm there is no active disease. Do not administer upadacitinib to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of upadacitinib.

** Risk factors for TB include: Persons with close contact to people with infectious TB disease; persons who have recently immigrated from areas of the world with high rates of TB (e.g., Africa, Asia, Eastern Europe, Latin America, Russia); children less than 5 years of age who have a positive TB test; groups with high rates of TB transmission (e.g., homeless persons, injection drug users, persons with HIV infection); persons who work or reside with people who are at an increased risk for active TB (e.g., hospitals, long-term care facilities, correctional facilities, homeless shelters).

For all indications: Member cannot use Rinvoq concomitantly with any biologic DMARD, targeted synthetic DMARD, or potent immunosuppressants such as azathioprine or cyclosporine.

V. APPENDICES

Appendix A: Examples of Contraindications to Methotrexate

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
4. Elevated liver transaminases
5. History of intolerance or adverse event
6. Hypersensitivity
7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
8. Myelodysplasia
9. Pregnancy or planning pregnancy
10. Renal impairment
11. Significant drug interaction

VI. REFERENCES

1. Rinvoq [package insert]. North Chicago, IL; AbbVie, Inc.; August 2019.
2. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. *Arthritis Rheumatol*. 2016;68(1):1-26.
3. Smolen JS, Landewé R, Billsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. *Ann Rheum Dis*. 2017;0:1-18.
4. Tuberculosis (TB). TB risk factors. Centers for Disease Control and Prevention. Retrieved on 21 June 2019 from: <https://www.cdc.gov/tb/topic/basics/risk.htm>.

SPECIALTY GUIDELINE MANAGEMENT

RITUXAN HYCELA (rituximab and hyaluronidase human)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Adult patients with follicular lymphoma (FL):
 - i. Relapsed or refractory, follicular lymphoma as a single agent
 - ii. Previously untreated follicular lymphoma in combination with first line chemotherapy and, in patients achieving a complete or partial response to rituximab in combination with chemotherapy, as single-agent maintenance therapy
 - iii. Non-progressing (including stable disease), follicular lymphoma as a single agent after first-line CVP (cyclophosphamide, vincristine, and prednisone) chemotherapy
2. Adult patients with previously untreated diffuse large B-cell lymphoma (DLBCL) in combination with cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) or other anthracycline-based chemotherapy regimens
3. Adult patients with previously untreated and previously treated chronic lymphocytic leukemia (CLL), in combination with fludarabine and cyclophosphamide (FC)

Limitations of Use:

Initiate treatment with Rituxan Hycela only after patients have received at least one full dose of a rituximab product by intravenous infusion.

Rituxan Hycela is not indicated for the treatment of non-malignant conditions.

B. Compendial Uses

1. Acquired immune deficiency syndrome (AIDS)-related B-cell lymphoma
2. Burkitt lymphoma
3. Castleman's disease (CD)
4. High-grade B-cell lymphoma
5. Gastric mucosa-associated lymphoid tissue (MALT) lymphoma
6. Mantle cell lymphoma
7. Nodal marginal zone lymphoma
8. Nongastric MALT lymphoma
9. Primary cutaneous B-cell lymphoma (e.g., cutaneous marginal zone lymphoma or cutaneous follicle center lymphomas)
10. Post-transplant lymphoproliferative disorder (PTLD)
11. Small lymphocytic lymphoma (SLL)
12. Splenic marginal zone lymphoma

All other indications are considered experimental/investigational and are not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Testing or analysis confirming CD20 protein on the surface of the B-cell

III. CRITERIA FOR INITIAL APPROVAL

Prior to initiating therapy, all members must receive at least one full dose of a rituximab product by intravenous infusion without experiencing severe adverse reactions.

A. Follicular lymphoma (FL)

Authorization of 12 months may be granted for treatment of CD20 positive FL.

B. Diffuse large B-cell lymphoma (DLBCL)

Authorization of 12 months may be granted for treatment of CD20 positive DLBCL.

C. Chronic lymphocytic leukemia (CLL)/ Small lymphocytic lymphoma (SLL)

Authorization of 12 months may be granted for treatment of CD20 positive CLL or SLL.

D. B-cell lymphomas

Authorization of 12 months may be granted for treatment of any of the following oncologic disorders that are CD20-positive as confirmed by testing or analysis:

1. Acquired immune deficiency syndrome (AIDS)-related B-cell lymphoma
2. Burkitt lymphoma
3. Castleman's disease (CD)
4. Gastric MALT lymphoma
5. High-grade B-cell lymphoma
6. Mantle cell lymphoma
7. Nodal marginal zone lymphoma
8. Nongastric MALT lymphoma
9. Primary cutaneous B-cell lymphoma (e.g., cutaneous marginal zone lymphoma or cutaneous follicle center lymphomas)
10. Post-transplant lymphoproliferative disorder (PTLD)
11. Splenic marginal zone lymphoma

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced an unacceptable toxicity.

V. REFERENCES

1. Rituxan Hycela [package insert]. South San Francisco, CA: Genentech, Inc.; April 2018.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed April 17, 2019.

SPECIALTY GUIDELINE MANAGEMENT

RITUXAN (rituximab) RUXIENCE (rituximab-pvvr) TRUXIMA (rituximab-abbs)

Treatment of Hematologic and Oncologic Conditions

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Rituxan, Ruxience, and Truxima are indicated for:

1. Non-Hodgkin's Lymphoma (NHL) in adult patients with:
 - a. Relapsed or refractory, low-grade or follicular, CD20-positive, B-cell NHL as a single agent
 - b. Previously untreated follicular, CD20-positive, B-cell NHL in combination with first line chemotherapy and, in patients achieving a complete or partial response to a rituximab product in combination with chemotherapy, as single-agent maintenance therapy
 - c. Non-progressing (including stable disease), low-grade, CD20-positive, B-cell NHL, as a single agent after first-line CVP (cyclophosphamide, vincristine, and prednisone) chemotherapy
 - d. Previously untreated diffuse large B-cell, CD20-positive NHL in combination with cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) or other anthracycline-based chemotherapy regimens
2. Chronic lymphocytic leukemia (CLL), in combination with fludarabine and cyclophosphamide (FC), for the treatment of adult patients with previously untreated and previously treated CD20-positive CLL.
3. Granulomatosis with polyangiitis (Wegener's Granulomatosis) and microscopic polyangiitis (MPA) (Not addressed in this policy – Refer to Rituxan-Ruxience-Truxima-RA+Other SGM)

Rituxan and Truxima are also indicated for:

Moderately to severely active rheumatoid arthritis in adult patients who have had an inadequate response to one or more TNF antagonist therapies

(Not addressed in this policy – Refer to Rituxan-Ruxience-Truxima-RA+Other SGM)

Rituxan is also indicated for:

Moderate to severe pemphigus vulgaris in adult patients

(Not addressed in this policy – Refer to Rituxan- Ruxience-Truxima-RA+Other SGM)

B. Compendial Uses

1. Non-Hodgkin's Lymphoma
 - a. Small lymphocytic lymphoma (SLL)
 - b. Mantle cell lymphoma
 - c. Marginal zone lymphomas (nodal, splenic, gastric MALT, nongastric MALT)
 - d. Burkitt lymphoma
 - e. Primary cutaneous B-cell lymphoma

- f. High-grade B-cell lymphoma with translocations of MYC and BCL2 and/or BCL6 (double/triple hit lymphoma)
 - g. High-grade B-cell lymphoma, not otherwise specified
 - h. Castleman's disease
 - i. Acquired immunodeficiency syndrome (AIDS)-related B-cell lymphoma
 - j. Hairy cell leukemia
 - k. Post-transplant lymphoproliferative disorder (PTLD)
 - l. B-cell lymphoblastic lymphoma
2. Relapsed/refractory immune or idiopathic thrombocytopenic purpura (ITP)
 3. Autoimmune hemolytic anemia
 4. Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma (LPL)
 5. Thrombotic thrombocytopenic purpura
 6. Myasthenia gravis, refractory
 7. Hodgkin's lymphoma, nodular lymphocyte-predominant
 8. Chronic graft-versus-host disease (GVHD)
 9. Central nervous system (CNS) cancers
 - a. Leptomeningeal metastases from lymphomas
 - b. Primary CNS lymphoma
 10. B-cell acute lymphoblastic leukemia (ALL)
 11. Prevention of Epstein-Barr virus (EBV)-related PTLD in high risk patients
 12. Immune checkpoint inhibitor-related toxicities
 13. For other compendial uses, refer to Rituxan-Ruxience-Truxima-RA+Other SGM

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Testing or analysis confirming CD20 protein on the surface of the B-cell (if applicable)

III. CRITERIA FOR INITIAL APPROVAL

A. Oncologic indications

Authorization of 12 months may be granted for treatment of any of the following oncologic disorders that are CD20-positive as confirmed by testing or analysis:

1. Non-Hodgkin's Lymphoma (NHL) with any of the following subtypes:
 - a. Diffuse large B-cell lymphoma
 - b. High-grade B-cell lymphoma with translocations of MYC and BCL2 and/or BCL6 (double/triple hit lymphoma)
 - c. High-grade B-cell lymphoma, not otherwise specified
 - d. Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL)
 - e. Follicular lymphoma
 - f. Mantle cell lymphoma
 - g. Marginal zone lymphomas (nodal, splenic, gastric/non-gastric MALT)
 - h. Burkitt lymphoma
 - i. Primary cutaneous B-cell lymphoma
 - j. Castleman's disease
 - k. AIDS-related B-cell lymphoma
 - l. Hairy cell leukemia

- m. Post-transplant lymphoproliferative disorder (PTLD)
- n. B-cell lymphoblastic lymphoma
- 2. Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma (LPL)
- 3. Hodgkin's lymphoma, nodular lymphocyte-predominant
- 4. Central nervous system (CNS) cancers with either of the following:
 - a. Leptomeningeal metastases from lymphomas
 - b. Primary CNS lymphoma
- 5. B-cell acute lymphoblastic leukemia (ALL)

B. Hematologic indications

Authorization of 12 months may be granted for treatment of any of the following indications:

- 1. Refractory immune or idiopathic thrombocytopenic purpura (ITP)
- 2. Autoimmune hemolytic anemia
- 3. Thrombotic thrombocytopenic purpura
- 4. Chronic graft-versus-host disease (GVHD)
- 5. Prevention of Epstein-Barr virus (EBV)-related PTLD

C. Myasthenia gravis

Authorization of 12 months may be granted for treatment of refractory myasthenia gravis.

D. Immune checkpoint inhibitor-related toxicities

Authorization of 3 months may be granted for treatment of immune checkpoint inhibitor-related toxicities.

IV. CONTINUATION OF THERAPY

For oncologic indications: Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an oncologic indication listed in Section III A. who have not experienced an unacceptable toxicity.

For immune checkpoint inhibitor-related toxicities: Authorization of 3 months may be granted for continued treatment in members requesting reauthorization for treatment of immune checkpoint inhibitor-related toxicities who are experiencing benefit from therapy.

For all other indications: Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III B.-C. who are experiencing benefit from therapy.

V. REFERENCES

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Reference number(s)
1704-A

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SPECIALTY GUIDELINE MANAGEMENT

RITUXAN (rituximab) RUXIENCE (rituximab-pvvr) TRUXIMA (rituximab-abbs)

Treatment of Rheumatoid Arthritis and Other Conditions

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Rituxan, Ruxience, and Truxima are indicated for:

1. Granulomatosis with Polyangiitis (GPA) (Wegener's Granulomatosis) and Microscopic Polyangiitis (MPA) in combination with glucocorticoids.
2. Non-Hodgkin's lymphoma (NHL)
(Not addressed in this policy – Refer to Rituxan-Ruxience-Truxima-Oncology SGM)
3. Chronic lymphocytic leukemia (CLL)
(Not addressed in this policy – Refer to Rituxan-Ruxience-Truxima-Oncology SGM)

Rituxan and Truxima are also indicated for:

Rheumatoid Arthritis (RA)

Rituxan or Truxima, in combination with methotrexate, is indicated for the treatment of adult patients with moderately- to severely- active rheumatoid arthritis who have had an inadequate response to one or more TNF antagonist therapies.

Rituxan is also indicated for:

Pemphigus Vulgaris (PV)

Rituxan is indicated for the treatment of adult patients with moderate to severe pemphigus vulgaris.

B. Compendial Uses

1. Sjögren's syndrome
2. Multiple sclerosis, relapsing remitting
3. Neuromyelitis optica (Devic disease)
4. Autoimmune blistering disease
5. Cryoglobulinemia
6. Solid organ transplant
7. Opsoclonus-myoclonus ataxia
8. Systemic lupus erythematosus
9. For other compendial uses, refer to Rituxan-Ruxience-Truxima-Oncology SGM

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

- A. Coverage will not be provided for requests for the treatment of rheumatoid arthritis (RA) when planned date of administration is less than 16 weeks since date of last dose received.
- B. Member will not receive Rituxan, Ruxience, or Truxima with other biologics for RA.
- C. Member will not receive Rituxan, Ruxience, or Truxima with other multiple sclerosis (MS) drugs excluding Ampyra

III. CRITERIA FOR INITIAL APPROVAL

A. Rheumatoid arthritis (RA)

1. Authorization of 12 months may be granted for the treatment of moderately to severely active rheumatoid arthritis (RA) in combination with methotrexate (MTX) unless the member has a contraindication (see V. Appendix) or intolerance to MTX and either of the following criteria are met:
 - a. The member has previously received any biologic disease-modifying antirheumatic drug (DMARD) or targeted synthetic DMARD (e.g., Xeljanz) indicated for the treatment of moderately to severely active rheumatoid arthritis; or
 - b. The member has received at least two full doses of Rituxan, Ruxience, or Truxima for the treatment of RA, where the most recent dose was given within 6 months of the request.
2. Authorization of 12 months may be granted for treatment of moderately to severely active RA in combination with MTX when either of the following criteria are met:
 - a. The member has experienced an inadequate response to at least a 3-month trial of MTX despite adequate dosing (i.e., titrated to 20 mg/week); or
 - b. The member had an intolerable adverse effect or contraindication to MTX (see V. Appendix), and an inadequate response to another conventional DMARD (e.g., hydroxychloroquine, leflunomide, sulfasalazine).

B. Granulomatosis with polyangiitis (GPA) (Wegener's granulomatosis) and microscopic polyangiitis (MPA) and Churg-Strauss and pauciimmune glomerulonephritis

Authorization of 12 months may be granted for treatment of GPA, MPA or and Churg-Strauss and pauciimmune glomerulonephritis.

C. Sjögren's syndrome

Authorization of 12 months may be granted for treatment of Sjögren's syndrome when corticosteroids and other immunosuppressive agents were ineffective.

D. Multiple sclerosis

Authorization of 12 months may be granted for treatment of relapsing remitting multiple sclerosis (MS).

E. Neuromyelitis optica

Authorization of 12 months may be granted for treatment of neuromyelitis optica when at least one other immunotherapy was ineffective.

F. Autoimmune blistering disease

Authorization of 12 months may be granted for treatment of corticosteroid refractory autoimmune blistering disease (e.g., pemphigus vulgaris, pemphigus foliaceus, bullous pemphigoid, cicatricial pemphigoid, epidermolysis bullosa acquisita and paraneoplastic pemphigus).

G. Cryoglobulinemia

Authorization of 12 months may be granted for treatment of cryoglobulinemia when corticosteroids and other immunosuppressive agents were ineffective.

H. Solid organ transplant

Authorization of 3 months may be granted for treatment of solid organ transplant and prevention of antibody mediated rejection in solid organ transplant.

I. Opsoclonus-myoelonus-ataxia

Authorization of 12 months may be granted for treatment of opsoclonus-myoelonus-ataxia associated with neuroblastoma when the member is refractory to steroids and chemotherapy.

J. Systemic Lupus Erythematosus

Authorization of 12 months may be granted for the treatment of systemic lupus erythematosus that is refractory to immunosuppressive therapy.

IV. CONTINUATION OF THERAPY

A. Rheumatoid arthritis

Authorization of 12 months may be granted for continued treatment in all members (including new members) requesting reauthorization who meet all initial authorization criteria and achieve or maintain positive clinical response after at least two doses of therapy with Rituxan, Ruxience, or Truxima as evidenced by low disease activity or improvement in signs and symptoms of the condition.

B. Multiple Sclerosis

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for relapsing remitting multiple sclerosis (MS) who are experiencing disease stability or improvement while receiving Rituxan, Ruxience, or Truxima.

C. Other indications

Authorization of 12 months may be granted for continued treatment in all members (including new members) requesting reauthorization who meet all initial authorization criteria and are receiving benefit from therapy.

V. APPENDIX

Examples of contraindications to methotrexate

- A. Alcoholism, alcoholic liver disease or other chronic liver disease
- B. Breastfeeding
- C. Blood dyscrasias (e.g., bone marrow hypoplasia, thrombocytopenia, leukopenia, significant anemia)
- D. Elevated liver transaminases
- E. Hypersensitivity
- F. Interstitial pneumonitis or clinically significant pulmonary fibrosis
- G. Myelodysplasia
- H. Pregnancy or planning pregnancy (male or female)
- I. Renal impairment
- J. Significant drug interaction

VI. REFERENCES

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22. Ruxience [package insert]. NY, NY: Pfizer Biosimilars; July 2019.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME* (generic)

FINACEA
(azelaic acid)

MIRVASO
(brimonidine)

NORITATE
(metronidazole)

RHOFADE
(oxymetazoline)

SOOLANTRA
(ivermectin)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

Ref # 1486-A

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Finacea

Finacea (azelaic acid) is indicated for topical treatment of inflammatory papules and pustules of mild to moderate rosacea.

Mirvaso

Mirvaso (brimonidine) is indicated for the topical treatment of persistent (non-transient) facial erythema of rosacea in adults 18 years of age or older.

Noritate

Noritate (metronidazole) is indicated for the topical treatment of inflammatory lesions and erythema of rosacea.

Rhofade

Rhofade (oxymetazoline) is indicated for the topical treatment of persistent facial erythema associated with rosacea in adults.

Soolantra

Soolantra (ivermectin) is indicated for the treatment of inflammatory lesions of rosacea.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has a diagnosis of rosacea

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Finacea (azelaic acid) is indicated for topical treatment of inflammatory papules and pustules of mild to moderate rosacea. Noritate is indicated for the topical treatment of inflammatory lesions and erythema of rosacea. Mirvaso (brimonidine) is indicated for the topical treatment of persistent (non-transient) facial erythema of rosacea in adults 18 years of age or older. Rhofade (oxymetazoline) is indicated for the topical treatment of persistent facial erythema associated with rosacea in adults. Soolantra (ivermectin) is indicated for the treatment of inflammatory lesions of rosacea.

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2. Mirvaso [package insert]. Fort Worth, TX: Galderma Labs; June 2018.
3. Noritate [package insert]. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; March 2018.
4. Rhofade [package insert]. Irvine, CA: Allergan; January 2017.
5. Soolantra [package insert]. Fort Worth, TX: Galderma Labs; May 2018.
6. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed June 2019.
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Written by: UM Development (SF)
Date Written: 06/2016
Revised: 09/2016 (added target drugs); MS) 02/2017(added Rhofade), (SF) 06/2017 (no clinical changes), (ME) 06/2018 (no clinical changes), 06/2019 (no clinical changes)
Reviewed: Medical Affairs (LMS) 06/2016, (JG) 02/2017
External Review: 09/2016, 02/2016, 04/2017, 10/2017, 10/2018, 10/2019

CRITERIA FOR APPROVAL

1	Does the patient have the diagnosis of rosacea?	Yes	No
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Mapping Instructions			
	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Approve, 36 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have rosacea. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]

SPECIALTY GUIDELINE MANAGEMENT

ROZLYTREK (entrectinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

1. Solid tumors
Rozlytrek is indicated for the treatment of adult and pediatric patients 12 years and older with solid tumors that:
 - a. have a neurotrophic receptor tyrosine kinase (NTRK) gene fusion without a known acquired resistance mutation,
 - b. are metastatic or where surgical resection is likely to result in severe morbidity, and
 - c. have no satisfactory alternative treatments or that have progressed following treatment.
2. Non-small cell lung cancer
Rozlytrek is indicated for the treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are ROS1-positive.

All other indications are considered experimental/investigational and are not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: NTRK gene fusion status or ROS1 status (where applicable).

III. CRITERIA FOR INITIAL APPROVAL

A. Solid tumors

Authorization of 12 months may be granted for treatment of solid tumors when all of the following criteria are met:

1. The tumors have a NTRK gene fusion without a known acquired resistance mutation, as demonstrated by laboratory testing (e.g., next-generation sequencing [NGS] or fluorescence in situ hybridization [FISH]).
2. The disease is metastatic or surgical resection is likely to result in severe morbidity.
3. No satisfactory alternative treatments are available or the disease has progressed following standard systemic treatment for the disease.

B. Non-small cell lung cancer (NSCLC)

Authorization of 12 months may be granted for treatment of metastatic ROS1-positive NSCLC.

Reference number(s)
3165-A

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication in Section III who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES

1. Rozlytrek [package insert]. South San Francisco, CA: Genentech, Inc. August 2019.

SPECIALTY GUIDELINE MANAGEMENT

RUBRACA (rucaparib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

1. Treatment of adult patients with deleterious BRCA mutation (germline and/or somatic) associated epithelial ovarian, fallopian tube, or primary peritoneal cancer who have been treated with two or more chemotherapies.
2. Maintenance treatment for adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
Documentation of laboratory report confirming BRCA mutation status, where applicable.

III. CRITERIA FOR INITIAL APPROVAL

Epithelial ovarian, fallopian tube, or primary peritoneal cancer

- A. Authorization of 12 months may be granted for treatment of epithelial ovarian, fallopian tube, or primary peritoneal cancer as a single agent when all of the following criteria are met:
 1. Tumor has deleterious BRCA mutation (germline, somatic, or both) as detected by an FDA-approved companion diagnostic test
 2. Member has received two or more prior chemotherapies
- B. Authorization of 12 months may be granted for the maintenance treatment of recurrent disease as a single agent when all of the following criteria are met:
 1. Members is in complete or partial response to platinum based chemotherapy
 2. Member has received at least two prior platinum-containing regimens

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced disease progression or an unacceptable toxicity.

Reference number(s)
2256-A

V. REFERENCES

1. Rubraca [package insert]. Boulder, CO: Clovis Oncology, Inc.; April 2018.

ENHANCED SPECIALTY GUIDELINE MANAGEMENT

RUCONEST (recombinant C1 esterase inhibitor)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Treatment of acute attacks in adults and adolescent patients with hereditary angioedema (HAE)

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

- A. C4 levels and C1 inhibitor functional and antigenic protein levels
- B. F12, angiopoietin-1 or plasminogen gene mutation testing, if applicable
- C. Chart notes confirming family history of angioedema, if applicable

III. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of acute hereditary angioedema attacks when Ruconest will not be used in combination with Berinert, Firazyr, or Kalbitor and either of the following criteria is met:

- A. Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing.
 1. C1 inhibitor (C1-INH) antigenic level below the lower limit of normal as defined by the laboratory performing the test; or
 2. Normal C1-INH antigenic level and a low C1-INH functional level (functional C1-INH less than 50% or C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test)
- B. Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
 1. Member has an F12, angiopoietin-1, or plasminogen gene mutation as confirmed by genetic testing, or
 2. Member has a documented family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine (e.g., cetirizine) for at least one month.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy when all of the following criteria are met:

- A. Member meets the criteria for initial approval.

- B. Member has experienced reduction in severity, and/or duration of attacks when they use the requested medication to treat an acute attack.

V. REFERENCES

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SPECIALTY GUIDELINE MANAGEMENT

RUZURGI (amifampridine)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Ruzurgi is indicated for the treatment of Lambert-Eaton myasthenic syndrome (LEMS) in patients 6 to less than 17 years of age.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of either of the following diagnostic tests is necessary to initiate prior authorization review:

- A. Electromyography (EMG)
- B. Anti-P/Q type voltage-gated calcium channel antibody test

III. EXCLUSIONS

Coverage will not be provided for members with a history of seizures.

IV. CRITERIA FOR INITIAL APPROVAL

Lambert-Eaton Myasthenic Syndrome (LEMS)

Authorization of 6 months may be granted for treatment of Lambert-Eaton myasthenic syndrome (LEMS) when all of the following criteria are met:

- A. Diagnosis is confirmed by either of the following:
 - 1. EMG showing compound muscle action potential (CMAP) that increased at least 2-fold after maximum voluntary contraction of the tested muscle
 - 2. A positive anti- P/Q type voltage-gated calcium channel antibody test
- B. Member has proximal muscle weakness
- C. For treatment-naïve members, the Quantitative Myasthenia Gravis (QMG) score is at least 5

V. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for LEMS who are responding to therapy (i.e., there is stability or improvement in symptoms relative to the natural course of LEMS).

Reference number(s)
3073-A

VI. REFERENCES

1. Ruzurgi [package insert]. Princeton, NJ: Jacobus Pharmaceutical Co, Inc.; May 2019.
2. A Phase 3 Study of Amifampridine Phosphate in Patients With Lambert Eaton Myasthenic Syndrome (LEMS). (2018). Retrieved from <https://clinicaltrials.gov/ct2> (Identification No. NCT01377922)

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS **GLUCAGON-LIKE PEPTIDE 1 (GLP-1) RECEPTOR AGONIST**

BRAND NAME*
(generic)

RYBELSUS
(semaglutide)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

Ref #3318-A

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Rybelsus is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use

- Rybelsus is not recommended as a first-line therapy for patients who have inadequate glycemic control on diet and exercise because of the uncertain relevance of rodent C-cell tumor findings to humans.
- Rybelsus has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.
- Rybelsus is not indicated for use in patients with type 1 diabetes mellitus or for the treatment of patients with diabetic ketoacidosis, as it would not be effective in these settings.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has been receiving GLP-1 Agonist therapy for at least 3 months and has demonstrated a reduction in A1c (hemoglobin A1c) since starting GLP-1 Agonist therapy
[Note: Examples of GLP-1 Agonists are Adlyxin, Bydureon, Byetta, Ozempic, Rybelsus, Tanzeum, Trulicity, Victoza]

OR

- The patient has a diagnosis of type 2 diabetes mellitus
AND
 - The patient has experienced an inadequate treatment response, intolerance or contraindication to metformin
OR
 - The patient requires combination therapy **AND** has an A1c (hemoglobin A1c) of 7.5 percent or greater

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Rybelsus is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Clinical guidelines from the American Diabetes Association and the American Association of Clinical Endocrinologists and American College of Endocrinology for the management of hyperglycemia in type 2 diabetes indicate that metformin monotherapy should be started at diagnosis of type 2 diabetes unless there are contraindications. Metformin is effective and safe, is inexpensive, and may reduce risk of cardiovascular events and death. In patients with contraindications or intolerance of metformin, initial therapy should be based on patient factors; consider a drug from another class.⁴⁻⁵

The clinical guidelines also state that the A1c test is the major tool for assessing glycemic control and has strong predictive value for diabetes complications. Thus, A1c testing should be performed routinely in all patients with diabetes at initial assessment and as part of continuing care. The guidelines set goals for therapeutic effectiveness which must be evaluated frequently (e.g., every 3 months) until stable, using multiple criteria, including A1c. Less frequent monitoring is acceptable once targets are achieved.⁴⁻⁵ Therefore; continued use of any GLP-1 Agonist (e.g., Adlyxin, Bydureon, Byetta, Ozempic, Rybelsus, Tanzeum, Trulicity, and Victoza) will be approved for patients who have demonstrated a reduction in A1c since starting GLP-1 Agonist therapy for at least three months.

If the A1c target is not achieved after approximately 3 months and patient does not have atherosclerotic cardiovascular disease (ASCVD) or chronic kidney disease (CKD), consider a combination of metformin and one of the preferred six treatment options: sulfonylurea, thiazolidinedione, dipeptidyl peptidase 4 (DPP-4) inhibitors, sodium-glucose cotransporter 2 (SGLT2) inhibitors, glucagon-like peptide 1 (GLP-1) receptor agonists, or basal insulin; the choice of which agent to add is based on drug-specific effects and patient factors. For patients in whom ASCVD, Heart Failure, or CKD predominates, the best choice for a second agent is a GLP-1 receptor agonist or SGLT2 inhibitor with demonstrated cardiovascular risk reduction, after consideration of drug-specific and patient factors.⁴⁻⁵

In patients with an initial A1c of 7.5% or greater, or in patients who are unable to achieve their glycemic goals with monotherapy, combination therapy is recommended.⁴⁻⁵

REFERENCES

1. Rybelsus [package insert]. Plainsboro, NJ: Novo Nordisk Inc; September 2019.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed September 2019.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed September 2019.
4. American Diabetes Association (ADA) Standards of Medical Care in Diabetes-2019—*Diabetes Care*. 2019; 42(Supplement 1).
5. Garber AJ, et al. AACE/ACE Consensus Statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the Comprehensive Type 2 Diabetes Management Algorithm 2019, *Endocr Pract*. 2019; 25 (No 1); 69-100.

Written by: UM Development (SF)
 Date Written: 09/2019
 Revised:
 Reviewed: Medical Affairs (CHART) 09/26/2019
 External Review: 10/2019

CRITERIA FOR APPROVAL

1	Has the patient been receiving GLP-1 Agonist therapy for at least 3 months? [Note: Examples of GLP-1 Agonists are Adlyxin, Bydureon, Byetta, Ozempic, Rybelsus, Tanzeum, Trulicity, Victoza] [If no, then skip to question 3.]	Yes	No
2	Has the patient demonstrated a reduction in A1c (hemoglobin A1c) since starting GLP-1 Agonist therapy? [No further questions.]	Yes	No
3	Does the patient have a diagnosis of type 2 diabetes mellitus?	Yes	No
4	Has the patient experienced an inadequate treatment response, intolerance, or contraindication to metformin? [If yes, then no further questions.]	Yes	No

5	Does the patient require combination therapy AND have an A1c (hemoglobin A1c) of 7.5 percent or greater?	Yes	No
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Guidelines for Approval

Duration of Approval 36 Months

Set 1		Set 2		Set 3	
Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)
1	None	3	1	3	1
2		4		5	4

Mapping Instructions

DENIAL REASONS – DO NOT USE FOR MEDICARE PART D			
	Yes	No	
1.	Go to 2	Go to 3	
2.	Approve, 36 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions: - You have been receiving this drug or another drug in the same class for at least 3 months - You had a reduction in A1c (hemoglobin A1c) since starting therapy Your request has been denied based on the information we have. [Short Description: No response to treatment]
3.	Go to 4	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have type 2 diabetes mellitus. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
4.	Approve, 36 months	Go to 5	
5.	Approve, 36 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet one of these conditions: - You have tried metformin and it did not work for you, or you cannot use it - You require combination therapy and you have an A1c (hemoglobin A1c) of 7.5 percent or greater Your request has been denied based on the information we have. [Short description: No inadequate treatment response, intolerance or contraindication to metformin, no requirement for combination therapy]

Reference number
1817-A

SPECIALTY GUIDELINE MANAGEMENT

RYDAPT (midostaurin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Rydapt is indicated, in combination with standard cytarabine and daunorubicin induction and cytarabine consolidation chemotherapy, for the treatment of adult patients with newly diagnosed acute myeloid leukemia (AML) who are FLT3 mutation-positive, as detected by a FDA approved test.

Limitations of Use: Rydapt is not indicated as a single-agent induction therapy for the treatment of patients with AML.

2. Rydapt is indicated for the treatment of adult patients with aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated hematological neoplasm (SM-AHN), or mast cell leukemia (MCL).

B. Compendial Uses

1. Relapsed/refractory AML, as a component of repeating the initial successful induction if late relapse (≥ 12 months)
2. For post-remission therapy for AML, in combination with cytarabine
3. For re-induction of residual disease in AML, in combination with cytarabine and daunorubicin

All other indications are considered experimental/investigational and are not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review (new starts only):
For AML, medical record documentation of FLT3 mutation as detected by an FDA-approved test

III. CRITERIA FOR INITIAL APPROVAL

A. **Acute myeloid leukemia (AML)**

Authorization of 12 months may be granted for the treatment of FLT3 mutation-positive AML when it is not used as a single-agent for induction therapy.

B. **Aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated hematological neoplasm (SM-AHN), and mast cell leukemia (MCL)**

Authorization of 12 months may be granted for the treatment of ASM, SM-AHN, or MCL.

Reference number
1817-A

IV. CONTINUATION OF THERAPY

A. Acute myeloid leukemia (AML)

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization who have not experienced an unacceptable toxicity.

B. Aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated hematological neoplasm (SM-AHN), and mast cell leukemia (MCL)

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES

1. Rydapt [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2019.
2. National Comprehensive Cancer Network. The NCCN Drugs & Biologics Compendium. <http://www.nccn.org>. Accessed July 11, 2019.
3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Acute Myeloid Leukemia. Version 3.2019. https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf. Accessed July 10, 2019.
4. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Mastocytosis. Version 2.2019. https://www.nccn.org/professionals/physician_gls/pdf/mastocytosis.pdf. Accessed July 11, 2019.

SPECIALTY GUIDELINE MANAGEMENT

SAMSCA (tolvaptan)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Treatment of clinically significant hypervolemic and euvolemic hyponatremia (serum sodium <125 mEq/L or less marked hyponatremia that is symptomatic and has resisted correction with fluid restriction), including patients with heart failure and Syndrome of Inappropriate Antidiuretic Hormone (SIADH)

Important Limitations

Patients requiring intervention to raise serum sodium urgently to prevent or to treat serious neurological symptoms should not be treated with Samsca. It has not been established that raising serum sodium with Samsca provides a symptomatic benefit to patients.

All other indications are considered experimental/investigational and are not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Hypervolemic/Euvolemic Hyponatremia

Authorization of 30 days may be granted for members prescribed Samsca when all of the following criteria are met:

- A. Therapy was initiated (or re-initiated) in the hospital, for hypervolemic or euvolemic hyponatremia; and
- B. Serum sodium was less than 125 mEq/L or serum sodium was less than 135 mEq/L with symptoms (e.g., nausea, vomiting, headache, lethargy, confusion) at the time of therapy initiation; and
- C. The member will not receive Samsca continually for greater than 30 days.

III. REFERENCE

1. Samsca [package insert]. Rockville, MD: Otsuka America Pharmaceutical, Inc.; June 2018.

SPECIALTY GUIDELINE MANAGEMENT

SCENESSE (afamelanotide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

A melanocortin 1 receptor (MC1-R) agonist indicated to increase pain free light exposure in adult patients with a history of phototoxic reactions from erythropoietic protoporphyria

All other indications are considered experimental/investigational and are not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
Increased level of protoporphyrin in peripheral red blood cells.

III. CRITERIA FOR INITIAL APPROVAL

Erythropoietic protoporphyria

Authorization of 12 months may be granted for the treatment of biochemically confirmed erythropoietic protoporphyria in adult members who have protoporphyrin above the lab reference range in peripheral red blood cells.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for adult members who are experiencing benefit from therapy while receiving Scenesse.

V. REFERENCES

1. Scenesse [package insert]. West Menlo Park, CA: Clinuvel; October 2019.
2. Scenesse. *Micromedex*. Micromedex [database online]. Truven Health Analytics, Inc. Ann Arbor, MI. Available at <http://www.micromedexsolutions.com>. Accessed October 11, 2019.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

SCENESSE
(afamelanotide)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

MDC
Ref # 3359-A

FDA-APPROVED INDICATIONS¹

SCENESSE

Erythropoietic protoporphyria

Scenesse is a melanocortin 1 receptor (MC1-R) agonist indicated to increase pain free light exposure in adult patients with a history of phototoxic reactions from erythropoietic protoporphyria (EPP).

B vs D CRITERIA FOR DETERMINATION

1	Is the requested drug being supplied from the physician and/or office stock supply and billed as part of a physician service (i.e., the drug is being furnished "incident to a physician's service")? [If yes, no further questions].	Yes	No
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CRITERIA FOR APPROVAL

2	Does the patient have a diagnosis of erythropoietic protoporphyria? [If no, no further questions].	Yes	No
3	Is the patient 18 years of age or older?	Yes	No

Continue to Clinical Questions if:

Guidelines for Determination	
Process through Medicare Part D	
Set 1	
Yes to question(s)	No to question(s)
None	1

For any other scenarios other than the Set above, close PA, drug is not covered as Part D

Approve if:

Guidelines for Approval	
Duration of Approval	12 months
Set 1: Erythropoietic protoporphyria	
Yes to question(s)	No to question(s)
2	None
3	

Mapping Instructions		
	Yes	No
1.	Close PA, drug is not covered as Part D	Go to 2
2.	Go to 3	Deny
3.	Approve, 12 months	Deny

RATIONALE

These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to:

1. Determine if the medication should be processed through Medicare Part D.
2. Ensure that patients follow selection elements noted in labeling and/or practice guidelines in order to decrease the potential for inappropriate utilization.

REFERENCES

1. Scenesse [package insert]. West Menlo Park, CA: Clinuvel; October 2019.
2. Medicare Part B versus Part D Coverage Issues. July 2005. <https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovContra/downloads/BvsDCoverageIssues.pdf> Accessed June 2019.
3. Medicare Prescription Drug Benefit Manual. Chapter 6- Part D Drugs and Formulary Requirements. (Rev. 18, 01-15-16). <https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovContra/Downloads/Part-D-Benefits-Manual-Chapter-6.pdf> Accessed October 2019.

DOCUMENT HISTORY

Created: Specialty Clinical Development (AS) 11/2019
Revised:
Reviewed: CDPR / DNC 10/2019
External Review: 11/2019

SPECIALTY GUIDELINE MANAGEMENT

Subcutaneous Immune Globulin (SCIG):

Hizentra®, HyQvia®, Cutaquig®, Cuvitru™ and Xembify®

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Cutaquig (Immune Globulin Subcutaneous [Human] - hipp, 16.5% Solution)
Cutaquig is indicated as replacement therapy for primary humoral immunodeficiency (PI) in adults.
2. Cuvitru (Immune Globulin Subcutaneous [Human], 20% Solution)
Cuvitru is indicated as replacement therapy for primary humoral immunodeficiency in adult and pediatric patients two years of age and older.
3. Hizentra (Immune Globulin Subcutaneous [Human], 20% Liquid)
 - a. Hizentra is indicated as replacement therapy for primary humoral immunodeficiency in adults and pediatric patients 2 years of age and older.
 - b. Hizentra is indicated for the treatment of adult patients with chronic inflammatory demyelinating polyneuropathy (CIDP) as maintenance therapy to prevent relapse of neuromuscular disability and impairment.
Limitations of Use:
Hizentra maintenance therapy in CIDP has been systematically studied for 6 months and for a further 12 months in a follow-up study. Maintenance therapy beyond these periods should be individualized based upon the patient's response and need for continued therapy.
4. HyQvia (Immune Globulin Infusion 10% [Human] with Recombinant Human Hyaluronidase)
HyQvia is indicated for the treatment of primary immunodeficiency in adults.
Limitation of Use: Safety and efficacy of chronic use of recombinant human hyaluronidase in HyQvia have not been established in conditions other than primary immunodeficiency.
5. Xembify (Immune Globulin Subcutaneous [Human] – klhw, 20% Solution)
Xembify is indicated for treatment of primary humoral immunodeficiency (PI) in patients 2 years of age and older.

B. Compendial Uses

1. Idiopathic thrombocytopenic purpura (ITP)
2. Multifocal motor neuropathy
3. Kawasaki syndrome
4. B-cell chronic lymphocytic leukemia (CLL)
5. Prophylaxis of bacterial infections in pediatric human immunodeficiency virus (HIV) infection
6. Prophylaxis of bacterial infections in bone marrow transplant (BMT)/hematopoietic stem cell transplant (HSCT) recipients
7. Dermatomyositis
8. Polymyositis

Reference number(s)
2043-A

9. Myasthenia gravis
10. Guillain-Barré syndrome
11. Lambert-Eaton myasthenic syndrome
12. Fetal/neonatal alloimmune thrombocytopenia
13. Parvovirus B19-induced pure red cell aplasia
14. Stiff-person syndrome
15. Management of immune checkpoint inhibitor-related nervous system adverse events
16. Acquired red cell aplasia
17. Acute disseminated encephalomyelitis
18. Autoimmune mucocutaneous blistering diseases
19. Autoimmune hemolytic anemia
20. Autoimmune neutropenia
21. Birdshot retinochoroidopathy
22. BK virus associated nephropathy
23. Churg-Strauss Syndrome
24. Enteroviral meningoencephalitis
25. Hematophagocytic lymphohistiocytosis (HLH) or macrophage activation syndrome (MAS)
26. Hemolytic disease of newborn
27. HIV-associated thrombocytopenia
28. Hyperimmunoblobulinemia E Syndrome
29. Hypogammaglobulinemia from chimeric antigen receptor T (CAR-T) therapy
30. Multiple myeloma
31. Neonatal hemochromatosis, prophylaxis
32. Opsoclonus-myoclonus
33. Paraneoplastic opsonus-myoclonus ataxia associated with neuroblastoma
34. Post-transfusion purpura
35. Rasmussen encephalitis
36. Renal transplantation from a live donor with ABO incompatibility or positive cross match
37. Secondary immunosuppression associated with major surgery, hematological malignancy, major burns, and collagen-vascular diseases
38. Solid organ transplantation, for allosensitized members
39. Toxic epidermal necrolysis and Stevens-Johnson syndrome
40. Toxic shock syndrome
41. Systemic lupus erythematosus (SLE)
42. Toxic necrotizing fasciitis due to group A streptococcus

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

The following information is necessary to initiate the prior authorization review:

- A. Primary immunodeficiency
 1. Diagnostic test results (when applicable)
 - a. Copy of laboratory report with serum immunoglobulin levels: IgG, IgA, IgM, and IgG subclasses
 - b. Vaccine response to pneumococcal polysaccharide vaccine (post-vaccination *Streptococcus pneumoniae* antibody titers)
 - c. Pertinent genetic or molecular testing in members with a known genetic disorder
 - d. Copy of laboratory report with lymphocyte subset enumeration by flow cytometry
 2. IgG trough level for those continuing with IG therapy
- B. Myasthenia gravis

1. Clinical records describing standard treatments tried and failed
- C. Secondary hypogammaglobulinemia (CLL, HIV, BMT/HSCT recipients, surgery, malignancy, burns, collagen-vascular disease)
 1. Copy of laboratory report with pre-treatment serum IgG level (when applicable)
- D. Chronic inflammatory demyelinating polyneuropathy (CIDP) and multifocal motor neuropathy (MMN)
 1. Pre-treatment electrodiagnostic studies (electromyography [EMG] or nerve conduction studies [NCS])
 2. For CIDP, pre-treatment cerebrospinal fluid (CSF) analysis (when available)
- E. Dermatomyositis and polymyositis
 1. Pre-treatment electrodiagnostic studies (EMG/NCS)
 2. Pre-treatment muscle biopsy report (when available)
 3. Clinical records describing standard treatments tried and failed
- F. Lambert-Eaton Myasthenic Syndrome (LEMS)
 1. Neurophysiology studies (e.g., electromyography) (when applicable)
 2. A positive anti- P/Q type voltage-gated calcium channel antibody test (when applicable)
- G. Idiopathic thrombocytopenic purpura
 1. Laboratory report with pre-treatment/current platelet count
 2. Chronic/persistent ITP: copy of medical records supporting trial and failure with corticosteroid or anti-D therapy (unless contraindicated)
- H. Parvovirus B19-indicated Pure Red Cell Aplasia (PRCA)
 1. Copy of test result confirming presence of parvovirus B19
- I. Stiff-person syndrome
 1. Anti-glutamic acid decarboxylase (GAD) antibody testing results
 2. Clinical records describing standard treatments tried and failed
- J. Toxic shock syndrome or toxic necrotizing fasciitis due to group A streptococcus
 1. Documented presence of fasciitis (when applicable)
 2. Microbiological data (culture or Gram stain)

III. CRITERIA FOR INITIAL APPROVAL

A. Primary Immunodeficiency

Initial authorization of 6 months may be granted for members with any of the following diagnoses:

1. Severe combined immunodeficiency (SCID) or congenital agammaglobulinemia (eg, X-linked or autosomal recessive agammaglobulinemia)
 - a. Diagnosis confirmed by genetic or molecular testing, or
 - b. Pretreatment IgG level < 200 mg/dL, or
 - c. Absence or very low number of T cells (CD3 T cells < 300/microliter) or the presence of maternal T cells in the circulation (SCID only)
2. Wiskott-Aldrich syndrome, DiGeorge syndrome, or ataxia-telangiectasia (or other non-SCID combined immunodeficiency)
 - a. Diagnosis confirmed by genetic or molecular testing (if applicable), and
 - b. History of recurrent bacterial infections (eg, pneumonia, otitis media, sinusitis, sepsis, gastrointestinal), and
 - c. Impaired antibody response to pneumococcal polysaccharide vaccine (see Appendix A)
3. Common variable immunodeficiency (CVID)
 - a. Age 4 years or older, and
 - b. Other causes of immune deficiency have been excluded (eg, drug induced, genetic disorders, infectious diseases such as HIV, malignancy), and
 - c. Pretreatment IgG level < 500 mg/dL or ≥ 2 SD below the mean for age, and
 - d. History of recurrent bacterial infections, and

- e. Impaired antibody response to pneumococcal polysaccharide vaccine (see Appendix A)
- 4. Hypogammaglobulinemia (unspecified), IgG subclass deficiency, selective IgA deficiency, selective IgM deficiency, or specific antibody deficiency
 - a. History of recurrent bacterial infections
 - b. Impaired antibody response to pneumococcal polysaccharide vaccine (see Appendix A)
 - c. Any of the following pre-treatment laboratory findings:
 - i. Hypogammaglobulinemia: IgG < 500 mg/dL or ≥ 2 SD below the mean for age
 - ii. Selective IgA deficiency: IgA level < 7 mg/dL with normal IgG and IgM levels
 - iii. Selective IgM deficiency: IgM level < 30 mg/dL with normal IgG and IgA levels
 - iv. IgG subclass deficiency: IgG1, IgG2, or IgG3 ≥ 2 SD below mean for age assessed on at least 2 occasions; normal IgG (total) and IgM levels, normal/low IgA levels
 - v. Specific antibody deficiency: normal IgG, IgA and IgM levels
- 5. Other predominant antibody deficiency disorders must meet a., b., and c.i. in section 4. above.
- 6. Other combined immunodeficiency must meet criteria in section 2. above.

Re-authorization of 6 months may be granted when the following criteria are met:

- 1. A reduction in the frequency of bacterial infections has been demonstrated since initiation of IG therapy, AND
- 2. IgG trough levels are monitored at least yearly and maintained at or above the lower range of normal for age (when applicable for indication), OR
- 3. The prescriber will re-evaluate the dose of IG and consider a dose adjustment (when appropriate).

B. Myasthenia Gravis

- 1. Authorization of 1 month may be granted to members who are prescribed IG for worsening weakness, acute exacerbation, or in preparation for surgery.
 - a. Worsening weakness includes an increase in any of the following symptoms: diplopia, ptosis, blurred vision, difficulty speaking (dysarthria), difficulty swallowing (dysphagia), difficulty chewing, impaired respiratory status, fatigue, and limb weakness. Acute exacerbations include more severe swallowing difficulties and/or respiratory failure
 - b. Pre-operative management (eg, prior to thymectomy)
- 2. Authorization of 6 months may be granted to members with refractory myasthenia gravis who have tried and failed 2 or more of standard therapies (eg, corticosteroids, azathioprine, cyclosporine, mycophenolate mofetil, rituximab).

C. Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

- 1. Initial authorization of 3 months may be granted when the following criteria are met:
 - a. Disease course is progressive or relapsing/remitting for 2 months or longer
 - b. Moderate to severe functional disability
 - c. The diagnosis was confirmed by electrodiagnostic studies and the evaluation of cerebrospinal fluid (CSF)
- 2. Re-authorization of 6 months may be granted when the following criteria are met:
 - a. Significant improvement in disability and maintenance of improvement since initiation of IG therapy
 - b. IG is being used at the lowest effective dose and frequency

D. Dermatomyositis or Polymyositis

- 1. Initial authorization of 3 months may be granted when the following criteria are met:
 - a. Member has at least 4 of the following:
 - i. Proximal muscle weakness (upper or lower extremity and trunk)
 - ii. Elevated serum creatine kinase (CK) or aldolase level

- iii. Muscle pain on grasping or spontaneous pain
 - iv. Myogenic changes on EMG (short-duration, polyphasic motor unit potentials with spontaneous fibrillation potentials)
 - v. Positive anti-Jo-1 (histadyl tRNA synthetase) antibody
 - vi. Non-destructive arthritis or arthralgias
 - vii. Systemic inflammatory signs (fever: more than 37°C at axilla, elevated serum CRP level or accelerated ESR of more than 20 mm/h by the Westergren method,
 - viii. Pathological findings compatible with inflammatory myositis (inflammatory infiltration of skeletal evidence of active regeneration may be seen), and
 - b. Standard first-line treatments (corticosteroids) and second-line treatments (immunosuppressants) have been tried but were unsuccessful or not tolerated, or
 - c. Member is unable to receive standard first-line and second-line therapy because of a contraindication or other clinical reason.
2. Re-authorization of 6 months may be granted when the following criterion is met:
- a. Significant improvement in disability and maintenance of improvement since initiation of IG therapy

E. Idiopathic Thrombocytopenic Purpura (Immune Thrombocytopenia)

1. Newly diagnosed ITP (diagnosed within the past 3 months) or initial therapy: authorization of 1 month may be granted when the following criteria are met
 - a. Children (< 18 years of age)
 - i. Significant bleeding symptoms (mucosal bleeding or other moderate/severe bleeding) or
 - ii. High risk for bleeding* (see Appendix B), or
 - iii. Rapid increase in platelets is required* (eg, surgery or procedure)
 - b. Adults (≥ 18 years of age)
 - i. Platelet count < 30,000/mcL, or
 - ii. Platelet count < 50,000/mcL and significant bleeding symptoms, high risk for bleeding or rapid increase in platelets is required*, and
 - iii. Corticosteroid therapy is contraindicated and IG will be used alone or IG will be used in combination with corticosteroid therapy
2. Chronic/persistent ITP (≥ 3 months from diagnosis) or ITP unresponsive to first-line therapy: authorization of 6 months may be granted when the following criteria are met:
 - a. Platelet count < 30,000/mcL, or
 - b. Platelet count < 50,000/mcL and significant bleeding symptoms, high risk for bleeding* or rapid increase in platelets is required*, and
 - c. Relapse after previous response to IG or inadequate response/intolerance/contraindication to corticosteroid or anti-D therapy
3. Adults with refractory ITP after splenectomy: authorization of 6 months may be granted when either of the following criteria is met:
 - a. Platelet count < 30,000/mcL, or
 - b. Significant bleeding symptoms
4. ITP in pregnant women: authorization through delivery may be granted to pregnant women with ITP.

* The member's risk factor(s) for bleeding (see Appendix B) or reason requiring a rapid increase in platelets must be provided.

F. B-cell Chronic Lymphocytic Leukemia (CLL)

1. Initial authorization of 6 months may be granted when all of the following criteria are met:
 - a. IG is prescribed for prophylaxis of bacterial infections.

- b. Member has a history of recurrent sinopulmonary infections requiring intravenous antibiotics or hospitalization.
- c. Member has a pretreatment serum IgG level <500 mg/dL.
- 2. Re-authorization of 6 months may be granted when a reduction in the frequency of bacterial infections has been demonstrated since initiation of IG therapy.

G. Prophylaxis of Bacterial Infections in HIV-Infected Pediatric Patients

- 1. Initial authorization of 6 months may be granted to pediatric members with HIV infection when any of the following criteria are met:
 - a. IG is prescribed for primary prophylaxis of bacterial infections and pretreatment serum IgG < 400 mg/dL, or
 - b. IG is prescribed for secondary prophylaxis of bacterial infections for members with a history of recurrent bacterial infections (> 2 serious bacterial infections in a 1-year period), or
 - c. Member has failed to form antibodies to common antigens, such as measles, pneumococcal, and/or Haemophilus influenzae type b vaccine, or
 - d. Member lives in an area where measles is highly prevalent and who have not developed an antibody response after two doses of measles, mumps, and rubella virus vaccine live, or
 - e. Member has been exposed to measles and request is for a single dose, or
 - f. Member has chronic bronchiectasis that is suboptimally responsive to antimicrobial and pulmonary therapy
- 2. Re-authorization of 6 months may be granted when a reduction in the frequency of bacterial infections has been demonstrated since initiation of IG therapy.

H. Prophylaxis of Bacterial Infections in BMT/HSCT Recipients

- 1. Initial authorization of 6 months may be granted to members who are BMT/HSCT recipients when the following criteria are met:
 - a. IG is prescribed for prophylaxis of bacterial infections.
 - b. Either of the following:
 - i. IG is requested within the first 100 days post-transplant.
 - ii. Member has a pretreatment serum IgG < 400 mg/dL.
- 2. Re-authorization of 6 months may be granted when a reduction in the frequency of bacterial infections has been demonstrated since initiation of IG therapy.

I. Multifocal Motor Neuropathy (MMN)

- 1. Initial authorization of 3 months may be granted when the following criteria are met:
 - a. Member experienced progressive, multifocal, asymmetrical weakness without objective sensory loss in 2 or more nerves for at least 1 month
 - b. The diagnosis was confirmed by electrodiagnostic studies
- 2. Re-authorization of 6 months may be granted when significant improvement in disability and maintenance of improvement have occurred since initiation of IG therapy

J. Guillain-Barre Syndrome (GBS)

Authorization of 2 months total may be granted for GBS when the following criteria are met:

- 1. Member has severe disease with significant weakness (eg inability to stand or walk without aid, respiratory weakness)
- 2. Onset of neurologic symptoms occurred less than 4 weeks from the anticipated start of therapy

K. Lambert-Eaton Myasthenic Syndrome (LEMS)

- 1. Initial authorization of 6 months may be granted for LEMS when the following criteria are met:
 - a. Diagnosis has been confirmed by either of the following:
 - i. Neurophysiology studies (e.g., electromyography)

- ii. A positive anti- P/Q type voltage-gated calcium channel antibody test
 - b. Anticholinesterases (eg pyridostigmine) and amifampridine (eg 3,4-diaminopyridine phosphate, Firdapse) have been tried but were unsuccessful or not tolerated
 - c. Weakness is severe or there is difficulty with venous access for plasmapheresis
 - 2. Re-authorization of 6 months may be granted when member is responding to therapy (i.e., there is stability or improvement in symptoms relative to the natural course of LEMS).
- L. Kawasaki Syndrome**
Authorization of 1 month may be granted for pediatric members with Kawasaki syndrome.
- M. Fetal/Neonatal Alloimmune Thrombocytopenia (F/NAIT)**
Authorization of 6 months may be granted for treatment of F/NAIT.
- N. Parvovirus B19-induced Pure Red Cell Aplasia (PRCA)**
Authorization of 6 months may be granted for severe, refractory anemia associated with bone marrow suppression, with parvovirus B19 viremia.
- O. Stiff-person Syndrome**
Authorization of 6 months may be granted for stiff-person syndrome when the following criteria are met:
- 1. Diagnosis has been confirmed by anti-glutamic acid decarboxylase (GAD) antibody testing
 - 2. Member had an inadequate response to first-line treatment (benzodiazepines and/or baclofen)
- P. Management of immune checkpoint inhibitor-related nervous system adverse events**
Authorization of 1 month may be granted for management of immune checkpoint-inhibitor toxicities when all of the following criteria are met:
- 1. Member has experienced a moderate or severe adverse event to a PD-1 or PD-L1 inhibitor (eg, pembrolizumab, nivolumab, atezolizumab, avelumab, durvalumab)
 - 2. The offending medication has been held or discontinued
 - 3. Member experienced one or more of the following nervous system adverse events: pneumonitis, myasthenia gravis, peripheral neuropathy, encephalitis, transverse myelitis, or severe inflammatory arthritis
- Q. Acquired Red Cell Aplasia**
Authorization of 6 months may be granted for acquired red cell aplasia.
- R. Acute Disseminated Encephalomyelitis**
Authorization of 6 months may be granted for acute disseminated encephalomyelitis in members who have had an insufficient response to intravenous corticosteroid treatment.
- S. Autoimmune Mucocutaneous Blistering Disease**
Authorization of 6 months may be granted for autoimmune mucocutaneous blistering disease (includes pemphigus vulgaris, pemphigus foliaceus, bullous pemphigoid, mucous membrane pemphigoid, and epidermolysis bullosa aquisita) when the following criteria are met:
- 1. Diagnosis has been proven by biopsy and confirmed by pathology report, and
 - 2. Condition is rapidly progressing, extensive or debilitating, and
 - 3. Member has failed or experienced significant complications (eg diabetes, steroid-induced osteoporosis) from standard treatment (corticosteroids, immunosuppressive agents).
- T. Autoimmune Hemolytic Anemia**
Authorization of 6 months may be granted for warm-type autoimmune hemolytic anemia in members who do not respond or have a contraindication to corticosteroids or splenectomy.

- U. Autoimmune Neutropenia**
Authorization of 6 months may be granted for autoimmune neutropenia where treatment with G-CSF (granulocyte colony stimulating factor) is not appropriate.
- V. Birdshot Retinochoroidopathy**
Authorization of 6 months may be granted for birdshot (vitiliginous) retinochoroidopathy that is not responsive to immunosuppressives (eg corticosteroids, cyclosporine).
- W. BK Virus Associated Nephropathy**
Authorization of 6 months may be granted for BK virus associated nephropathy.
- X. Churg-Strauss Syndrome**
Authorization of 6 months may be granted for severe, active Churg-Strauss syndrome as adjunctive therapy for members who have experienced failure, intolerance, or are contraindicated to other interventions.
- Y. Enteroviral Meningoencephalitis**
Authorization of 6 months may be granted for severe cases of enteroviral meningoencephalitis.
- Z. Hematophagocytic Lymphohistiocytosis (HLH) or Macrophage Activation Syndrome (MAS)**
Authorization of 6 months may be granted for treatment of hypogammaglobulinemia in HLH or MAS when total IgG is less than 400 mg/dL or two standard deviations below the mean for age.
- AA. Hemolytic Disease of Newborn**
Authorization of 6 months may be granted for isoimmune hemolytic disease in neonates.
- BB. HIV-associated Thrombocytopenia**
Authorization of 6 months may be granted for HIV-associated thrombocytopenia when the following criteria are met:
 1. Pediatric members with IgG < 400 mg/dL and has one of the following:
 - a. 2 or more bacterial infections in a 1-year period despite antibiotic chemoprophylaxis with TMP-SMZ or another active agent, or
 - b. Received 2 doses or measles vaccine and lives in a region with a high prevalence or measles, or
 - c. HIV-associated thrombocytopenia despite anti-retroviral therapy, or
 - d. Chronic bronchiectasis that is suboptimally responsive to antimicrobial and pulmonary therapy, or
 - e. T4 cell count $\geq 200/\text{mm}^3$
 2. Adult members with significant bleeding, platelet count < 20,000/mcL, and failure of RhIG in Rh-positive patients
- CC. Hyperimmunoglobulinemia E Syndrome**
Authorization of 6 months may be granted to treat severe eczema in hyperimmunoglobulinemia E syndrome.
- DD. Hypogammaglobulinemia from CAR-T therapy**
Authorization of 6 months may be granted for members with IgG < 400 mg/dL receiving treatment with CAR-T therapy (tisagenlecleucel [Kymriah] or axicabtagene ciloleucel [Yescarta]).
- EE. Multiple Myeloma**

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Authorization of 6 months may be granted for multiple myeloma in members who have recurrent, serious infections despite the use of prophylactic antibiotics.

FF. Neonatal Hemochromatosis

Authorization of 6 months may be granted for prophylaxis in members who are pregnant with a history of pregnancy ending in documented neonatal hemochromatosis.

GG. Opsoclonus-myoclonus

Authorization of 6 months may be granted for treatment of either of the following:

1. Paraneoplastic opsoclonus-myoclonus-ataxia associated with neuroblastoma
2. Refractory opsoclonus-myoclonus, as last-resort treatment

HH. Post-transfusion Purpura

Authorization of 1 month may be granted for post-transfusion purpura.

II. Rasmussen Encephalitis

Authorization of 6 months may be granted for Rasmussen encephalitis in members whose symptoms do not improve with anti-epileptic drugs and corticosteroids.

JJ. Renal Transplantation

Authorization of 6 months may be granted for a member undergoing renal transplantation from a live donor with ABO incompatibility or positive cross match.

KK. Secondary Immunosuppression Associated with Major Surgery, Hematological Malignancy, Major Burns, and Collagen-Vascular Diseases

Authorization of 6 months may be granted to prevent or modify recurrent bacterial or viral infections in members with secondary immunosuppression (IgG < 400 mg/dL) associated with major surgery, hematological malignancy, extensive burns, or collagen-vascular disease.

LL. Solid Organ Transplantation

Authorization of 6 months may be granted for solid organ transplantation for allosensitized members.

MM. Toxic Epidermal Necrolysis and Stevens-Johnson Syndrome

Authorization of 1 month may be granted for severe cases of toxic epidermal necrolysis or Stevens-Johnson syndrome.

NN. Toxic Shock Syndrome

Authorization of 1 month may be granted for staphylococcal or streptococcal toxic shock syndrome when the infection is refractory to several hours of aggressive therapy, an undrainable focus is present, or the member has persistent oliguria with pulmonary edema.

OO. Systemic Lupus Erythematosus

Authorization of 6 months may be granted for severe, active SLE in members who have experienced inadequate response, intolerance or have a contraindication to first and second line therapies.

PP. Toxic Necrotizing Fasciitis Due To Group A Streptococcus

Authorization of 1 month may be granted for members with fasciitis due to invasive streptococcal infection.

IV. CONTINUATION OF THERAPY

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Authorization may be granted for continuation of therapy when either the following criteria is met:

- A. For conditions with reauthorization criteria listed under section III: Members who are currently receiving IG therapy must meet the applicable reauthorization criteria for the member's condition.
- B. For all other conditions, all members (including new members) must meet initial authorization criteria.

V. APPENDICES

Appendix A: Impaired Antibody Response to Pneumococcal Polysaccharide Vaccine

- Age 2 years and older: impaired antibody response demonstrated to vaccination with a pneumococcal polysaccharide vaccine
- Not established for children less than 2 years of age
- Excludes the therapy initiated in the hospital setting

Appendix B: Examples of Risk Factors for Bleeding (not all inclusive)

- Undergoing a medical or dental procedure where blood loss is anticipated
- Comorbidity (eg, peptic ulcer disease, hypertension)
- Mandated anticoagulation therapy
- Profession or lifestyle predisposes patient to trauma (eg, construction worker, fireman, professional athlete)

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PRIOR AUTHORIZATION CRITERIA

CLASS SELECT ARTIFICIAL SALIVA MEDICAL DEVICES

PRODUCT NAME
(brand/generic)

SELECT ARTIFICIAL SALIVA MEDICAL DEVICES RX ONLY
[Use RxClaim List ID CMKJMED001 for target list]

Status: CVS Caremark Criteria

Type: Initial Prior Authorization

Ref # 2506-A

INDICATIONS¹⁻⁸

Artificial Saliva Medical Devices

- Indicated for dryness of the mouth or throat (hyposalivation, xerostomia, mucositis)
- Indicated for dryness of the oral mucosa due to drugs such as antihistamines or atropine or other anticholinergic agents that suppress salivary secretion
- May be used as part of an oral hygiene program for patients with dry mouth, also provides intensive hygiene of the oral cavity
- Indicated as an adjunct to standard oral care in relieving the discomfort associated with oral mucositis that may be caused by radiation or high dose chemotherapy. Relief of dryness of the oral mucosa in these conditions is associated with amelioration of pain.
- May be used for relief of dryness of the oral mucosa when hyposalivation results from any of the following: surgery, radiotherapy, chemotherapy, infection or dysfunction of the salivary glands, inflammation of the mouth or throat, fever, emotional factors such as fear or anxiety, obstruction of the salivary ducts, Bell's Palsy, Sjogren's syndrome
- Provide relief from dry mouth due to certain diseases, medication use, inflammation, medication, chemo or radiotherapy, stress or aging. Relieves symptoms of dry mouth such as difficulties in swallowing, speech, and changes in taste.
- Relieves the symptoms of dry mouth by enhancing swallowing, improving speech mechanics, and lubricating the oral cavity like natural saliva.

COVERAGE CRITERIA

The requested medical device will be covered with prior authorization when the following criteria are met:

- The medical device is being prescribed for dryness of the oral mucosa

AND

- The patient experienced an inadequate response, intolerance, or contraindication to all over-the-counter (OTC) artificial salivas (e.g. Biotene, MouthKote, Oasis, Xylimelts)

AND

- The patient experienced an inadequate treatment response, intolerance, or contraindication to FDA-approved salivary stimulant drugs (pilocarpine/Salagen, cevimeline/Evoxac)

OR

- FDA-approved salivary stimulant drugs (pilocarpine/Salagen, cevimeline/Evoxac) are not indicated for the patient's medical condition

RATIONALE

The intent of the criteria is to ensure that patients follow selection elements noted in labeling in order to decrease the potential for inappropriate utilization and to confirm the appropriate coverage of select artificial saliva medical devices. A medical device is an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part or accessory which is:

- recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them

- intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, or
- intended to affect the structure or any function of the body, and which does not achieve any of its primary intended purposes through chemical action within or on the body and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes.⁹

This policy is intended to ensure that select artificial saliva medical devices are utilized in accordance with indications or uses within the manufacturer's guidelines and to foster cost-effective, first-line use of available FDA-approved medications and OTC products. If the patient has dryness of the oral mucosa and has experienced an inadequate treatment response, intolerance, or contraindication to all over-the-counter (OTC) artificial salivas, and to prescription salivary stimulants or prescription salivary stimulants are not indicated for the patient's medical condition, the prior authorization will be approved. If criteria for coverage are met, the requested artificial saliva will be approved for 12 months.

Artificial saliva is indicated as an adjunct to standard oral care in relieving the discomfort associated with oral mucositis that may be caused by radiation or high dose chemotherapy. Relief of dryness of the oral mucosa in these conditions is associated with amelioration of pain. Artificial saliva may be used for relief of dryness of the oral mucosa when hyposalivation results from the following: surgery, radiotherapy near the salivary glands, chemotherapy, infection or dysfunction of the salivary glands, inflammation of the mouth or throat, fever, emotional factors such as fear or anxiety, obstruction of the salivary ducts, Sjogren's syndrome.¹⁻⁴

Pilocarpine (Salagen) tablets are indicated for: the treatment of symptoms of dry mouth from salivary gland hypofunction caused by radiotherapy for cancer of the head and neck; and the treatment of symptoms of dry mouth in patients with Sjogren's Syndrome.⁹ Cevimeline (Evoxac) is indicated for the treatment of symptoms of dry mouth in patients with Sjogren's Syndrome.¹⁰

Biotene Oral Balance Gel, Biotene Dry Mouth Oral Rinse and Biotene Moisturizing Mouth Spray are over-the-counter (OTC) artificial salivas intended to relieve the symptoms of dry mouth, refresh, moisturize, clean, soothe oral irritation and lubricate oral dryness.⁵ Under the supervision of a healthcare professional, Oasis dry mouth relief discs have been formulated for the relief of chronic and temporary xerostomia (dry mouth), which may be a result of diseases such as Sjogren's Syndrome, oral inflammation, medication, chemo or radiotherapy, stress or aging. Oasis mouth moisturizing discs have been formulated for relief of dry mouth symptoms such as difficulties in swallowing, speech and changes in taste. These symptoms may be brought on by disease, stress, aging or medication.⁶ MouthKote relieves dry mouth conditions.⁷ Xylimelts helps stimulate saliva, helps coat, moisturize and lubricate, promotes comfortable sleeping, may help reduce risk of cavities, and helps freshen breath.⁸

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Written by: UM Development (AJ/JK/TM/KC)
 Date Written: 02/2018
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 Reviewed: Medical Affairs (SD) 05/2018; (AN) 05/2019
 MDCCommittee 05/2018, 05/2019

CRITERIA FOR APPROVAL

1	Is the requested medical device being prescribed for dryness of the oral mucosa?	Yes	No
2	Has the patient experienced an inadequate response, intolerance, or contraindication to all over-the-counter (OTC) artificial salivas (e.g. Biotene, MouthKote, Oasis, Xylimelts)?	Yes	No
3	Has the patient experienced an inadequate treatment response, intolerance, or contraindication to FDA-approved salivary stimulant drugs (pilocarpine/Salagen, cevimeline/Evoxac)? [If yes, then no further questions.]	Yes	No
4	Are FDA-approved salivary stimulant drugs (pilocarpine/Salagen, cevimeline/Evoxac) indicated for the patient's medical condition?	Yes	No

Mapping Instructions			
	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this medical device when you have dry mouth. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
2.	Go to 3	Deny	You do not meet the requirements of your plan. Your plan covers this medical device when you meet any of these conditions: - You tried all over-the-counter (OTC) artificial salivas (e.g. Biotene, MouthKote, Oasis, Xylimelts) and they did not work for you - You cannot use OTC artificial salivas (e.g. Biotene, MouthKote, Oasis, Xylimelts) Your request has been denied based on the information we have. [Short Description: No inadequate response, intolerance or contraindication to OTC artificial salivas]
3.	Approve, 12 Months	Go to 4	
4.	Deny	Approve, 12 Months	You do not meet the requirements of your plan. Your plan covers this medical device when you meet any of these conditions: - You have tried FDA-approved salivary stimulant drugs (pilocarpine/Salagen, cevimeline/Evoxac) and they did not work for you - You cannot use FDA-approved salivary stimulant drugs (pilocarpine/Salagen, cevimeline/Evoxac) - FDA-approved salivary stimulant drugs (pilocarpine/Salagen, cevimeline/Evoxac) are not used for your medical condition Your request has been denied based on the information we have. [Short Description: No inadequate response, intolerance or contraindication to FDA-approved salivary stimulant drugs (pilocarpine, cevimeline)]

SPECIALTY GUIDELINE MANAGEMENT

SENSIPAR (cinacalcet)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Secondary hyperparathyroidism (HPT) in adult patients with chronic kidney disease (CKD) on dialysis
2. Hypercalcemia in adult patients with parathyroid carcinoma
3. Hypercalcemia in adult patients with primary HPT for whom parathyroidectomy would be indicated on the basis of serum calcium levels, but who are unable to undergo parathyroidectomy

B. Compendial Use

Tertiary hyperparathyroidism in post-kidney transplant patients not receiving dialysis

All other indications are considered experimental/investigational and are not medically necessary.

II. INITIAL CRITERIA FOR APPROVAL

A. **Secondary Hyperparathyroidism with CKD on Dialysis**

Authorization of 12 months may be granted for treatment of secondary hyperparathyroidism in a member with chronic kidney disease on dialysis who has a serum calcium level (corrected for albumin) greater than or equal to 8.4 mg/dL (see Appendix).

B. **Primary Hyperparathyroidism**

Authorization of 12 months may be granted for treatment of primary hyperparathyroidism in a member who is not able to undergo parathyroidectomy and has a serum calcium level (corrected for albumin) greater than or equal to 8.4 mg/dL (see Appendix).

C. **Tertiary Hyperparathyroidism in Post-Kidney Transplant Patients Not Receiving Dialysis**

Authorization of 12 months may be granted for treatment of tertiary hyperparathyroidism in a member who has had a kidney transplant, is not receiving dialysis, and has a serum calcium level (corrected for albumin) greater than or equal to 8.4 mg/dL (see Appendix).

D. **Parathyroid Carcinoma**

Authorization of 12 months may be granted for the treatment of parathyroid carcinoma in a member who has a serum calcium level (corrected for albumin) greater than or equal to 8.4 mg/dL (see Appendix).

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when the following criteria are met:

Reference number(s)
1624-A

A. Secondary Hyperparathyroidism with CKD on Dialysis

Member is experiencing benefit from therapy as evidenced by a decrease in intact parathyroid hormone (iPTH) levels from pretreatment baseline.

B. All other indications

Member is experiencing benefit from therapy (e.g., decreased or normalized corrected serum calcium levels since starting therapy).

IV. APPENDIX

Corrected calcium = measured total calcium + 0.8(4.0 – serum albumin)

V. REFERENCES

1. Sensipar [package insert]. Thousand Oaks, CA: Amgen, Inc.; March 2019.
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SPECIALTY GUIDELINE MANAGEMENT

SEROSTIM (somatropin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Serostim is indicated for the treatment of HIV patients with wasting or cachexia to increase lean body mass and body weight, and improve physical endurance. Concomitant antiretroviral therapy is necessary.

All other indications are considered experimental/investigational and are not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Treatment of HIV patients with wasting or cachexia to increase lean body mass and body weight, and improve physical endurance.

Authorization of 12 weeks may be granted when all of the following criteria are met:

- A. Member is diagnosed with HIV-associated wasting/cachexia
- B. Member is currently on antiretroviral therapy
- C. Trial with suboptimal response to alternative therapies (See Appendix A) or contraindication or intolerance to alternative therapies
- D. BMI was less than 18.5 kg/m² prior to initiating therapy with Serostim (See Appendix B)

III. CONTINUATION OF THERAPY

Treatment of HIV patients with wasting or cachexia to increase lean body mass and body weight, and improve physical endurance.

Authorization of 12 weeks may be granted when all of the following criteria are met:

- A. Member is diagnosed with HIV-associated wasting/cachexia
- B. Member is currently on antiretroviral therapy
- C. Member is currently receiving treatment with Serostim excluding obtainment as samples or via manufacturer's patient assistance programs
- D. Current BMI is less than 27 kg/m² (See Appendix B)

IV. APPENDICES

Appendix A – Alternative therapies for HIV Wasting

- Cyproheptadine
- Marinol (dronabinol)
- Megace (megestrol acetate)
- Testosterone therapy if hypogonadal

Appendix B – Calculation of BMI and IBW

$$\text{BMI} = \frac{\text{Weight (pounds)} \times 703}{[\text{Height (inches)}]^2} \quad \text{OR} \quad \frac{\text{Weight (kg)}}{[\text{Height (m)}]^2}$$

BMI classification:	Underweight	< 18.5 kg/m ²
	Normal weight	18.5 – 24.9 kg/m ²
	Overweight	25 – 29.9 kg/m ²
	Obesity (class 1)	30 – 34.9 kg/m ²
	Obesity (class 2)	35 – 39.9 kg/m ²
	Extreme obesity	≥ 40 kg/m ²

V. REFERENCES

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SPECIALTY GUIDELINE MANAGEMENT

SIGNIFOR (pasireotide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Signifor is indicated for the treatment of adult patients with Cushing's disease for whom pituitary surgery is not an option or has not been curative.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

- A. For initial requests: pretreatment urinary free cortisol level
- B. For continuation of therapy: current urinary free cortisol level

III. CRITERIA FOR APPROVAL

Cushing's syndrome/disease

Authorization of 6 months may be granted for the treatment of Cushing's disease/syndrome in members who either have had surgery that was not curative OR for members who are not a candidates for surgery.

IV. CONTINUATION OF THERAPY

Cushing's syndrome/disease

Authorization of 12 months for continuation of therapy may be granted if the member has lower urinary free cortisol levels since the start of therapy or has improvement in signs or symptoms of the disease.

V. REFERENCES

1. Signifor [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; January 2019.
2. Nieman LK, Biller B, Findling JW, et al. Treatment of Cushing's Syndrome: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*. 2015;100:2807-2831.

SPECIALTY GUIDELINE MANAGEMENT

SIGNIFOR LAR (pasireotide injectable suspension)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

1. Treatment of patients with acromegaly who have had an inadequate response to surgery and/or for whom surgery is not an option
2. Treatment of patients with Cushing's disease for whom pituitary surgery is not an option or has not been curative

All other indications are considered experimental/investigational and are not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

- A. For acromegaly:
 1. For initial approval: Laboratory report indicating high pretreatment insulin-like growth factor-1 (IGF-1) level and chart notes indicating an inadequate or partial response to surgery or a clinical reason for not having surgery.
 2. For continuation: Laboratory report indicating normal current IGF-1 levels or chart notes indicating that the member's IGF-1 level has decreased or normalized since initiation of therapy
- B. Cushing's syndrome: Chart notes indicating that surgery is not an option for the member or was not curative.

III. CRITERIA FOR INITIAL APPROVAL

A. Acromegaly

Authorization of 12 months may be granted for the treatment of acromegaly when all of the following criteria are met:

1. Member has a high pretreatment IGF-1 level for age and/or gender based on the laboratory reference range.
2. Member had an inadequate or partial response to surgery OR there is a clinical reason why the member has not had surgery.

B. Cushing's syndrome/disease

Authorization of 12 months may be granted for the treatment of Cushing's disease/syndrome when the member has had surgery that was not curative OR the member is not a candidate for surgery.

IV. CONTINUATION OF THERAPY

A. Acromegaly

Authorization of 12 months may be granted for continuation of therapy for acromegaly when the member's IGF-1 level has decreased or normalized since initiation of therapy.

B. Cushing's syndrome/disease

Authorization of 12 months may be granted for continuation of therapy for Cushing's syndrome/disease when the member meets ALL initial authorization criteria.

V. REFERENCES

1. Signifor LAR [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Company; April 2019.
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SPECIALTY GUIDELINE MANAGEMENT

Revatio (sildenafil tablets and oral suspension) sildenafil tablets (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Sildenafil/Revatio is indicated for the treatment of pulmonary arterial hypertension (World Health Organization [WHO] Group 1) in adults to improve exercise ability and delay clinical worsening.

Limitation of use: Adding sildenafil to bosentan therapy does not result in any beneficial effect on exercise capacity.

B. Compendial Use

Secondary Raynaud's phenomenon (*Tablets only*)

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Pulmonary Arterial Hypertension**

Authorization of 12 months may be granted for treatment of PAH when ALL of the following criteria are met:

1. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
2. PAH was confirmed by either criterion (i) or criterion (ii) below:
 - i. Pretreatment right heart catheterization with all of the following results:
 - a. mPAP \geq 25 mmHg
 - b. PCWP \leq 15 mmHg
 - c. PVR $>$ 3 Wood units
 - ii. For infants less than one year of age with any of the following conditions, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed:
 - a. Post cardiac surgery
 - b. Chronic heart disease
 - c. Chronic lung disease associated with prematurity
 - d. Congenital diaphragmatic hernia

B. **Secondary Raynaud's Phenomenon**

Authorization of 12 months may be granted for treatment of secondary Raynaud's phenomenon when the patient has had an inadequate response to one of the following medications:

1. Calcium channel blockers

2. Angiotensin receptor blockers
3. Selective serotonin reuptake inhibitors
4. Alpha blockers
5. Topical nitrates

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with an indication listed in Section II who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

IV. APPENDIX

WHO Classification of Pulmonary Hypertension

1 PAH

- 1.1 Idiopathic (PAH)
- 1.2 Heritable PAH
- 1.3 Drug- and toxin-induced PAH
- 1.4. PAH associated with:
 - 1.4.1 Connective tissue diseases
 - 1.4.2 HIV infection
 - 1.4.3 Portal hypertension
 - 1.4.4 Congenital heart diseases
 - 1.4.5 Schistosomiasis
- 1.5 PAH long-term responders to calcium channel blockers
- 1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement
- 1.7 Persistent PH of the newborn syndrome

2 PH due to left heart disease

- 2.1 PH due to heart failure with preserved LVEF
- 2.2 PH due to heart failure with reduced LVEF
- 2.3 Valvular heart disease
- 2.4 Congenital/acquired cardiovascular conditions leading to post-capillary PH

3 PH due to lung diseases and/or hypoxia

- 3.1 Obstructive lung disease
- 3.2 Restrictive lung disease
- 3.3 Other lung disease with mixed restrictive/obstructive pattern
- 3.4 Hypoxia without lung disease
- 3.5 Developmental lung disorders

4 PH due to pulmonary artery obstruction

- 4.1 Chronic thromboembolic PH
- 4.2 Other pulmonary artery obstructions
 - 4.2.1 Sarcoma (high or intermediate grade) or angiosarcoma
 - 4.2.2 Other malignant tumors
 - Renal carcinoma
 - Uterine carcinoma
 - Germ cell tumours of the testis
 - Other tumours

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1651-A

- 4.2.3 Non-malignant tumours
Uterine leiomyoma
- 4.2.4 Arteritis without connective tissue disease
- 4.2.5 Congenital pulmonary artery stenosis
- 4.2.6 Parasites
Hydatidosis

5 PH with unclear and/or multifactorial mechanisms

- 5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders
- 5.2 Systemic and metabolic disorders: Pulmonary Langerhans cell histiocytosis, Gaucher disease, glycogen storage disease, neurofibromatosis, sarcoidosis
- 5.3 Others: chronic renal failure with or without hemodialysis, fibrosing mediastinitis
- 5.4 Complex congenital heart disease

V. REFERENCES

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1651-A

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SPECIALTY GUIDELINE MANAGEMENT

SILIQ (brodalumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy and have failed to respond or have lost response to other systemic therapies

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Moderate to severe plaque psoriasis

- A. Authorization of 12 months may be granted for members who have previously received Otezla or a biologic indicated for the treatment of moderate to severe plaque psoriasis.
- B. Authorization of 12 months may be granted for treatment of moderate to severe plaque psoriasis when all of the following criteria are met:
 1. At least 3% of body surface area (BSA) is affected OR crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
 2. Member meets any of the following criteria:
 - a. Member has had an inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) or pharmacologic treatment with methotrexate, cyclosporine or acitretin.
 - b. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine and acitretin (see Appendix).
 - c. Member has severe psoriasis that warrants a biologic DMARD as first-line therapy (i.e. at least 10% of the body surface area (BSA) or crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected).

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who are using Siliq for an indication outlined in section II and who achieve or maintain positive clinical response with Siliq as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

For all indications: Member has had a documented negative TB test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons

Reference number
1731-A

who are naïve to biologic DMARDs or targeted synthetic DMARDs (e.g., Xeljanz), and repeated yearly for members with risk factors** for TB that are continuing therapy with biologics.

* If the screening testing for TB is positive, there must be documentation of further testing to confirm there is no active disease. Do not administer brodalumab to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of brodalumab.

** Risk factors for TB include: Persons with close contact to people with infectious TB disease; persons who have recently immigrated from areas of the world with high rates of TB (e.g., Africa, Asia, Eastern Europe, Latin America, Russia); children less than 5 years of age who have a positive TB test; groups with high rates of TB transmission (e.g., homeless persons, injection drug users, persons with HIV infection); persons who work or reside with people who are at an increased risk for active TB (e.g., hospitals, long-term care facilities, correctional facilities, homeless shelters).

For all indications: Member cannot use Siliq concomitantly with any other biologic DMARD or targeted synthetic DMARD.

V. APPENDIX

Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine or Acitretin

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Cannot be used due to risk of treatment-related toxicity
4. Drug interaction
5. Pregnancy or planning pregnancy
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

VI. REFERENCES

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SPECIALTY GUIDELINE MANAGEMENT

SIMPONI (golimumab for subcutaneous injection)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Moderately to severely active rheumatoid arthritis (RA) in combination with methotrexate
2. Active psoriatic arthritis (PsA)
3. Active ankylosing spondylitis (AS)
4. Moderately to severely active ulcerative colitis (UC)

B. Compendial Use

Axial spondyloarthritis

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Moderately to severely active rheumatoid arthritis (RA)**

1. Authorization of 12 months may be granted for members who have previously received a biologic or targeted synthetic DMARD (e.g., Rinvoq, Xeljanz) indicated for moderately to severely active rheumatoid arthritis. Simponi must be prescribed in combination with methotrexate unless the member has a clinical reason not to use methotrexate (see Appendix A).
2. Authorization of 12 months may be granted for treatment of moderately to severely active RA when all of the following criteria are met:
 - a. Member is prescribed Simponi in combination with methotrexate or has a clinical reason not to use methotrexate.
 - b. Member meets any of the following criteria:
 - i. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to 20 mg/week).
 - ii. Member has an intolerance or contraindication to methotrexate (see Appendix A).

B. **Active psoriatic arthritis (PsA)**

Authorization of 12 months may be granted for treatment of active psoriatic arthritis (PsA).

C. **Active ankylosing spondylitis (AS) and axial spondyloarthritis**

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for active ankylosing spondylitis or axial spondyloarthritis.
2. Authorizations of 12 months may be granted for treatment of active ankylosing spondylitis and axial spondyloarthritis when any of the following criteria is met:

- a. Member has experienced an inadequate response to at least two non-steroidal anti-inflammatory drugs (NSAIDs).
- b. Member has an intolerance or contraindication to two or more NSAIDs.

D. Moderately to severely active ulcerative colitis (UC)

1. Authorization of 12 months may be granted for members who have previously received a biologic or targeted synthetic drug (e.g., Xeljanz) indicated for moderately to severely active ulcerative colitis.
2. Authorization of 12 months may be granted for the treatment of moderately to severely active UC for members who had an inadequate response, intolerance or contraindication to at least one conventional therapy option (See Appendix B).

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who are using Simponi for an indication outlined in section II and who achieve or maintain positive clinical response with Simponi as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

For all indications: Member has had a documented negative TB test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic DMARDs or targeted synthetic DMARDs (e.g., Xeljanz), and repeated yearly for members with risk factors** for TB that are continuing therapy with biologics.

* If the screening testing for TB is positive, there must be documentation of further testing to confirm there is no active disease. Do not administer golimumab to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of golimumab.

** Risk factors for TB include: Persons with close contact to people with infectious TB disease; persons who have recently immigrated from areas of the world with high rates of TB (e.g., Africa, Asia, Eastern Europe, Latin America, Russia); children less than 5 years of age who have a positive TB test; groups with high rates of TB transmission (e.g., homeless persons, injection drug users, persons with HIV infection); persons who work or reside with people who are at an increased risk for active TB (e.g., hospitals, long-term care facilities, correctional facilities, homeless shelters).

For all indications: Member cannot use Simponi concomitantly with any other biologic DMARD or targeted synthetic DMARD.

V. APPENDICES

Appendix A: Examples of Contraindications to Methotrexate

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
4. Elevated liver transaminases
5. History of intolerance or adverse event
6. Hypersensitivity
7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
8. Myelodysplasia

9. Pregnancy or planning pregnancy
10. Renal impairment
11. Significant drug interaction

Appendix B: Examples of Conventional Therapy Options for UC

1. Mild to moderate disease – induction of remission:
 - a. Oral mesalamine (e.g., Asacol, Asacol HD, Lialda, Pentasa), balsalazide, olsalazine
 - b. Rectal mesalamine (e.g., Canasa, Rowasa)
 - c. Rectal hydrocortisone (e.g., Colocort, Cortifoam)
 - d. Alternatives: prednisone, azathioprine, mercaptopurine, sulfasalazine
2. Mild to moderate disease – maintenance of remission:
 - a. Oral mesalamine, balsalazide, olsalazine, rectal mesalamine
 - b. Alternatives: azathioprine, mercaptopurine, sulfasalazine
3. Severe disease – induction of remission:
 - a. Prednisone, hydrocortisone IV, methylprednisolone IV
 - b. Alternatives: cyclosporine IV, tacrolimus, sulfasalazine
4. Severe disease – maintenance of remission:
 - a. Azathioprine, mercaptopurine
 - b. Alternative: sulfasalazine
5. Pouchitis: Metronidazole, ciprofloxacin
 - a. Alternative: rectal mesalamine

VI. REFERENCES

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Reference number(s)
2014-A

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SPECIALTY GUIDELINE MANAGEMENT

SIMPONI ARIA (golimumab injection for intravenous use)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

1. Moderately to severely active rheumatoid arthritis (RA) in combination with methotrexate
2. Active psoriatic arthritis (PsA)
3. Active ankylosing spondylitis (AS)

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Moderately to severely active rheumatoid arthritis (RA)

1. Authorization of 12 months may be granted for members who have previously received a biologic or targeted synthetic DMARD (e.g. Rinvoq, Xeljanz) indicated for moderately to severely active rheumatoid arthritis. Simponi Aria must be prescribed in combination with methotrexate unless the member has a clinical reason not to use methotrexate (see Appendix A).
2. Authorization of 12 months may be granted for treatment of moderately to severely active RA when all of the following criteria are met:
 - a. Member is prescribed Simponi Aria in combination with methotrexate or has a clinical reason not to use methotrexate.
 - b. Member meets any of the following criteria:
 - i. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to 20 mg/week).
 - ii. Member has an intolerance or contraindication to methotrexate (See Appendix A).

B. Active psoriatic arthritis (PsA)

Authorization of 12 months may be granted for treatment of active psoriatic arthritis (PsA).

C. Active ankylosing spondylitis (AS)

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for active ankylosing spondylitis.
2. Authorization of 12 months may be granted for treatment of active ankylosing spondylitis when any of the following criteria is met:
 - a. Member has experienced an inadequate response to at least two non-steroidal anti-inflammatory drugs (NSAIDs).
 - b. Member has an intolerance or contraindication to two or more NSAIDs.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who are using Simponi Aria for an indication outlined in section II and who achieve or maintain positive clinical response with Simponi Aria as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

For all indications: Member has had a documented negative TB test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic DMARDs or targeted synthetic DMARDs (e.g., Xeljanz), and repeated yearly for members with risk factors** for TB that are continuing therapy with biologics.

* If the screening testing for TB is positive, there must be documentation of further testing to confirm there is no active disease. Do not administer golimumab to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of golimumab.

** Risk factors for TB include: Persons with close contact to people with infectious TB disease; persons who have recently immigrated from areas of the world with high rates of TB (e.g., Africa, Asia, Eastern Europe, Latin America, Russia); children less than 5 years of age who have a positive TB test; groups with high rates of TB transmission (e.g., homeless persons, injection drug users, persons with HIV infection); persons who work or reside with people who are at an increased risk for active TB (e.g., hospitals, long-term care facilities, correctional facilities, homeless shelters).

For all indications: Member cannot use Simponi Aria concomitantly with any other biologic DMARD or targeted synthetic DMARD.

V. APPENDICES

Appendix A: Examples of Contraindications to Methotrexate

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
4. Elevated liver transaminases
5. History of intolerance or adverse event
6. Hypersensitivity
7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
8. Myelodysplasia
9. Pregnancy or planning pregnancy
10. Renal impairment
11. Significant drug interaction

Appendix B: Examples of Contraindications to the Use of NSAIDs

1. Allergic-type reaction following aspirin or other NSAID administration
2. Asthma
3. Gastrointestinal bleeding
4. History of intolerance or adverse event
5. Significant drug interaction
6. Urticaria

VI. REFERENCES

1. Simponi Aria [package insert]. Horsham, PA: Janssen Biotech, Inc.; May 2018.
2. Smolen JS, Landewé R, Billsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. *Ann Rheum Dis*. 2017;0:1-18.
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PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

SIRTURO
(bedaquiline)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

MDC-1
Ref # 923-A

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Sirturo is a diarylquinoline antimycobacterial drug indicated as part of combination therapy in the treatment of adult and pediatric patients (12 to less than 18 years of age and weighing at least 30 kg) with pulmonary multi-drug resistant tuberculosis (MDR-TB). Reserve Sirturo for use when an effective treatment regimen cannot otherwise be provided. This indication is approved under accelerated approval based on time to sputum culture conversion. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Limitations of Use:

- Do not use SIRTURO for the treatment of:
 - Latent infection due to *Mycobacterium tuberculosis*
 - Drug-sensitive tuberculosis
 - Extra-pulmonary tuberculosis
 - Infections caused by non-tuberculous mycobacteria
- The safety and efficacy of SIRTURO in the treatment of HIV infected patients with MDR-TB have not been established as clinical data are limited.

Off Label Uses

Combination regimen with pretomanid and linezolid for the treatment of pulmonary extensively drug resistant (XDR) or treatment-intolerant or nonresponsive multidrug-resistant (MDR) tuberculosis (TB)^{5,6}

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed as part of combination therapy in a patient with pulmonary multi-drug resistant tuberculosis (MDR-TB)

AND

- Another effective treatment regimen cannot be used instead of Sirturo (bedaquiline)

OR

- The requested drug is being prescribed for pulmonary extensively drug resistant (XDR) or treatment-intolerant/nonresponsive multidrug-resistant (MDR) tuberculosis

AND

- The requested drug is being prescribed as part of a combination regimen with Pretomanid and Zyvox (linezolid)

RATIONALE

These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Sirturo (bedaquiline) is indicated as part of combination therapy in the treatment of adult and pediatric patients (12 to less than 18 years of age and weighing at least

30 kg) with pulmonary multi-drug resistant tuberculosis (MDR-TB). Sirturo should be reserved for use when an effective treatment regimen cannot otherwise be provided.

Sirturo should only be initiated as part of combination therapy with at least 3 drugs to which the patient's MDR-TB isolate has been shown to be effective in vitro. If in vitro testing results are unavailable, Sirturo treatment may be initiated in combination with at least 4 other drugs to which the patient's MDR-TB isolate is likely to be susceptible.¹ The recommended dosage of Sirturo is 400 mg orally once daily for 2 weeks, then 200 mg orally 3 times weekly (with at least 48 hours between doses) for 22 weeks. The total duration of treatment with Sirturo is 24 weeks.

The Centers for Disease Control and Prevention (CDC) provisional guidelines for the use of bedaquiline for the treatment of multidrug-resistant tuberculosis, go beyond current FDA-approved labeling for bedaquiline. The guidelines state the following: Bedaquiline may be used for 24 weeks of treatment in adults with laboratory-confirmed pulmonary MDR-TB (TB with an isolate showing genotypic or phenotypic resistance to both isoniazid and rifampin) when an effective treatment regimen cannot otherwise be provided; bedaquiline may be used on a case-by-case basis in children, HIV-infected persons, pregnant women, persons with extrapulmonary MDR-TB, and patients with comorbid conditions on concomitant medications when an effective treatment regimen cannot otherwise be provided; and bedaquiline may be used on a case-by-case basis for durations longer than 24 weeks when an effective treatment regimen cannot be provided otherwise.⁴ Additionally, new evidence is available from the World Health Organization (WHO) on the use of bedaquiline longer than six months duration for MDR/Rifampin Resistant (RR)-TB, concurrent use of bedaquiline and delamanid for MDR/RR-TB, and use of bedaquiline, pretomanid and linezolid in combination for patients with extensively drug resistant tuberculosis (XDR-TB).⁶

Pretomanid is a newly approved FDA drug indicated as part of a combination regimen with bedaquiline (Sirturo) and linezolid (Zyvox) for the treatment of pulmonary XDR-TB or treatment-intolerant or nonresponsive MDR-TB.⁵ The recommended dosage and duration for this combination regimen are as follows⁵:

- Pretomanid Tablet 200 mg orally (1 tablet of 200 mg), once daily, for 26 weeks. Swallow Pretomanid Tablets whole with water
- Bedaquiline 400 mg orally once daily for 2 weeks followed by 200 mg 3 times per week, with at least 48 hours between doses, for 24 weeks for a total of 26 weeks

If either bedaquiline or Pretomanid Tablets are discontinued, the entire combination regimen should also be discontinued.

- Linezolid starting at 1,200 mg orally per day for 26 weeks, with dose adjustments to 600 mg daily and further reduction to 300 mg daily or interruption of dosing as necessary for known linezolid adverse reactions of myelosuppression, peripheral neuropathy, and optic neuropathy.

If linezolid is permanently discontinued during the initial four consecutive weeks of treatment, bedaquiline and Pretomanid Tablets should also be discontinued. If linezolid is discontinued after the initial four weeks of consecutive treatment, continue administering bedaquiline and Pretomanid Tablets.⁵

The duration of approval is set at 12 months based on the new evidence per the WHO and because the dosing of the combination regimen of Pretomanid, bedaquiline, and linezolid can be extended beyond 26 weeks, if necessary.^{5,6}

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1. Sirturo [package insert]. Titusville, New Jersey: Janssen Therapeutics; August 2019.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed February 2019.
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Sirturo MDC-1 923-A 02-2019_7-10-20.doc

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External Review: 01/2013, 02/2013, 12/2013, 10/2014, 10/2015, 08/2016, 08/2017, 06/2018, 06/2019, 10/2019

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed as part of combination therapy in a patient with pulmonary multi-drug resistant tuberculosis (MDR-TB)? [If no, then skip to question 3.]	Yes	No
2	Can another effective treatment regimen be used instead of Sirturo (bedaquiline)? [No further questions.]	Yes	No
3	Is the requested drug being prescribed for pulmonary extensively drug resistant (XDR) or treatment-intolerant/nonresponsive multidrug-resistant (MDR) tuberculosis?	Yes	No
4	Is the requested drug being prescribed as part of a combination regimen with Pretomanid and Zyvox (linezolid)?	Yes	No

Guidelines for Approval

Duration of Approval		12 Months
Set 1		
Yes to question(s)		No to question(s)
1		2
Set 2		
Yes to question(s)		No to question(s)
3		1
4		

Mapping Instructions

	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Go to 3	
2.	Deny	Approve, 12 months	You do not meet the requirements of your plan. Your plan covers this drug when other drugs cannot be used for the infection. Your request has been denied based on the information we have. [Short Description: Another effective treatment regimen can be used]
3.	Go to 4	Deny	You do not meet the requirements of your plan. Your plan covers this drug when it is used with other drugs for a certain infection in the lungs that is resistant to multiple drugs. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
4.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when it is used with Pretomanid and Zyvox (linezolid) for the infection. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis/combination regimen]

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

SIVEXTRO
(tedizolid)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

Ref # 1161-A

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Sivextro is an oxazolidinone-class antibacterial indicated for the treatment of acute bacterial skin and skin structure infections (ABSSSI) caused by susceptible isolates of the following Gram-positive microorganisms: *Staphylococcus aureus* (including methicillin-resistant [MRSA] and methicillin-susceptible [MSSA] isolates), *Streptococcus pyogenes*, *Streptococcus agalactiae*, *Streptococcus anginosus* Group (including *Streptococcus anginosus*, *Streptococcus intermedius*, and *Streptococcus constellatus*), and *Enterococcus faecalis*.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Sivextro and other antibacterial drugs, Sivextro should be used only to treat ABSSSI that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient is being converted from IV (intravenous) tedizolid (Sivextro) as prescribed by or in consultation with an Infectious Disease specialist

OR

- The patient has an acute bacterial skin or skin structure infection (ABSSSI) proven or strongly suspected to be caused by susceptible isolates of the following Gram-positive microorganisms: A) *Staphylococcus aureus* (including methicillin-resistant [MRSA] and methicillin-susceptible [MSSA] isolates), B) *Streptococcus pyogenes*, C) *Streptococcus agalactiae*, D) *Streptococcus anginosus* Group (including *Streptococcus anginosus*, *Streptococcus intermedius*, and *Streptococcus constellatus*), E) *Enterococcus faecalis*

AND

- The patient experienced an inadequate treatment response, intolerance, or contraindication to alternative therapies or the bacteria are not susceptible to any other antibiotics

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Sivextro is an oxazolidinone-class antibacterial indicated for the treatment of acute bacterial skin and skin structure infections (ABSSSI) caused by susceptible isolates of the following Gram-positive microorganisms: *Staphylococcus aureus* (including methicillin-resistant [MRSA] and methicillin-susceptible [MSSA] isolates), *Streptococcus pyogenes*, *Streptococcus agalactiae*, *Streptococcus anginosus* Group (including *Streptococcus anginosus*, *Streptococcus intermedius*, and *Streptococcus constellatus*), and *Enterococcus faecalis*.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Sivextro and other antibacterial drugs, Sivextro should be used only to treat ABSSSI that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

The recommended dosage of Sivextro is 200 mg administered once daily for 6 days either orally or as an intravenous (IV) infusion. No dose adjustment is necessary when changing from intravenous to oral Sivextro. Sivextro will be approved if being requested for a patient converted from IV Sivextro as prescribed by or in consultation with an Infectious Disease specialist.

REFERENCES

1. Sivextro [package insert]. Whitehouse Station, NJ: Merck & Co, Inc.; August 2017.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed February 2019.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed February 2019.
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 External Review: 08/2014, 10/2015, 08/2016, 08/2017, 06/2018, 06/2019

CRITERIA FOR APPROVAL

1	Is the patient being converted from IV (intravenous) tedizolid (Sivextro) as prescribed by or in consultation with an Infectious Disease specialist? [If yes, then no further questions.]	Yes	No
2	Does the patient have an acute bacterial skin or skin structure infection (ABSSSI) proven or strongly suspected to be caused by susceptible isolates of the following Gram-positive microorganisms: A) Staphylococcus aureus (including methicillin-resistant [MRSA] and methicillin-susceptible [MSSA] isolates), B) Streptococcus pyogenes, C) Streptococcus agalactiae, D) Streptococcus anginosus Group (including Streptococcus anginosus, Streptococcus intermedius, and Streptococcus constellatus), E) Enterococcus faecalis?	Yes	No
3	Has the patient experienced an inadequate treatment response, intolerance, or contraindication to alternative therapies OR are the bacteria NOT susceptible to any other antibiotics?	Yes	No

Mapping Instructions

	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Approve, 6 days	Go to 2	
2.	Go to 3	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet any of these conditions: - You are changing from IV (intravenous) tedizolid (Sivextro) as discussed with an Infectious Disease specialist

			<p>- You have an infection shown or strongly suspected to be caused by bacteria that are susceptible to the drug.</p> <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No approvable diagnosis.]</p>
3.	Approve, 6 days	Deny	<p>You do not meet the requirements of your plan.</p> <p>Your plan covers this drug when you meet any of these conditions:</p> <ul style="list-style-type: none"> - You tried other drugs and they either did not work for you or you cannot use them - The bacteria are not susceptible to any other drugs <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No trial of other drugs.]</p>

SPECIALTY GUIDELINE MANAGEMENT

SKYRIZI (risankizumab-rzaa)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Treatment of moderate-to-severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Moderate to severe plaque psoriasis

- A. Authorization of 12 months may be granted for members who have previously received Otezla or a biologic indicated for the treatment of moderate to severe plaque psoriasis.
- B. Authorization of 12 months may be granted for treatment of moderate to severe plaque psoriasis when all of the following criteria are met:
 1. At least 3% of body surface area (BSA) is affected OR crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
 2. Member meets any of the following criteria:
 - a. Member has had an inadequate response to either phototherapy (e.g., UVB, PUVA) or pharmacologic treatment with methotrexate, cyclosporine or acitretin.
 - b. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine and acitretin (see Appendix).
 - c. Member has severe psoriasis that warrants a biologic DMARD as first-line therapy (i.e. at least 10% of the body surface area (BSA) or crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected).

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who are using Skyrizi for an indication outlined in section II and who achieve or maintain positive clinical response Skyrizi as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

For all indications: Member has had a documented negative TB test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons

who are naïve to biologic DMARDs or targeted synthetic DMARDs (e.g., Xeljanz), and repeated yearly for members with risk factors** for TB that are continuing therapy with biologics.

* If the screening testing for TB is positive, there must be documentation of further testing to confirm there is no active disease. Do not administer risankizumab-rzaa to members with active TB infection. If there is latent disease, TB treatment must be started before initiation risankizumab-rzaa.

** Risk factors for TB include: Persons with close contact to people with infectious TB disease; persons who have recently immigrated from areas of the world with high rates of TB (e.g., Africa, Asia, Eastern Europe, Latin America, Russia); children less than 5 years of age who have a positive TB test; groups with high rates of TB transmission (e.g., homeless persons, injection drug users, persons with HIV infection); persons who work or reside with people who are at an increased risk for active TB (e.g., hospitals, long-term care facilities, correctional facilities, homeless shelters).

For all indications: Member cannot use Skyrizi concomitantly with any other biologic DMARD or targeted synthetic DMARD.

V. APPENDIX

Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine and Acitretin

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Cannot be used due to risk of treatment-related toxicity
4. Drug interaction
5. Pregnancy or planning pregnancy
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

VI. REFERENCES

1. Skyrizi [package insert]. North Chicago, IL: AbbVie Inc.; April 2019.
2. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 4: Guidelines of care for the management and treatment of psoriasis with traditional systemic agents. *J Am Acad Dermatol*. 2009;61:451-485.
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SPECIALTY GUIDELINE MANAGEMENT

SOLIRIS (eculizumab) ENHANCED SGM

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

- A. Paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis
- B. Atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy
- C. Generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) antibody positive
- D. Neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive

Limitations of Use: Soliris is not indicated for the treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS).

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review for new requests for treatment of:

- A. Atypical hemolytic uremic syndrome: ADAMTS 13 level
- B. Paroxysmal nocturnal hemoglobinuria: flow cytometry used to show results of GPI-APs deficiency
- C. Generalized myasthenia gravis: anti-acetylcholine receptor (AChR) antibody positive, clinical classification of myasthenia gravis score, MG activities of daily living score, use of IVIG and rituximab, use of two immunosuppressive therapies
- D. Neuromyelitis optica spectrum disorder: immunoassay used to confirm anti-aquaporin-4 (AQP4) antibody is present

III. CRITERIA FOR INITIAL APPROVAL

A. Atypical hemolytic uremic syndrome

Authorization of 6 months may be granted for treatment of atypical hemolytic uremic syndrome not caused by Shiga toxin when all of the following criteria are met:

1. ADAMTS 13 activity level above 5%
2. Absence of Shiga toxin

B. Paroxysmal nocturnal hemoglobinuria

Authorization of 6 months may be granted for treatment of paroxysmal nocturnal hemoglobinuria (PNH) when all of the following criteria are met:

- A. The diagnosis of PNH was confirmed by detecting a deficiency of glycosylphosphatidylinositol-anchored proteins (GPI-APs) as demonstrated by either of the following:
 - 1. At least 5% PNH cells
 - 2. At least 51% of GPI-anchored protein deficient poly-morphonuclear cells
- B. Flow cytometry is used to demonstrate GPI-anchored proteins deficiency

C. Generalized myasthenia gravis (gMG)

Authorization of 6 months may be granted for treatment of generalized myasthenia gravis (gMG) when all of the following criteria are met:

- 1. Anti-acetylcholine receptor (AChR) antibody positive
- 2. Myasthenia Gravis Foundation of America (MGFA) clinical classification II to IV
- 3. MG activities of daily living (MG-ADL) total score ≥ 6
- 4. Meets both of the following:
 - a. Patient has had an inadequate response to at least two immunosuppressive therapies listed below:
 - i. azathioprine
 - ii. cyclosporine
 - iii. mycophenolate mofetil
 - iv. tacrolimus
 - v. methotrexate
 - vi. cyclophosphamide
 - b. Member has inadequate response to chronic IVIG AND rituximab

D. Neuromyelitis Optica Spectrum Disorder (NMOSD)

Authorization of 6 months may be granted for treatment of neuromyelitis optica spectrum disorder (NMOSD) when all of the following criteria are met:

- 1. Anti-aquaporin-4 (AQP4) antibody positive
- 2. Member exhibits one of the following core clinical characteristics of NMOSD:
 - a. Optic neuritis
 - b. Acute myelitis
 - c. Area postrema syndrome (episode of otherwise unexplained hiccups or nausea and vomiting)
 - d. Acute brainstem syndrome
 - e. Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions
 - f. Symptomatic cerebral syndrome with NMOSD-typical brain lesions
- 3. The member will not be treated with rituximab and eculizumab concomitantly

IV. CONTINUATION OF THERAPY

A. Atypical hemolytic uremic syndrome

Authorization of 12 months may be granted to all members requesting continuation of therapy provided they meet all initial authorization criteria and demonstrate a positive response to therapy (e.g., normalization of lactate dehydrogenase (LDH) levels, platelet counts).

B. Paroxysmal nocturnal hemoglobinuria

Authorization of 12 months may be granted to all members requesting continuation of therapy provided they meet all initial authorization criteria and demonstrate a positive response to therapy (e.g., improvement in hemoglobin levels, normalization of LDH levels).

C. Generalized myasthenia gravis (gMG)

Authorization of 12 months may be granted to all members requesting continuation of therapy provided they meet all initial authorization criteria and demonstrate a positive response to therapy

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(e.g., improvement in MG-ADL scores, changes in baseline in Quantitative Myasthenia Gravis (QMG) total score).

D. Neuromyelitis optica spectrum disorder (NMOSD)

Authorization of 12 months may be granted to all members requesting continuation of therapy provided they meet all initial authorization criteria and demonstrate a positive response to therapy (e.g., reduction in number of relapses).

IV. REFERENCES

1. Soliris [package insert]. New Haven, CT: Alexion Pharmaceuticals, Inc.; June 2019.
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3. Parker CJ. Management of paroxysmal nocturnal hemoglobinuria in the era of complement inhibitory therapy. *Hematology*. 2011; 21-29.
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5. Jaretzki A, Barohn RJ, Ernstoff RM et al. Myasthenia Gravis: Recommendations for Clinical Research Standards. *Ann Thorac Surg*. 2000;70: 327-34.
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SPECIALTY GUIDELINE MANAGEMENT

SOMATULINE DEPOT (lanreotide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Somatuline Depot is indicated for the long-term treatment of acromegalic patients who have had an inadequate response to surgery and/or radiotherapy, or for whom surgery and/or radiotherapy is not an option.
2. Somatuline Depot is indicated for the treatment of patients with unresectable, well- or moderately-differentiated, locally advanced or metastatic gastroenteropancreatic neuroendocrine tumors (GEP-NETs) to improve progression-free survival.
3. Somatuline Depot is indicated for the treatment of adults with carcinoid syndrome; when used, it reduces the frequency of short-acting somatostatin analog rescue therapy.

B. Compendial Uses

Neuroendocrine tumors (NETs):

1. Tumors of the gastrointestinal (GI) tract, lung, and thymus (carcinoid tumors)
2. Tumors of the pancreas
3. Pheochromocytoma and paraganglioma
4. Zollinger-Ellison syndrome

All other indications are considered experimental/investigational and are not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review for acromegaly:

- A. For initial approval: Laboratory report indicating high pretreatment insulin-like growth factor-1 (IGF-1) level and chart notes indicating an inadequate or partial response to surgery or radiotherapy or a clinical reason for not having surgery or radiotherapy.
- B. For continuation: Laboratory report indicating normal current IGF-1 levels or chart notes indicating that the member's IGF-1 level has decreased or normalized since initiation of therapy

III. CRITERIA FOR INITIAL APPROVAL

A. **Acromegaly**

Authorization of 12 months may be granted for the treatment of acromegaly when all of the following criteria are met:

1. Member has a high pretreatment IGF-1 level for age and/or gender based on the laboratory reference range.
2. Member had an inadequate or partial response to surgery or radiotherapy OR there is a clinical reason why the member has not had surgery or radiotherapy.

B. Neuroendocrine tumors (NETs)

1. Tumors of the gastrointestinal (GI) tract (carcinoid tumor)
Authorization of 12 months may be granted for treatment of locoregional advanced or metastatic NETs of the GI tract or unresected primary gastrinoma.
2. Tumors of the thymus (carcinoid tumor)
Authorization of 12 months may be granted for treatment unresectable or metastatic of NETs of the thymus.
3. Tumors of the lung (carcinoid tumor)
Authorization of 12 months may be granted for treatment of unresectable or metastatic NETs of the lung.
4. Tumors of the pancreas
Authorization of 12 months may be granted for treatment of NETs of the pancreas.
5. Gastroenteropancreatic neuroendocrine tumors (GEP-NETs)
Authorization of 12 months may be granted for treatment of unresectable, well- or moderately-differentiated, locally advanced or metastatic GEP-NETs.

C. Carcinoid syndrome

Authorization of 12 months may be granted for treatment of carcinoid syndrome when it is used in any of the following clinical settings:

1. As a single agent
2. In combination with telotristat for persistent diarrhea due to poorly controlled carcinoid syndrome
3. In combination with other systemic therapy options for persistent symptoms such as flushing or diarrhea, or for progressive disease

D. Pheochromocytoma and paraganglioma

Authorization of 12 months may be granted for treatment of locally unresectable or metastatic pheochromocytoma and paraganglioma.

E. Zollinger-Ellison syndrome

Authorization of 12 months may be granted for treatment of Zollinger-Ellison syndrome.

IV. CONTINUATION OF THERAPY

A. Acromegaly

Authorization of 12 months may be granted for continuation of therapy for acromegaly when the member's IGF-1 level has decreased or normalized since initiation of therapy.

B. Carcinoid syndrome and Zollinger-Ellison syndrome

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization when the member is experiencing clinical benefit as evidenced by improvement or stabilization in clinical signs and symptoms since starting therapy.

C. All other indications

Members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. REFERENCES

1. Somatuline Depot [package insert]. Basking Ridge, NJ: Ipsen Biopharmaceuticals, Inc.; April 2019.

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3. Katznelson L, Laws ER, Melmed S, et al. Acromegaly: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab*. 2014;99:3933-3951.
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5. The NCCN Clinical Practice Guidelines in Oncology® Neuroendocrine and Adrenal Tumors (Version 1.2019). © 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed June 11, 2019.
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SPECIALTY GUIDELINE MANAGEMENT

SOMAVERT (pegvisomant)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Somavert is indicated for the treatment of acromegaly in patients who have had an inadequate response to surgery or radiation therapy, or for whom these therapies are not appropriate.

All other indications are considered experimental/investigational and are not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

- A. For initial approval: Laboratory report indicating high pretreatment insulin-like growth factor-1 (IGF-1) level and chart notes indicating an inadequate or partial response to surgery or radiotherapy or a clinical reason for not having surgery or radiotherapy.
- B. For continuation: Laboratory report indicating normal current IGF-1 levels or chart notes indicating that the member's IGF-1 level has decreased or normalized since initiation of therapy

III. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for the treatment of acromegaly when all of the following criteria are met:

- A. Member has a high pretreatment IGF-1 level for age and/or gender based on the laboratory reference range.
- B. Member had an inadequate or partial response to surgery or radiotherapy OR there is a clinical reason why the member has not had surgery or radiotherapy.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy for acromegaly when the member's IGF-1 level has decreased or normalized since initiation of therapy.

V. REFERENCES

1. Somavert [package insert]. New York, NY: Pharmacia & Upjohn Co; April 2016.
2. Katznelson L, Laws ER, Melmed S, et al. Acromegaly: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2014; 99:3933-3951.

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3. American Association of Clinical Endocrinologists Acromegaly Guidelines Task Force. Medical guidelines for clinical practice for the diagnosis and treatment of acromegaly – 2011 update. Endocr Pract. 2011;17(suppl 4):1-44.

SPECIALTY GUIDELINE MANAGEMENT

SOVALDI (sofosbuvir)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Sovaldi is indicated for the treatment of:

- Adult patients with chronic hepatitis C virus (HCV) infection as a component of a combination antiviral treatment regimen
 - genotype 1 or 4 infection without cirrhosis or with compensated cirrhosis for use in combination with pegylated interferon and ribavirin
 - genotype 2 or 3 infection without cirrhosis or with compensated cirrhosis for use in combination with ribavirin.
- Chronic HCV genotype 2 or 3 infection in pediatric patients 12 years of age and older or weighing at least 35 kg without cirrhosis or with compensated cirrhosis for use in combination with ribavirin.

All other indications are considered experimental/investigational and not medically necessary.

Compendial Uses

Chronic hepatitis C genotype 5 or 6 infection (refer to Daklinza SGM)

II. CRITERIA FOR APPROVAL

A. Chronic hepatitis C virus infection, in combination with peginterferon alfa (PEG-IFN) and ribavirin (RBV)

1. Genotype 1 infection

Authorization of up to 12 weeks total may be granted for members who are treatment-naïve.

2. Genotype 4 infection

Authorization of up to 12 weeks total may be granted for members who are treatment-naïve.

B. Chronic hepatitis C virus infection, in combination with ribavirin

1. Genotype 1 infection

Authorization of up to 24 weeks total may be granted for members who have documented interferon (IFN) ineligibility (see Section III).

2. Genotype 2 infection

Authorization of up to 12 weeks total may be granted for members who are treatment-naïve or failed prior treatment with PEG-IFN and RBV.

3. Genotype 3 infection

Authorization of up to 24 weeks total may be granted for members who are treatment-naïve or failed prior treatment with PEG-IFN and RBV.

4. Members with hepatocellular carcinoma awaiting liver transplantation

Authorization of up to 48 weeks total or until liver transplantation, whichever occurs first, may be granted for members with genotype 1, 2, 3, or 4 infection and hepatocellular carcinoma who meet the MILAN criteria, defined as the following:

- a. Tumor size 5 cm or less in diameter with single hepatocellular carcinomas OR 3 tumor nodules or less, each 3 cm or less in diameter with multiple tumors AND
- b. No extrahepatic manifestations of the cancer or evidence of vascular invasion of tumor

C. Chronic hepatitis C virus infection, in combination with Olysio (with or without ribavirin)

Authorization of up to 24 weeks total (as applicable) may be granted for members prescribed Sovaldi in combination with Olysio (with or without ribavirin as applicable) who meet the criteria for approval for the requested regimen. Refer to the Olysio SGM for the specific criteria for approval and approval durations.

D. Chronic hepatitis C virus infection, in combination with Daklinza (with or without ribavirin)

Authorization of up to 24 weeks total (as applicable) may be granted for members prescribed Sovaldi in combination with Daklinza (with or without ribavirin as applicable) who meet the criteria for approval for the requested regimen. Refer to the Daklinza SGM for the specific criteria for approval and approval durations.

E. Chronic hepatitis C virus infection, in combination with Zepatier

Authorization of up to 12 weeks total (as applicable) may be granted for members prescribed Sovaldi in combination with Zepatier who meet the criteria for approval for the requested regimen. Refer to the Zepatier SGM for the specific criteria for approval and approval durations.

F. HCV and HIV coinfection

Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in Section A, B, C, D, or E above are met.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. APPENDIX: INTERFERON INELIGIBILITY

IFN ineligible is defined as one or more of the below:

- Intolerance to IFN
- Autoimmune hepatitis and other autoimmune disorders
- Hypersensitivity to PEG-IFN or any of its components
- Major uncontrolled depressive illness
- A baseline neutrophil count < 1,500/mcL
- A baseline platelet count < 90,000/mcL
- A baseline hemoglobin < 10 g/dL
- History of pre-existing cardiac disease

V. REFERENCES

1. Sovaldi [package insert]. Foster City, CA: Gilead Sciences, Inc.; November 2017.
2. AASLD/IDSA/IAS–USA. Recommendations for testing, managing, and treating hepatitis C. <http://www.hcvguidelines.org>. Last changes made on May 24, 2018. Accessed August 02, 2018.

This policy applies to the following:

	Standard Opt-in		PDPD		VF		Medical Benefit	✓	Medical Benefit: Biosimilars First
	Standard Opt-out		ACSF		MMT		Medical Benefit: Managed Medicaid		Medical Benefit: Add-on
			Balanced		Marketplace		Medicare Part B		Medicare Part B: Biosimilars First

Reference #
3657-D

EXCEPTIONS CRITERIA

DISEASE-MODIFYING ANTIRHEUMATIC DRUG PRODUCTS

PREFERRED PRODUCTS: AVSOLA, ENTYVIO, ILUMYA, INFLECTRA, RENFLEXIS, SIMPONI ARIA, STELARA IV

POLICY

This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the disease-modifying antirheumatic drug (DMARD) products specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred product and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. For Remicade, this program applies to all adult members. For Actemra, Cimzia and Orencia, this program applies to adult members who are new to treatment with a targeted product for the first time, except if the request is for the treatment of psoriasis.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Disease-modifying antirheumatic drugs for autoimmune conditions

	Products	
Preferred	<ul style="list-style-type: none"> • Avsola (infliximab-axxq) • Entyvio (vedolizumab) • Ilumya (tildrakizumab-asmn) • Inflectra (infliximab-dyyb) 	<ul style="list-style-type: none"> • Renflexis (infliximab-abda) • Simponi Aria (golimumab, intravenous) • Stelara IV (ustekinumab)*
Targeted	<ul style="list-style-type: none"> • Actemra (tocilizumab) • Cimzia (certolizumab pegol) 	<ul style="list-style-type: none"> • Orencia (abatacept) • Remicade (infliximab)

*Stelara IV is indicated for a one time induction dose for Crohn's disease and ulcerative colitis.

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for an indication that is FDA-approved for the preferred products.

Coverage for a targeted product is provided when any of the following criteria is met:

- A. For Remicade, when member meets both of the following:

This policy applies to the following:

	Standard Opt-in		PDPD		VF		Medical Benefit	✓	Medical Benefit: Biosimilars First
	Standard Opt-out		ACSF		MMT		Medical Benefit: Managed Medicaid		Medical Benefit: Add-on
			Balanced		Marketplace		Medicare Part B		Medicare Part B: Biosimilars First

Reference #
3657-D

1. Member has a documented intolerable adverse event with all of the preferred products, Avsola, Inflectra, and Renflexis, and the adverse event was not an expected adverse event attributed to the active ingredient as described in the prescribing information.
 2. Member has a documented inadequate response or intolerable adverse event with Entyvio, Ilumya, and Simponi Aria where the product's indications overlap.
- B. For Cimzia, when any of the following criteria are met:
1. Member is currently receiving treatment with the requested targeted product, excluding when the requested targeted product is obtained as samples or via manufacturer's patient assistance programs, unless the request is for psoriasis.
 2. Member has a documented inadequate response or intolerable adverse event with each of the following where the product's indications overlap:
 - a. Avsola, Inflectra, or Renflexis
 - b. Entyvio
 - c. Ilumya
 - d. Simponi Aria
 3. Member is currently pregnant or breastfeeding
- C. For all other targeted products, when any of the following criteria are met:
1. Member is currently receiving treatment with the requested targeted product, excluding when the requested targeted product is obtained as samples or via manufacturer's patient assistance programs.
 2. Member has a documented inadequate response or intolerable adverse event with each of the following where the product's indications overlap:
 - a. Avsola, Inflectra, or Renflexis
 - b. Entyvio
 - c. Ilumya
 - d. Simponi Aria
 3. Member has a documented inadequate response or intolerable adverse event with Entyvio or Ilumya where the product's indications overlap and there is a documented clinical reason to avoid TNF inhibitors (Appendix).

III. Appendix: Clinical reasons to avoid TNF inhibitors

- History of demyelinating disorder
- History of congestive heart failure
- History of hepatitis B virus infection
- Autoantibody formation/lupus-like syndrome
- Risk of lymphoma

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1. Actemra [package insert]. South San Francisco, CA: Genentech, Inc.; June 2019.
2. Avsola [package insert]. Thousand Oaks, CA: Amgen; December 2019.
3. Cimzia [package insert]. Smyrna, GA: UCB, Inc.; September 2019.
4. Entyvio [package insert]. Deerfield, IL: Takeda Pharmaceutical America, Inc.; May 2019.
5. Ilumya [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; August 2018.
6. Inflectra [package insert]. Lake Forest, IL: Hospira, a Pfizer Company; June 2019.

This policy applies to the following:

	Standard Opt-in		PDPD		VF		Medical Benefit	✓	Medical Benefit: Biosimilars First
	Standard Opt-out		ACSF		MMT		Medical Benefit: Managed Medicaid		Medical Benefit: Add-on
			Balanced		Marketplace		Medicare Part B		Medicare Part B: Biosimilars First

Reference #
3657-D

7. Orencia [package insert]. Princeton, NJ: Bristol-Meyers Squibb Company; March 2019.
8. Remicade [package insert]. Horsham, PA: Janssen Biotech, Inc.; June 2018.
9. Renflexis [package insert]. Kenilworth, NJ. Merck &Co., Inc; October 2019.
10. Simponi Aria [package insert]. Horsham, PA: Janssen Biotech, Inc.; September 2019.
11. Stelara [package insert]. Horsham, PA: Janssen Biotech, Inc.; November 2019.

This policy applies to the following:

	Standard Opt-in		PDPD		VF		Medical Benefit		Medical Benefit: Biosimilars First
	Standard Opt-out		ACSF		MMT		Medical Benefit: Managed Medicaid		Medical Benefit: Add-on
			Balanced		Marketplace		Medicare Part B	✓	Medicare Part B: Biosimilars First

Reference #
3658-D

EXCEPTIONS CRITERIA

DISEASE-MODIFYING ANTIRHEUMATIC DRUG PRODUCTS

PREFERRED PRODUCTS: AVSOLA, ENTYVIO, ILUMYA, INFLECTRA, RENFLEXIS, SIMPONI ARIA, STELARA IV

POLICY

This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the disease-modifying antirheumatic drug (DMARD) products specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred product and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to adult members who are new to treatment with a targeted product for the first time.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Disease-modifying antirheumatic drugs for autoimmune conditions

	Products	
Preferred	<ul style="list-style-type: none"> • Avsola (infliximab-axxq) • Entyvio (vedolizumab) • Ilumya (tildrakizumab-asmn) • Inflectra (infliximab-dyyb) 	<ul style="list-style-type: none"> • Renflexis (infliximab-abda) • Simponi Aria (golimumab, intravenous) • Stelara IV (ustekinumab)*
Targeted	<ul style="list-style-type: none"> • Actemra (tocilizumab) • Cimzia (certolizumab pegol) 	<ul style="list-style-type: none"> • Orencia (abatacept) • Remicade (infliximab)

*Stelara IV is indicated for a one time induction dose for Crohn's disease and ulcerative colitis.

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for an indication that is FDA-approved for the preferred products.

Coverage for a targeted product is provided when any of the following criteria is met:

- A. For Remicade when either of the following criteria are met:
 1. Member has received treatment with the targeted product in the past 365 days.
 2. When both of the following criteria are met:
 - a. Member has a documented intolerable adverse event with all of the preferred products: Avsola, Inflectra, and Renflexis, and the adverse event was not an expected adverse event attributed to the active ingredient as described in the prescribing information.

This policy applies to the following:

	Standard Opt-in		PDPD		VF		Medical Benefit		Medical Benefit: Biosimilars First
	Standard Opt-out		ACSF		MMT		Medical Benefit: Managed Medicaid		Medical Benefit: Add-on
			Balanced		Marketplace		Medicare Part B	✓	Medicare Part B: Biosimilars First

Reference #
3658-D

- b. Member has a documented inadequate response or intolerable adverse event with Entyvio, Ilumya, and Simponi Aria where the product's indications overlap.

B. For Cimzia, when any of the following criteria are met:

1. Member has received treatment with the targeted product in the past 365 days.
2. Member has a documented inadequate response or intolerable adverse event with each of the following where the product's indications overlap:
 - a. Avsola, Inflectra, or Renflexis
 - b. Entyvio
 - c. Ilumya
 - d. Simponi Aria
3. Member is currently pregnant or breastfeeding

C. For all other targeted products, when any of the following criteria are met:

1. Member has received treatment with the targeted product in the past 365 days.
2. Member has a documented inadequate response or intolerable adverse event with each of the following where the product's indications overlap:
 - a. Avsola, Inflectra, or Renflexis
 - b. Entyvio
 - c. Ilumya
 - d. Simponi Aria
3. Member has a documented inadequate response or intolerable adverse event with Entyvio or Ilumya where the product's indications overlap and there is a documented clinical reason to avoid TNF inhibitors (Appendix).

III. Appendix: Clinical reasons to avoid TNF inhibitors

- History of demyelinating disorder
- History of congestive heart failure
- History of hepatitis B virus infection
- Autoantibody formation/lupus-like syndrome
- Risk of lymphoma

REFERENCES

1. Actemra [package insert]. South San Francisco, CA: Genentech, Inc.; June 2019.
2. Avsola [package insert]. Thousand Oaks, CA: Amgen; December 2019.
3. Cimzia [package insert]. Smyrna, GA: UCB, Inc.; September 2019.
4. Entyvio [package insert]. Deerfield, IL: Takeda Pharmaceutical America, Inc.; May 2019.
5. Ilumya [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; August 2018.
6. Inflectra [package insert]. Lake Forest, IL: Hospira, a Pfizer Company; June 2019.
7. Orencia [package insert]. Princeton, NJ: Bristol-Meyers Squibb Company; March 2019.
8. Remicade [package insert]. Horsham, PA: Janssen Biotech, Inc.; June 2018.
9. Renflexis [package insert]. Kenilworth, NJ. Merck & Co., Inc; October 2019.
10. Simponi Aria [package insert]. Horsham, PA: Janssen Biotech, Inc.; September 2019.
11. Stelara [package insert]. Horsham, PA: Janssen Biotech, Inc.; November 2019.

SPECIALTY POST LIMIT QUANTITY EXCEPTION CRITERIA

I. PROGRAM DESCRIPTION

Coverage is provided for an amount of drug sufficient for most members based on the most common uses of the drug. The submitted prescription is covered up to this standard limit without a review process. In situations where an additional quantity of drug is needed to adequately treat the member, prior authorization is required to determine if clinical exceptions are met.

Coverage for an additional quantity of drug is provided for duration sufficient for most uses (e.g., shorter period of time to accommodate loading doses or dose titration when a member requires additional amounts to adequately treat his/her condition).

In situations where coverage for additional quantities is not approved through the prior authorization process, an appeals process exists to review specific or unique cases where additional drug may be necessary.

II. RATIONALE

The intent of this program is to provide coverage for quantities sufficient for treatment for most members based on the most common uses of the drug. Quantity limits are based on dosage recommendations in product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. In situations where greater amounts of drug are needed, prior authorization criteria allow approval of these quantities based on clinical exceptions such as to accommodate loading doses, compendial supported dosing, drug interactions, or dosing by body weight or body surface area, and to allow for dose adjustments using a particular strength of the drug, as applicable.

III. CRITERIA FOR APPROVAL

The use of medication at the requested quantity is supported by the manufacturer's prescribing information or dosing guidelines found in the compendia or current literature (e.g., AHFS, Micromedex DrugDex, NCCN compendia, current treatment guidelines) and the member meets the criteria set A, B or C.

- A. Authorization for a quantity up to the exception limit may be granted for up to 90 days for initiation of treatment at a higher dose or frequency of administration (e.g., loading dose).
- B. Authorization for a quantity up to the exception limit may be granted for up to 6 months when a greater quantity is necessary to adjust the dose using a lower strength due to intolerance to the recommended maintenance dose.
- C. Authorization for a quantity up to the exception limit may be granted for up to 12 months or for the remaining duration of any other existing prior authorization (e.g., Specialty Guideline Management) in the following situations:
 - 1. Member is prescribed a drug dosed by weight or body surface area and requires a greater quantity to achieve the appropriate dose OR
 - 2. A greater quantity is necessary to accommodate a higher dose following an inadequate response OR
 - 3. A greater quantity is necessary for a compendial use or an FDA-approved indication OR
 - 4. A greater quantity is necessary to adjust the dose or frequency of administration to account for a drug interaction.

Reference number
1718-J

IV. COVERED QUANTITIES

Coverage is provided without prior authorization up to the standard limits. Coverage of an additional quantity may be provided up to the exception limit with prior authorization. These limits are specified in the Specialty Quantity Limit Program policies for the applicable products.

SPECIALTY QUANTITY LIMIT PROGRAM

ENDARI (L-glutamine oral powder)

I. PROGRAM DESCRIPTION

The standard limit is designed to allow a quantity sufficient for the most common uses of the medication. The recommended dosing parameters for all FDA-approved indications fall within the standard limits. Coverage of an additional quantity may be reviewed on a case-by-case basis upon request.

II. COVERED QUANTITIES

Medication	Standard Limit	FDA-recommended dosing
Endari (L-glutamine oral powder) 5 g packets	180 packets per 30 days	5 grams to 15 grams orally, twice daily based on body weight* *Less than 30 kg = 5 g per dose; 30 to 65 kg = 10 g per dose; Greater than 65 kg = 15 g per dose

III. REFERENCES

1. Endari [package insert]. Torrance, CA: Emmaus Medical, Inc; July 2017.

SPECIALTY QUANTITY LIMIT PROGRAM

FOLLITROPINS

I. PROGRAM DESCRIPTION

The initial limit is designed to allow a quantity sufficient for the most common uses of the medication. The recommended dosing parameters for all FDA-approved indications fall within the standard limits. Coverage of an additional quantity may be reviewed on a case-by-case basis upon request.

II. COVERED QUANTITIES

Medication	Standard Limit	FDA-recommended dosing
Follitropin Beta (Follistim AQ) 75 unit vial	60 vials per 28 days	Ovulation induction: starting dose of 75 IU daily for at least 7 days, increased by 25 to 50 IU at weekly intervals until adequate ovarian response. Maximum daily dose of 300 IU. Assisted reproductive technology: starting dose of 150 to 225 IU daily for at least 4 days with subsequent doses adjusted based upon ovarian response. Maximum daily dose of 600 IU. Induction of spermatogenesis: 450 IU per week
Follitropin Beta (Follistim AQ) 300 unit cartridge	15 cartridges per 28 days	Ovulation induction: starting dose of 50 IU daily for at least 7 days, increased by 25 to 50 IU at weekly intervals until adequate ovarian response. Maximum daily dose of 250 IU.
Follitropin Beta (Follistim AQ) 600 unit cartridge	10 cartridges per 28 days	Controlled ovarian stimulation as part of an in vitro fertilization or intracytoplasmic sperm injection cycle: starting dose of 200 IU daily for at least 7 days with subsequent doses adjusted up or down based upon ovarian response. Maximum daily dose of 500 IU. Induction of spermatogenesis: 450 IU per week
Follitropin Beta (Follistim AQ) 900 unit cartridge	7 cartridges per 28 days	
Follitropin Alfa (Gonal-f) 450 units vial	10 vials per 28 days	Ovulation induction: first cycle starting dose of 75 IU daily with incremental adjustment of up to 37.5 IU after 14 days. If necessary, increase dose by same magnitude every 7 days (in general up to 35 days of treatment). The initial dose in subsequent cycles is individualized based on prior response. Maximum daily dose of 300 IU.

Follitropin Alfa (Gonal-f) 1050 units vial	6 vials per 28 days	<p>Assisted reproductive technology: starting dose of 150 IU per day until adequate follicular development (up to 10 days of therapy in most cases). In patients whose endogenous gonadotropin levels are suppressed, starting dose of 225 IU daily. Consider dose adjustment after 5 days based on response (adjust no more frequently than every 3-5 days by no more than 75-150 IU). Maximum daily dose of 450 IU.</p> <p>Hypogonadotropic hypogonadism: 150 IU three times per week. Maximum dose of 300 IU three times per week.</p>
Follitropin Alfa (Gonal-f RFF) 300/0.5ml pen injector	15 cartridges per 28 days	<p>Ovulation induction: first cycle starting dose of 75 IU daily for 14 days. If indicated by the ovarian response after the initial 14 days, adjust dose by up to 37.5 IU every 7 days. Continue until adequate ovarian response (up to 35 days). The initial dose in subsequent cycles is based on prior response. Maximum daily dose of 300 IU.</p>
Follitropin Alfa (Gonal-f RFF) 450/0.75ml pen injector	10 cartridges per 28 days	
Follitropin Alfa (Gonal-f RFF) 900/1.5ml pen injector	7 cartridges per 28 days	<p>Assisted reproductive technology: starting dose of 150 IU per day until adequate follicular development (up to 10 days of therapy in most cases). In patients whose endogenous gonadotropin levels are suppressed, starting dose of 150 IU per day (if under 35 years old) or 225 IU per day (if 35 years old or older). Adjust dose after 5 days based on response (adjust no more frequently than every 3-5 days by no more than 75-150 IU). Maximum daily dose of 450 IU.</p>
Follitropin Alfa (Gonal-f RFF) 75 unit vial	60 vials per 28 days	<p>Ovulation induction: first cycle starting dose of 75 IU daily with incremental adjustment of up to 37.5 IU after 14 days. If necessary, increase dose by same magnitude every 7 days (in general up to 35 days of treatment). The initial dose in subsequent cycles is individualized based on prior response. Maximum daily dose of 300 IU.</p> <p>Assisted reproductive technology: starting dose of 150 IU per day until adequate follicular development (up to 10 days of therapy in most cases). In patients whose endogenous gonadotropin levels are suppressed, starting dose of 150 IU per day (if under 35 years old) or 225 IU per day (if 35 years old or older). Adjust dose after 5 days based on response (adjust no more frequently than every 3-5 days by no more than 75-150 IU). Maximum daily dose of 450 IU.</p>

Reference number
2047-H

III. REFERENCES

1. Follistim AQ [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; December 2013.
2. Follistim AQ Cartridge [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; December 2014.
3. Gonal-f Multi-Dose [package insert]. Rockland, MA: EMD Serono, Inc.; December 2012.
4. Gonal-f RFF [package insert]. Rockland, MA: EMD Serono, Inc.; May 2018.
5. Gonal-f RFF Redi-ject [package insert]. Rockland, MA: EMD Serono, Inc.; May 2018.
6. National Institute for Health and Clinical Excellence clinical guidelines 156. Fertility: Assessment and treatment for people with fertility problems. NICE 02/2013.

SPECIALTY QUANTITY LIMIT PROGRAM

OXBRYTA (voxelotor)

I. PROGRAM DESCRIPTION

The standard limit is designed to allow a quantity sufficient for the most common uses of the medication. If the member's plan allows a quantity limit exception review for the requested medication, coverage of an additional quantity may be provided up to the exception limit with prior authorization.

II. COVERED QUANTITIES

Medication	Standard Limit	Exception Limit*	FDA-recommended dosing
Oxbryta 500 mg tablet	90 per 30 days	150 per 30 days	Sickle cell disease: 1,500 mg orally once daily Dose modifications: <ul style="list-style-type: none"> Severe hepatic impairment: 1,000 mg orally once daily Strong CYP3A4 inhibitors or fluconazole: 1,000 mg orally once daily Strong or moderate CYP3A4 inducers: 2,500 mg orally once daily

*Coverage up to the exception limits may be provided with prior authorization via the Specialty Post Limit Quantity Exception Criteria for approval.

III. REFERENCES

- Oxbryta [package insert]. South San Francisco, CA: Global Blood Therapeutics, Inc.; December 2019.

SPECIALTY QUANTITY LIMIT PROGRAM

VISTOGARD (uridine triacetate)

I. PROGRAM DESCRIPTION

The standard limit is designed to allow a quantity sufficient for the most common uses of the medication. The recommended dosing parameters for all FDA-approved indications fall within the standard limits. Coverage of an additional quantity may be reviewed on a case-by-case basis upon request.

II. COVERED QUANTITIES

Medication	Standard Limit	FDA-recommended dosing
Vistogard Pak, oral granules 10 gram packet	20 packets per 5 days	Adults: 10 grams (1 packet) orally every 6 hours for 20 doses Pediatric: 6.2 grams/m ² of body surface area (not to exceed 10 grams per dose) orally every 6 hours for 20 doses

III. REFERENCES

- Vistogard [package insert]. Rockville, MD: Wellstat Therapeutics Corporation; February 2017.

SPECIALTY QUANTITY LIMIT PROGRAM

VISTOGARD (uridine triacetate)

I. PROGRAM DESCRIPTION

The standard limit is designed to allow a quantity sufficient for the most common uses of the medication. The recommended dosing parameters for all FDA-approved indications fall within the standard limits. Coverage of an additional quantity may be reviewed on a case-by-case basis upon request.

II. COVERED QUANTITIES

Medication	Standard Limit	FDA-recommended dosing
Vistogard Pak, oral granules 10 gram packet	20 packets per 5 days	Adults: 10 grams (1 packet) orally every 6 hours for 20 doses Pediatric: 6.2 grams/m ² of body surface area (not to exceed 10 grams per dose) orally every 6 hours for 20 doses

III. REFERENCES

- Vistogard [package insert]. Rockville, MD: Wellstat Therapeutics Corporation; February 2017.

SPECIALTY GUIDELINE MANAGEMENT

SPINRAZA (nusinersen)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Spinraza is indicated for the treatment of spinal muscular atrophy (SMA) in pediatric and adult patients.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. Initiation of therapy:

1. Deletion or mutation at the SMN1 allele confirmed by genetic testing.
2. Medical records (e.g., chart notes, laboratory values) of the baseline assessment for at least one of the following assessment tools (based on patient age and motor ability) to establish baseline motor ability:
 - i. Hammersmith Infant Neurological Exam Part 2 (HINE-2)
 - ii. Hammersmith Functional Motor Scale Expanded (HFMSE)
 - iii. Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND)

B. Continuation of therapy:

1. Medical records (e.g., chart notes, laboratory values) of the most recent (less than 1 month prior to continuation request) assessment by at least one of the following assessments:
 - i. HINE-2
 - ii. HFMSE
 - iii. CHOP-INTEND
 - iv. For members prescribed Spinraza due to clinical worsening after receiving gene therapy: Documentation of the impact of Spinraza therapy (e.g., impact on motor milestones)

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a physician who specializes in treatment of spinal muscular atrophy.

IV. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of SMA when all of the following criteria are met:

- A. Member has type 1, type 2 or type 3 SMA.

- B. There is genetic documentation of 5q SMA homozygous gene mutation, homozygous gene deletion, or compound heterozygote.
- C. The member is 15 years of age or younger at initiation of treatment.
- D. Member is not dependent on either of the following:
 - 1. Invasive ventilation or tracheostomy
 - 2. Use of non-invasive ventilation beyond naps and nighttime sleep
- E. Member meets one of the following criteria:
 - 1. Member has not previously received gene therapy for SMA, or
 - 2. Member has previously received gene therapy for SMA and has experienced a worsening in clinical status since receiving gene therapy as demonstrated by a decline of minimally clinical important difference from highest score achieved on one of the following exams (based on member age and motor ability):
 - i. HINE-2: Decline of at least 2 points on kicking and 1 point on any other milestone (excluding voluntary grasp)
 - ii. HFMSE: Decline of at least 3 points
 - iii. CHOP-INTEND: Decline of at least 4 points
- F. If the member has not received a loading dose, the loading dose will be dosed at 12 mg (5mL) on Day 0, 14, 28, and 58.

V. CONTINUATION OF THERAPY

Note: Members who were previously established on Spinraza and subsequently administered gene therapy must meet all initial criteria prior to re-starting therapy on Spinraza.

Authorization of 12 months may be granted for continued treatment of SMA when all of the following criteria are met:

- A. Member has type 1, type 2 or type 3 SMA.
- B. Member is not dependent on either of the following:
 - 1. Invasive ventilation or tracheostomy
 - 2. Use of non-invasive ventilation beyond naps and nighttime sleep
- C. Submission of medical records (e.g., chart notes, laboratory values) of the most recent (less than 1 month prior to continuation request) assessment documenting a positive clinical response from pretreatment baseline to Spinraza therapy, as demonstrated by at least one of the following assessments:
 - 1. HINE-2
 - i. One of the following:
 - a. Member exhibited improvement or maintenance of previous improvement of at least a 2 point (or maximal score) increase in ability to kick; *or*
 - b. Member exhibited improvement or maintenance of previous improvement of at least a 1 point (or maximal score) increase in any other HINE-2 milestone (e.g., head control, rolling, sitting, crawling, standing, or walking) excluding voluntary grasp; *and*
 - ii. One of the following:
 - a. Member exhibited improvement or maintenance of previous improvement in more HINE-2 motor milestones than worsening (net positive improvement); *or*
 - b. Member achieved and maintained any new motor milestones when they would otherwise be unexpected to do so (e.g., sit or stand unassisted, walk)
 - 2. HFMSE
 - i. One of the following:

- a. Member exhibited improvement or maintenance of previous improvement of at least a 3-point increase in score; *or*
 - b. Member has achieved and maintained any new motor milestone from pretreatment baseline when they would otherwise be unexpected to do so
3. CHOP-INTEND
- i. One of the following:
 - a. Member exhibited improvement or maintenance of previous improvement of at least a 4-point increase in score; *or*
 - b. Member has achieved and maintained any new motor milestone from pretreatment baseline when they would otherwise be unexpected to do so
4. Member was prescribed Spinraza due to clinical worsening after receiving gene therapy and there is documentation of stabilization or improvement in clinical status with Spinraza therapy (e.g., impact on motor milestones).
- D. If member has already received a loading dose, the maintenance dose will not exceed 12 mg (5 mL) every 4 months.

VI. REFERENCES

1. Spinraza [package insert]. Cambridge, MA: Biogen Inc.; June 2019.
2. Arnold WD, Kassar D, Kissel JT, et al. Spinal muscular atrophy: diagnosis and management in a new therapeutic era. *Muscle & Nerve*. 2015;51(2):157-167.
3. Burgunder JM, Schols L, Baets J, et al. EFNS guidelines for the molecular diagnosis of neurogenetic disorders: motoneuron, peripheral nerve and muscle disorders. *European J Neurol*. 2011;18:207-217.
4. Finkel RS, Chiriboga CA, Vajsar J, et al. Treatment of infantile-onset spinal muscular atrophy with nusinersen: a phase 2, open-label, dose-escalation study. *Lancet*. 2016;388:3017-26.
5. Finkel RS, Mercuri E, Darras BT, et al. Nusinersen versus sham control in infantile-onset spinal muscular atrophy. *N Engl J Med*. 2017; 377:1723-1732.
6. Ionis Pharmaceuticals, Inc. A Study to Assess the Efficacy and Safety of IONIS-SMN Rx in Infants with Spinal Muscular Atrophy. In: ClinicalTrials.gov [internet]. Bethesda (MD): National Library of Medicine (US). 2000- [2016 Feb 14]. Available from: <https://clinicaltrials.gov/ct2/show/NCT02193074>.
7. Mercuri E, Darras BT, Chiriboga CA, et al. Nusinersen versus sham control in later-onset spinal muscular atrophy. *N Engl J Med*. 2018; 378:625-635.
8. Wang CH, Finkel RS, Bertini ES, et al. Consensus statement for standard care in spinal muscular atrophy. *J Child Neurol*. 2007;22(8):1027-1049.

SPECIALTY GUIDELINE MANAGEMENT

SPRAVATO (esketamine) nasal spray

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Spravato is indicated, in conjunction with an oral antidepressant, for the treatment of treatment-resistant depression (TRD) in adults.

Limitations of Use: Spravato is not approved as an anesthetic agent. The safety and effectiveness of Spravato as an anesthetic agent have not been established.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

- A. For initial requests:
 1. Pretreatment depression severity score(s) from standardized rating scale(s) that reliably measure depressive symptoms (e.g., Beck Depression Scale [BDI], Hamilton Depression Rating Scale [HDRS], Montgomery-Asberg Depression Rating Scale [MADRS], etc.)
 2. Medical records documenting inadequate response with antidepressant and augmentation agents for the current depressive episode (if applicable)
- B. For continuation of therapy:

Current depression severity score(s) from standardized rating scale(s) that reliably measure depressive symptoms

III. EXCLUSION

Coverage will not be provided for members with current or recent history (i.e., within the last 6 months) of moderate or severe substance or alcohol use disorder.

IV. CRITERIA FOR INITIAL APPROVAL

Treatment-resistant depression (TRD)

Authorization of 1 month may be granted for treatment of TRD when all of the following criteria are met:

- A. Member has a confirmed diagnosis of severe major depressive disorder (single or recurrent episode), documented by standardized rating scales that reliably measure depressive symptoms (e.g., Beck

Depression Scale [BDI], Hamilton Depression Rating Scale [HDRS], Montgomery-Asberg Depression Rating Scale [MADRS]).

- B. Diagnosis is verified by a psychiatrist.
- C. Member is 18 years of age or older.
- D. Requested drug will be administered under the direct supervision of a healthcare provider.
- E. Member will be monitored by a health care provider for at least 2 hours after administration.
- F. Member meets either of the following criteria:
 1. Member must meet both of the following:
 - i. Member has experienced inadequate response during the current depressive episode with two antidepressants (e.g., selective serotonin reuptake inhibitor [SSRI], serotonin-norepinephrine reuptake inhibitor [SNRI], tricyclic antidepressant [TCA], bupropion, mirtazapine) from at least two different classes (different mechanisms of action) at the maximally tolerated labeled dose, each used for at least 8 weeks;
 - Aminoketone (Wellbutrin/SR/XL [bupropion])
 - Monoamine oxidase inhibitors (MAOIs) (e.g., Marplan, Nardil, Parnate, phenelzine, tranylcypromine)
 - Noradrenaline and specific serotonergic antidepressants (NASSAs) (e.g., amoxapine, maprotiline, mirtazapine/ODT, Oleptro ER, Remeron/Solutab, trazodone)
 - Selective serotonin reuptake inhibitors (SSRIs) (e.g., Celexa, citalopram, escitalopram, fluoxetine, fluvoxamine, Lexapro, Luvox/CR, paroxetine, Paxil/CR, Pexeva, Prozac/Weekly, sertraline, Zoloft)
 - Serotonin-norepinephrine reuptake inhibitors (SNRIs) (e.g., Cymbalta, desvenlafaxine/ER, duloxetine, Effexor/XR, Fetzima, Irenka, Khedezla, Pristiq, venlafaxine/ER)
 - Tricyclic antidepressants (TCAs) (e.g., amitriptyline, desipramine, doxepin, Elavil, imipramine, Norpramin, nortriptyline, Pamelor, Surmontil, Tofranil, trimipramine)
 - ii. Member has experienced an inadequate response with an adequate trial of augmentation therapy OR cognitive behavioral therapy during the current depressive episode
 - Augmentation therapy is defined as:
 - Two antidepressants with different mechanisms of action used concomitantly
 - An antidepressant and a second-generation antipsychotic used concomitantly
 - An antidepressant and lithium used concomitantly
 - An antidepressant and thyroid hormone used concomitantly
 - An antidepressant and buspirone used concomitantly
 2. Member has profound depression and persistent suicidal ideation defined as all of the following:
 - i. The prescriber represents that, in the absence of the requested drug, within the next 24 to 48 hours the member will require confinement in an acute care psychiatric institution.
 - ii. Member has a depressive episode so acute and so severe that the member is not able to participate in self-care (e.g., washing, eating) and is unable to participate at all in their usual daily activities (e.g., work). Member has persistent thoughts of hopelessness and helplessness as well as anhedonia.
 - iii. Member has thoughts of dying and/or self-harm for at least some part of each and every day.
- G. Requested drug will be used in combination with an oral antidepressant (e.g., duloxetine, escitalopram, sertraline, venlafaxine).

V. CONTINUATION OF THERAPY

Treatment-resistant depression (TRD)

Authorization of 3 months may be granted for the continuation of treatment of TRD when there is improvement or sustained improvement from baseline in depressive symptoms documented by standardized rating scales that reliably measure depressive symptoms (e.g., Beck Depression Scale [BDI], Hamilton Depression Rating Scale [HDRS], Montgomery-Asberg Depression Rating Scale [MADRS]).

Reference number(s)
2889-A

VI. REFERENCES

1. Spravato [package insert]. Titusville, NJ: Janssen Pharmaceuticals, Inc.; May 2019.

SPECIALTY GUIDELINE MANAGEMENT

SPRYCEL (dasatinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Newly diagnosed adults with Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) in chronic phase
2. Adults with chronic, accelerated, or myeloid or lymphoid blast phase Ph+ CML with resistance or intolerance to prior therapy including imatinib
3. Adults with Ph+ acute lymphoblastic leukemia (ALL) with resistance or intolerance to prior therapy
4. Pediatric patients with Ph+ CML in chronic phase
5. Pediatric patients with newly diagnosed Ph+ ALL in combination with chemotherapy

B. Compendial Uses

1. Primary treatment of advanced phase CML (accelerated phase or blast phase)
2. Follow-up therapy for CML patients after hematopoietic stem cell transplant (HSCT)
3. Ph+ ALL as a single agent or in combination with chemotherapy or corticosteroids
4. Induction therapy for Ph+ ALL in adults aged ≥ 65 years
5. Metastatic chondrosarcoma
6. Recurrent chordoma
7. Gastrointestinal stromal tumor (GIST) in patients with PDGFRA D842V mutation and disease progression on imatinib, sunitinib, or regorafenib

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review:

- A. Prior to initiation of therapy for treatment of CML or Ph+ ALL: results of cytogenetic and/or molecular testing for detection of the Ph chromosome or the BCR-ABL gene
- B. For members requesting initiation of Sprycel therapy for treatment of CML or ALL after experiencing resistance to prior tyrosine kinase inhibitor (TKI) therapy: results of T315I mutation testing

III. CRITERIA FOR INITIAL APPROVAL

A. **Chronic Myeloid Leukemia (CML)**

Authorization of 6 months may be granted for treatment of CML that has been confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing when any of the following criteria are met:

1. Member has not received prior therapy with a TKI (e.g., bosutinib, imatinib, nilotinib, ponatinib)
2. Member experienced toxicity or intolerance to prior therapy with a TKI

3. Member experienced resistance to prior therapy with a TKI and results of mutational testing are negative for T315I mutation
4. Member has received HSCT for CML

B. Ph+ Acute Lymphoblastic Leukemia (ALL)/Lymphoblastic Lymphoma (LL)

Authorization of 12 months may be granted for treatment of Ph+ ALL or LL that has been confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing when any of the following criteria are met:

1. Member has not received prior therapy with a TKI (e.g., bosutinib, imatinib, nilotinib, ponatinib)
2. Member experienced toxicity or intolerance to prior therapy with a TKI
3. Member experienced resistance to prior therapy with a TKI and results of mutational testing are negative for T315I mutation

C. Gastrointestinal Stromal Tumor (GIST)

Authorization of 12 months may be granted for treatment of GIST in members with PDGFRA D842V mutation who have experienced disease progression on imatinib, sunitinib, or regorafenib.

D. Bone Cancer

Authorization of 12 months may be granted for treatment of metastatic chondrosarcoma or recurrent chordoma.

IV. CONTINUATION OF THERAPY

A. CML

Authorization of 12 months may be granted for continued treatment of CML that has been confirmed by detection of Ph chromosome or BCR-ABL gene by cytogenetic and/ or molecular testing when any of the following criteria are met:

1. BCR-ABL1 \leq 10% for members who have been receiving Sprycel for \leq 12 months
2. No evidence of disease progression for members who have been receiving Sprycel for $>$ 12 months
3. Member has received HSCT

B. Ph+ ALL/LL

Authorization of 12 months may be granted for continued treatment of Ph+ ALL or LL that has been confirmed by detection of Ph chromosome or BCR-ABL gene by cytogenetic and/ or molecular testing in members who have not experienced disease progression or an unacceptable toxicity.

C. GIST and Bone Cancer

Authorization of 12 months may be granted for continued treatment of GIST, metastatic chondrosarcoma, or recurrent chordoma in members who have not experienced disease progression or an unacceptable toxicity.

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SPECIALTY GUIDELINE MANAGEMENT

STELARA (ustekinumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

1. FDA-Approved Indications
2. Moderate to severe plaque psoriasis (PsO)
3. Active psoriatic arthritis (PsA)
4. Moderately to severely active Crohn's disease (CD)
5. Moderately to severely active ulcerative colitis (UC)

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Moderate to severe plaque psoriasis (PsO)

1. Authorization of 12 months may be granted for members who previously received Otezla or a biologic indicated for the treatment of moderate to severe plaque psoriasis.
2. Authorization of 12 months may be granted for treatment of moderate to severe plaque psoriasis when all of the following criteria are met:
 - a. At least 3% of body surface area (BSA) is affected OR crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
 - b. Member meets any of the following criteria:
 - i. Member has had an inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) or a pharmacologic treatment with methotrexate, cyclosporine or acitretin.
 - ii. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine and acitretin (see Appendix A).
 - iii. Member has severe psoriasis that warrants a biologic DMARD as first-line therapy (i.e. at least 10% of the body surface area (BSA) or crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected).

B. Active psoriatic arthritis (PsA)

Authorization of 12 months may be granted for treatment of active psoriatic arthritis.

C. Moderately to severely active Crohn's disease (CD)

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for the treatment of Crohn's disease.

2. Authorization of 12 months may be granted for the treatment of moderately to severely active CD in members who had an inadequate response, intolerance or contraindication to at least one conventional therapy option (See Appendix B).

D. Moderately to severely active ulcerative colitis (UC)

1. Authorization of 12 months may be granted for members who have previously received a biologic or targeted synthetic DMARD (e.g., Xeljanz) indicated for moderately to severely active ulcerative colitis.
2. Authorization of 12 months may be granted for the treatment of moderately to severely active UC for members who had an inadequate response, intolerance or contraindication to at least one conventional therapy option (See Appendix C).

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who are using Stelara for an indication outlined in section II and achieve or maintain a positive clinical response with Stelara as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

For all indications: Member has had a documented negative TB test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic DMARDs or targeted synthetic DMARDs (e.g., Xeljanz), and repeated yearly for members with risk factors** for TB that are continuing therapy with biologics.

* If the screening testing for TB is positive, there must be documentation of further testing to confirm there is no active disease. Do not administer ustekinumab to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of ustekinumab.

** Risk factors for TB include: Persons with close contact to people with infectious TB disease; persons who have recently immigrated from areas of the world with high rates of TB (e.g., Africa, Asia, Eastern Europe, Latin America, Russia); children less than 5 years of age who have a positive TB test; groups with high rates of TB transmission (e.g., homeless persons, injection drug users, persons with HIV infection); persons who work or reside with people who are at an increased risk for active TB (e.g., hospitals, long-term care facilities, correctional facilities, homeless shelters).

For all indications: Member cannot use Stelara concomitantly with any other biologic DMARD or targeted synthetic DMARD.

Stelara for intravenous administration is FDA-approved for the treatment of Crohn's disease and ulcerative colitis and will only be authorized for these conditions.

V. APPENDICES

Appendix A: Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine or Acitretin.

1. Alcoholism, alcoholic liver disease or other chronic liver disease

2. Breastfeeding
3. Drug interaction
4. Cannot be used due to risk of treatment-related toxicity
5. Pregnancy or planning pregnancy
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

Appendix B: Examples of Conventional Therapy Options for CD

1. Mild to moderate disease – induction of remission:
 - a. Oral budesonide
 - b. Alternatives: metronidazole, ciprofloxacin, rifaximin
2. Mild to moderate disease – maintenance of remission:
 - a. Azathioprine, mercaptopurine
 - b. Alternatives: oral budesonide, methotrexate intramuscular (IM) or subcutaneous (SC), sulfasalazine
3. Moderate to severe disease – induction of remission:
 - a. Prednisone, methylprednisolone intravenously (IV)
 - b. Alternatives: methotrexate IM or SC
4. Moderate to severe disease – maintenance of remission:
 - a. Azathioprine, mercaptopurine
 - b. Alternative: methotrexate IM or SC
5. Perianal and fistulizing disease – induction of remission:
 - a. Metronidazole ± ciprofloxacin, tacrolimus
6. Perianal and fistulizing disease – maintenance of remission:
 - a. Azathioprine, mercaptopurine
 - b. Alternative: methotrexate IM or SC

Appendix C: Examples of conventional therapy options for UC

1. Mild to moderate disease – induction of remission:
 - a. Oral mesalamine (e.g., Asacol, Asacol HD, Lialda, Pentasa), balsalazide, olsalazine
 - b. Rectal mesalamine (e.g., Canasa, Rowasa)
 - c. Rectal hydrocortisone (e.g., Colocort, Cortifoam)
 - d. Alternatives: prednisone, azathioprine, mercaptopurine, sulfasalazine
2. Mild to moderate disease – maintenance of remission:
 - a. Oral mesalamine, balsalazide, olsalazine, rectal mesalamine
 - b. Alternatives: azathioprine, mercaptopurine, sulfasalazine
3. Severe disease – induction of remission:
 - a. Prednisone, hydrocortisone IV, methylprednisolone IV
 - b. Alternatives: cyclosporine IV, tacrolimus, sulfasalazine
4. Severe disease – maintenance of remission:
 - a. Azathioprine, mercaptopurine
 - b. Alternative: sulfasalazine
5. Pouchitis: Metronidazole, ciprofloxacin
 - a. Alternative: rectal mesalamine

VI. REFERENCES

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SPECIALTY GUIDELINE MANAGEMENT

STIMATE (desmopressin acetate nasal spray)

POLICY*

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Hemophilia A with factor VIII level >5%
2. Mild to moderate type 1 von Willebrand disease (vWD) with Factor VIII level >5%

B. Compendial Uses

1. Type 2A, 2M, 2N vWD
2. Qualitative platelet disorders
3. Acquired hemophilia A
4. Acquired von Willebrand syndrome

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Von Willebrand Disease**

1. Type 1 vWD
Indefinite authorization may be granted for treatment of mild or moderate type 1 vWD.
2. Type 2A, 2M, or 2N vWD
 - a. Authorization of one month may be granted for treatment of type 2A, 2M, or 2N vWD in members who are initiating therapy.
 - b. Indefinite authorization may be granted for treatment of type 2A, 2M, or 2N vWD in members who are continuing therapy and have demonstrated a response to an initial trial of Stimite.

B. **Hemophilia A**

Indefinite authorization may be granted for treatment of hemophilia A with factor VIII activity level greater than 5% (see Appendix).

C. **Qualitative Platelet Disorders**

Indefinite authorization may be granted for treatment of a qualitative platelet disorder.

D. **Acquired Hemophilia A**

Indefinite authorization may be granted for treatment of acquired hemophilia A.

E. **Acquired von Willebrand Syndrome**

Indefinite authorization may be granted for treatment of acquired von Willebrand syndrome.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. APPENDIX

Appendix: Classification of Hemophilia by Clotting Factor Level (% Activity) and Bleeding Episodes

Severity	Clotting Factor Level % activity*	Bleeding Episodes
Severe	<1%	Spontaneous bleeding episodes, predominantly into joints and muscles Severe bleeding with trauma, injury or surgery
Moderate	1% to 5%	Occasional spontaneous bleeding episodes Severe bleeding with trauma, injury or surgery
Mild	6% to 40%	Severe bleeding with serious injury, trauma or surgery

*Factor assay levels are required to determine the diagnosis and are of value in monitoring treatment response.¹²

*Note: **This program addresses the appropriate use of Stimate Nasal Spray only.** Stimate Nasal Spray and DDAVP (desmopressin) Nasal Spray are two distinct products and are not interchangeable. DDAVP Nasal Spray is not indicated for hemophilia or VWD.

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SPECIALTY GUIDELINE MANAGEMENT

STIMATE (desmopressin acetate nasal spray)

POLICY*

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Hemophilia A with factor VIII level >5%
2. Mild to moderate type 1 von Willebrand disease (VWD) with Factor VIII level >5%

B. Compendial Uses

1. Type 2A, 2M, 2N VWD
2. Qualitative platelet disorders
3. Acquired hemophilia A
4. Acquired von Willebrand syndrome

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Von Willebrand Disease**

1. Type 1 VWD
Indefinite authorization may be granted for treatment of mild or moderate type 1 VWD.
2. Type 2A, 2M, or 2N VWD
 - a. Authorization of one month may be granted for treatment of type 2A, 2M, or 2N VWD in members who are initiating therapy.
 - b. Indefinite authorization may be granted for treatment of type 2A, 2M, or 2N VWD in members who are continuing therapy and have demonstrated a response to an initial trial of Stimite.

B. **Hemophilia A**

Indefinite authorization may be granted for treatment of hemophilia A with factor VIII activity level greater than 5% (see Appendix).

C. **Qualitative Platelet Disorders**

Indefinite authorization may be granted for treatment of a qualitative platelet disorder.

D. **Acquired Hemophilia A**

Indefinite authorization may be granted for treatment of acquired hemophilia A.

E. **Acquired von Willebrand Syndrome**

Indefinite authorization may be granted for treatment of acquired von Willebrand syndrome.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. APPENDIX

Appendix: Classification of Hemophilia by Clotting Factor Level (% Activity) and Bleeding Episodes

Severity	Clotting Factor Level % activity*	Bleeding Episodes
Severe	<1%	Spontaneous bleeding episodes, predominantly into joints and muscles Severe bleeding with trauma, injury or surgery
Moderate	1% to 5%	Occasional spontaneous bleeding episodes Severe bleeding with trauma, injury or surgery
Mild	6% to 40%	Severe bleeding with serious injury, trauma or surgery

*Factor assay levels are required to determine the diagnosis and are of value in monitoring treatment response.

*Note: **This program addresses the appropriate use of Stimate Nasal Spray only.** Stimate Nasal Spray and DDAVP (desmopressin) Nasal Spray are two distinct products and are not interchangeable. DDAVP Nasal Spray is not indicated for hemophilia or VWD.

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SPECIALTY GUIDELINE MANAGEMENT

STIVARGA (regorafenib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. **Colorectal cancer**
Stivarga is indicated for the treatment of patients with metastatic colorectal cancer (CRC) who have been previously treated with fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, an anti-vascular endothelial growth factor (VEGF) therapy, and, if RAS wild type, an anti-epidermal growth factor receptor (EGFR) therapy.
2. **Gastrointestinal stromal tumors**
Stivarga is indicated for the treatment of patients with locally advanced, unresectable or metastatic gastrointestinal stromal tumor (GIST) who have been previously treated with imatinib mesylate and sunitinib malate.
3. **Hepatocellular carcinoma**
Stivarga is indicated for the treatment of patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib.

B. Compendial Uses

1. Unresectable, advanced, or metastatic colorectal cancer
2. Gastrointestinal stromal tumors (GIST)
3. Soft tissue sarcoma
 - a. Extremity/superficial trunk, head/neck
 - b. Retroperitoneal/Intra-Abdominal
 - c. Rhabdomyosarcoma
4. Hepatocellular Carcinoma

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Colorectal Cancer (CRC)**

Authorization of 12 months may be granted for the treatment of unresectable, advanced, or metastatic colorectal cancer as a single agent when the member has progressed on previous treatment with all the following regimens unless the member has a contraindication or intolerance:

1. Fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy; and
2. An anti-vascular endothelial growth factor (VEGF) therapy; and

Reference number(s)
1809-A

3. If RAS wild type, an anti-epidermal growth factor receptor (EGFR) therapy, such as Erbitux (cetuximab) or Vectibix (panitumumab)

B. Gastrointestinal stromal tumor (GIST)

Authorization of 12 months may be granted for the treatment of progressive disease in members when either of the following criteria are met:

1. Stivarga will be used following disease progression while previously treated with single-agent therapy with imatinib or sunitinib; or
2. Stivarga will be used in combination with everolimus following disease progression with imatinib, sunitinib, and regorafenib.

C. Hepatocellular carcinoma

Authorization of 12 months may be granted for the treatment of hepatocellular carcinoma as subsequent treatment as a single agent.

D. Soft tissue sarcomas

Authorization of 12 months may be for the treatment of retroperitoneal/intra-abdominal soft tissue sarcoma, rhabdomyosarcoma, and soft tissue sarcomas of the extremities, superficial trunk, or head and neck, as single agent palliative therapy.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in section II who have not experienced disease progression or an unacceptable toxicity.

IV. REFERENCES

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SPECIALTY GUIDELINE MANAGEMENT

STRENSIQ (asfotase alfa)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication¹

Strensiq is indicated for the treatment of patients with perinatal/infantile- and juvenile-onset hypophosphatasia (HPP).

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review:

Submission of the following:

- A. Documentation of presence of condition before the age of 18, if applicable
- B. Documentation confirming diagnosis which include one of the following:
 1. Genetic testing results confirming a mutation in the ALPL gene
 2. Submission of ALL of the following:
 - i. Radiographic imaging demonstrating skeletal abnormalities (See Appendix)
 - ii. A serum alkaline phosphatase level below the gender and age-specific reference range of the laboratory performing the test
 - iii. Elevated TNSALP substrate level (i.e., serum PLP level, serum or urine PEA level, urinary PPI level)

III. CRITERIA FOR INITIAL APPROVAL

Perinatal/infantile- and juvenile-onset hypophosphatasia (HPP)¹⁻⁴

Authorization of 12 months may be granted for treatment of HPP when all of the following criteria are met:

- A. The member has clinical signs and/or symptoms of hypophosphatasia (See Appendix A)
- B. The onset of the disease was perinatal/infantile or juvenile. If the member is 18 years of age or older at the time of the request, documentation of the presence of the condition before the age of 18 must be provided (e.g., member began experiencing symptoms at age 10).
- C. The diagnosis was confirmed by one of the following (1 or 2):
 1. The presence of a known pathological mutation in the ALPL gene as detected by ALPL molecular genetic testing
 2. The diagnosis is supported by ALL of the following:
 - i. Radiographic imaging demonstrating skeletal abnormalities (See Appendix B)
 - ii. A serum alkaline phosphatase level below the gender- and age-specific reference range of the laboratory performing the test

- iii. Elevated tissue-nonspecific alkaline phosphatase (TNSALP) substrate level (i.e., serum PLP level, serum or urine PEA level, urinary PPI level)

IV. CONTINUATION OF THERAPY

Authorization of 12 months will be granted for continued treatment in members requesting reauthorization for an indication listed in Section III are currently receiving the requested medication through a paid pharmacy or medical benefit and are experiencing benefit from therapy (e.g., improvement in skeletal manifestations, growth, gait/mobility, muscle strength).

V. APPENDIX

Appendix A. Examples of Signs and Symptoms of HPP²⁻⁴

A. Perinatal/infantile-onset HPP:

- Generalized hypomineralization with rachitic features, chest deformities and rib fractures
- Skeletal abnormalities (e.g., short limbs, abnormally shaped chest, soft skull bone)
- Respiratory problems (e.g., pneumonia)
- Hypercalcemia
- Failure to thrive
- Severe muscular hypotonia and weakness
- Nephrocalcinosis secondary to hypercalciuria
- Swallowing problems
- Seizures

B. Juvenile-onset HPP:

- Premature loss of deciduous teeth
- Failure to thrive with anorexia, nausea, and gastrointestinal problems
- Short stature with bowed legs or knock knees
- Skeletal deformities (e.g., enlarged wrist and ankle joints, abnormal skull shape)
- Bone and joint pain
- Rickets
- Fractures
- Delayed walking
- Waddling gait

Appendix B. Examples of Radiographic Findings that Support HPP Diagnosis²⁻⁴

- Infantile rickets
- Alveolar bone loss
- Focal bony defects of the metaphyses
- Metatarsal stress fractures
- Osteomalacia with lateral pseudofractures
- Osteopenia, osteoporosis, or low bone mineral content for age (as detected by dual-energy x-ray absorptiometry [DEXA])

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PRIOR AUTHORIZATION CRITERIA

DRUG CLASS **NARCOLEPSY AGENTS**

BRAND NAME*
(generic)

SUNOSI
(solriamfetol)

Status: CVS Caremark Criteria

Type: Initial Prior Authorization with Quantity Limit

Ref # 2915-C

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Sunosi is indicated to improve wakefulness in adult patients with excessive daytime sleepiness associated with narcolepsy or obstructive sleep apnea (OSA).

Limitations of use

Sunosi is not indicated to treat the underlying airway obstruction in OSA. Ensure that the underlying airway obstruction is treated (e.g., with continuous positive airway pressure (CPAP)) for at least one month prior to initiating Sunosi for excessive daytime sleepiness. Modalities to treat the underlying airway obstruction should be continued during treatment with Sunosi. Sunosi is not a substitute for these modalities.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has narcolepsy confirmed by sleep lab evaluation
AND
 - The patient has experienced an inadequate treatment response, intolerance or contraindication to a CNS stimulant (e.g., amphetamine, dextroamphetamine, methylphenidate)
AND
 - The patient has experienced an inadequate treatment response, intolerance or contraindication to modafinil OR armodafinil
- OR**
- The patient has obstructive sleep apnea (OSA) confirmed by polysomnography
AND
 - The patient has been receiving treatment for the underlying airway obstruction (e.g., continuous positive airway pressure [CPAP]) for at least one month
AND
 - The patient has experienced an inadequate treatment response, intolerance or contraindication to modafinil OR armodafinil

Quantity Limits Apply.

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Sunosi is indicated to improve wakefulness in adult patients with excessive daytime sleepiness associated with narcolepsy or obstructive sleep apnea (OSA). Sunosi is not indicated to treat the underlying airway obstruction in OSA. Ensure that the underlying airway obstruction is treated (e.g., with continuous positive airway pressure (CPAP)) for at least one month prior to initiating Sunosi for excessive

daytime sleepiness. Modalities to treat the underlying airway obstruction should be continued during treatment with Sunosi. Sunosi is not a substitute for these modalities.

According to the American Academy of Sleep Medicine (AASM), successful treatment of hypersomnia of central origin requires an accurate diagnosis, individual tailoring of therapy to produce the fullest possible return of normal function, and regular follow-up to monitor response to treatment. The evaluation should include a thorough evaluation of other possible contributing causes of excessive daytime sleepiness. The International Classification of Sleep Disorders, Third Edition (ICSD-3) specifies necessary diagnostic tests and criteria for each disorder of central origin. For narcolepsy, a sleep lab evaluation consisting of an overnight polysomnography (PSG) and mean sleep latency tests (MSLT) is recommended to confirm the diagnosis. Many other conditions produce such sleepiness and can mimic or coexist with a hypersomnia of central origin.⁴

According to AASM guidelines, modafinil is effective for treatment of daytime sleepiness due to narcolepsy. One additional study of 196 subjects involved assessment of armodafinil (the longer half-life enantiomer of modafinil) for treatment of excessive sleepiness in patients with narcolepsy.⁴ Subjects receiving armodafinil experienced significant improvement in sleepiness as measured by the Mean Wakefulness Test (MWT) mean sleep latency, and in the Clinical Global Impression of Change.⁴ The guidelines also state that amphetamine, dextroamphetamine, and methylphenidate are effective for treatment of daytime sleepiness due to narcolepsy.⁴ Therefore, patients with narcolepsy who have an inadequate treatment response, intolerance, or contraindication to a CNS stimulant and either modafinil or armodafinil will be considered for approval.

The presence or absence of obstructive sleep apnea (OSA) must be determined before initiating treatment. Diagnostic criteria for OSA are based on clinical signs and symptoms determined during a comprehensive sleep evaluation, which includes a sleep oriented history and physical examination, and findings defined by sleep testing.⁵ Following the history and physical examination, patients can be stratified according to their OSA disease risk. Those patients deemed high risk should have the diagnosis confirmed and severity determined with objective testing such as polysomnography with respiratory monitoring.⁵ OSA should be approached as a chronic disease requiring long-term, multidisciplinary management. The patient should be an active participant in the decision on treatment type and taught to contribute to the management of his or her own disease. Positive airway pressure (PAP) is the treatment of choice for mild, moderate, and severe OSA and should be offered as an option to all patients. Alternative therapies may be offered depending on the severity of the OSA and the patient's anatomy, risk factors, and preferences.⁵ Oral appliances (OA) may improve upper airway patency during sleep by enlarging the upper airway and/or by decreasing upper airway collapsibility (e.g., improving upper airway muscle tone). Although not as efficacious as PAP, OAs are indicated for use in patients with mild to moderate OSA who prefer OAs to CPAP or who do not respond to CPAP, are not appropriate candidates for CPAP, or who fail CPAP or other measures.⁵ Patients should be established on effective treatment of the underlying airway obstruction associated with OSA before considering pharmacologic therapy for excessive sleepiness associated with OSA.⁵ Patients should be continued on their treatment for the underlying airway obstruction while using pharmacologic treatment for excessive sleepiness due to OSA.^{1-3,5} Therefore, patients with OSA must be established on therapy to treat the underlying obstruction for approval of Sunosi.

Modafinil is recommended for the treatment of residual excessive daytime sleepiness in OSA patients who have sleepiness despite effective positive airway pressure (PAP) treatment and who are lacking any other identifiable cause for their sleepiness. Before using modafinil, other causes of residual sleepiness must be ruled out including: suboptimal objective adherence with PAP; ill-fitting PAP masks; insufficient sleep; poor sleep hygiene; other sleep disorders such as narcolepsy or restless legs syndrome/periodic limb movements of sleep; and depression. Modafinil should be used in addition to PAP therapy.⁵ Armodafinil (the longer half-life enantiomer of modafinil) is also indicated for the treatment of excessive daytime sleepiness associated with obstructive sleep apnea.^{2,3} Patients with OSA who have an inadequate treatment response, intolerance, or contraindication to modafinil or armodafinil will be considered for approval.

The recommended starting dosage of Sunosi in patients with narcolepsy is 75 mg once daily. Based on efficacy and tolerability, the dosage may be doubled at intervals of at least 3 days to a maximum recommended dose of 150 mg once daily. For OSA, Sunosi should be initiated at 37.5 mg once daily and may be doubled based on efficacy and tolerability at intervals of at least 3 days to a maximum recommended dose of 150 mg daily. Doses above 150 mg daily do not confer increased effectiveness sufficient to outweigh dose-related adverse reactions. Sunosi is available as 75 mg tablets that

are scored and can be split in half, and as 150 mg tablets. Therefore, the approval will be limited to a maximum of 30 tablets per month.

REFERENCES

1. Sunosi [package insert]. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; March 2019.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed April 2019.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed April 2019.
4. Morgenthaler TI, Vishesh KK, Brown T, et al. Practice Parameters for the Treatment of Narcolepsy and other Hypersomnias of Central Origin. *Sleep* 2007;30(12):1705-11.
5. Epstein LJ, Kristo D, Strollo PJ et al. Clinical Guidelines for the Evaluation, Management and Long-term Care of Obstructive Sleep Apnea in Adults. *J Clinical Sleep Medicine* 2009;5(3):263-276.

Written by: UM Development (KC)
 Date Written: 04/2019
 Revised:
 Reviewed: Medical Affairs (GAD) 04/2019
 External Review: 06/2019

CRITERIA FOR APPROVAL

1	Does the patient have a diagnosis of narcolepsy confirmed by sleep lab evaluation? [If no, then skip to question 3.]	Yes	No
2	Has the patient experienced an inadequate treatment response, intolerance, or contraindication to a central nervous system (CNS) stimulant (e.g., amphetamine, dextroamphetamine, methylphenidate)? [If yes, then skip to question 5.]	Yes	No
3	Does the patient have a diagnosis of obstructive sleep apnea (OSA) confirmed by polysomnography?	Yes	No
4	Has the patient been receiving treatment for the underlying airway obstruction (e.g., continuous positive airway pressure [CPAP]) for at least one month?	Yes	No
5	Has the patient experienced an inadequate treatment response, intolerance, or contraindication to armodafinil OR modafinil?	Yes	No
6	Does the patient require MORE than the plan allowance of 30 tablets per month? [RPh Note: If yes, then deny and enter a partial approval for 30 tablets per month.]	Yes	No

Mapping Instructions

	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Go to 3	
2.	Go to 5	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have tried a central nervous system (CNS) stimulant drug (e.g., amphetamine, dextroamphetamine, or methylphenidate) and it either did not work for you, or you cannot use it. Your request has been denied based on the information we have.

			[Short Description: No inadequate response, intolerance, or contraindication to a CNS stimulant drug]
3.	Go to 4	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet one of these conditions: - You have narcolepsy confirmed by sleep lab testing - You have obstructive sleep apnea confirmed by testing Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
4.	Go to 5	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have been on treatment for airway problems due to obstructive sleep apnea for at least one month. Your request has been denied based on the information we have. [Short Description: No underlying treatment for OSA]
5.	Go to 6	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have tried armodafinil or modafinil and it did not work for you, or you cannot use it. Your request has been denied based on the information we have. [Short Description: No inadequate response, intolerance, or contraindication to armodafinil or modafinil]
6.	Deny	Approve, 12 months, 30 tablets/25 days* or 90 tablets/75 days*	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 30 tablets/month of the requested drug and strength. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity]

*The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.

SPECIALTY GUIDELINE MANAGEMENT

Supprelin LA (histrelin acetate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Supprelin LA is indicated for the treatment of children with central precocious puberty (CPP).

B. Compendial Use

1. Gender dysphoria (also known as gender non-conforming or transgender persons)
NOTE: Some plans may opt-out of coverage for gender dysphoria.
2. Preservation of ovarian function
3. Prevention of recurrent menstrual related attacks in acute porphyria

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Central precocious puberty (CPP)**

1. Authorization up to age 12 may be granted for the treatment of CPP in a female member when all of the following criteria are met:
 - a. Intracranial tumor has been evaluated by appropriate lab tests and diagnostic imaging, such as computed tomography (CT scan), magnetic resonance imaging (MRI), or ultrasound.
 - b. The diagnosis of CPP has been confirmed by a pubertal response to a gonadotropin releasing hormone (GnRH) agonist test or a pubertal level of a third generation luteinizing hormone (LH) assay.
 - c. The assessment of bone age versus chronological age supports the diagnosis of CPP.
 - d. The member was less than 8 years of age at the onset of secondary sexual characteristics.
2. Authorization up to age 13 may be granted for the treatment of CPP in a male member when all of the following criteria are met:
 - a. Intracranial tumor has been evaluated by appropriate lab tests and diagnostic imaging, such as CT scan, MRI, or ultrasound.
 - b. The diagnosis of CPP has been confirmed by a pubertal response to a GnRH agonist test or a pubertal level of a third generation LH assay.
 - c. The assessment of bone age versus chronological age supports the diagnosis of CPP.
 - d. The member was less than 9 years of age at the onset of secondary sexual characteristics.

B. **Gender dysphoria**

1. Authorization of 12 months may be granted for pubertal suppression in preparation for gender reassignment in an adolescent member when all of the following criteria are met:
 - a. The member has a diagnosis of gender dysphoria.
 - b. The member has reached Tanner stage 2 of puberty.

Reference number(s)
1973-A, 2078-A

2. Authorization of 12 months may be granted for gender reassignment in an adult member when all of the following criteria are met:
 - a. The member has a diagnosis of gender dysphoria.
 - b. The member will receive Supprelin LA concomitantly with cross sex hormones.

C. Preservation of ovarian function

Authorization of 3 months may be granted for preservation of ovarian function when the member is premenopausal and undergoing chemotherapy.

D. Prevention of recurrent menstrual related attacks in acute porphyria

Authorization of 12 months may be granted for prevention of recurrent menstrual related attacks in members with acute porphyria when the requested medication is prescribed by or in consultation with a physician experienced in the management of porphyrias.

III. CONTINUATION OF THERAPY

A. Central precocious puberty (CPP)

1. Authorization up to age 12 may be granted for continuation of therapy for CPP in a female member if the member is currently less than 12 years of age.
2. Authorization up to age 13 may be granted for continuation of therapy for CPP in a male member if the member is currently less than 13 years of age.

B. Gender Dysphoria

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

C. All other indications

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Supprelin LA [package insert]. Malvern, PA: Endo Pharmaceuticals Solutions Inc.; May 2017.
2. Kletter GB, Klein KO, Wong YY. A pediatrician's guide to central precocious puberty. *Clin Pediatr*. 2015;54:414-424.
3. Carel J, Eugster EA, Rogol A, et al. Consensus statement on the use of gonadotropin-releasing hormone analogs in children. *Pediatrics*. 2009;123:e752-e762.
4. Houk CP, Kunselman AR, Lee PA. Adequacy of a single unstimulated luteinizing hormone level to diagnose central precocious puberty in girls. *Pediatrics*. 2009;123:e1059-e1063.
5. Kaplowitz P, Bloch C, the Section on Endocrinology. Evaluation and referral of children with signs of early puberty. *Pediatrics*. 2016;137:e20153732.
6. Hembree WC, Cohen-Kettenis PT, Gooren L, et al. Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*. 2017;102(11):3869-3903.
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11. Stein P, Badminton M, Barth J, Rees D, Stewart MF; British and Irish Porphyria Network. Best practice guidelines on clinical management of acute attacks of porphyria and their complications. *Ann Clin Biochem*. 2013 May;50(Pt 3):217-23.
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SPECIALTY GUIDELINE MANAGEMENT

SUTENT (sunitinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Gastrointestinal Stromal Tumor (GIST)
Sutent is indicated for the treatment of gastrointestinal stromal tumor after disease progression on or intolerance to imatinib mesylate.
2. Advanced Renal Cell Carcinoma (RCC)
Sutent is indicated for the treatment of advanced renal cell carcinoma.
3. Adjuvant Treatment of Renal Cell Carcinoma (RCC)
Sutent is indicated for the adjuvant treatment of adult patients at high risk of recurrent RCC following nephrectomy.
4. Advanced Pancreatic Neuroendocrine Tumors (pNET)
Sutent is indicated for the treatment of progressive, well-differentiated pancreatic neuroendocrine tumors in patients with unresectable locally advanced or metastatic disease.

B. Compendial Uses

1. Relapsed or stage IV RCC
2. Soft tissue sarcoma subtypes:
 - a. Angiosarcoma; as single-agent therapy
 - b. Solitary fibrous tumor; as single-agent therapy
 - c. Hemangiopericytoma, as single-agent therapy
 - d. Alveolar soft part sarcoma; as single-agent therapy
3. Gastrointestinal stromal tumors
 - a. Primary treatment for patients with life-threatening side effects on imatinib therapy and with disease documented as resectable with negative margins but with risk of significant morbidity, unresectable, recurrent, or metastatic
 - b. Postoperative treatment for patients who have life-threatening side effects on imatinib therapy
 - c. Treatment for limited or generalized progressive disease following progression on imatinib
 - d. Treatment in combination with everolimus for disease progression after single-agent therapy with imatinib, sunitinib, and regorafenib
4. Thymomas and thymic carcinomas, second-line therapy as a single agent
5. Thyroid carcinoma (papillary, Hürthle cell, or follicular), progressive and/or symptomatic iodine-refractory
6. Medullary thyroid carcinoma
 - a. Clinical trials, vandetanib, or cabozantinib are not available or appropriate
 - b. Disease progression on vandetanib or cabozantinib
7. Meningioma; surgically inaccessible recurrent or progressive disease for which radiation is not possible
8. Recurrent chordoma; as single-agent therapy

Reference number
2022-A

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Renal Cell Carcinoma

1. Authorization of 12 months may be granted for treatment of relapsed or metastatic renal cell carcinoma when any of the following criteria are met:
 - a. Sutent is given as first-line or subsequent therapy for disease with clear cell histology; OR
 - b. Sutent is given as systemic therapy for disease with non-clear cell histology.
2. Authorization of up to 54 weeks total may be granted for adjuvant treatment of members who are at high risk of recurrent renal cell carcinoma following nephrectomy.

B. Soft Tissue Sarcoma

Authorization of 12 months may be granted for treatment of the following subtypes of soft tissue sarcoma as single-agent therapy: alveolar soft-part sarcoma, angiosarcoma, solitary fibrous tumor, or hemangiopericytoma.

C. Gastrointestinal Stromal Tumor (GIST)

1. Authorization of 12 months may be granted for treatment of gastrointestinal stromal tumor after failure of imatinib due to progression or intolerable side effects.
2. Authorization of 12 months may be granted for treatment of gastrointestinal stromal tumor in combination with everolimus for disease progression after single-agent therapy with imatinib, sunitinib, and regorafenib.

D. Pancreatic Neuroendocrine Tumor

Authorization of 12 months may be granted for treatment of unresectable locally advanced or metastatic pancreatic neuroendocrine tumors.

E. Thymoma and Thymic Carcinoma

Authorization of 12 months may be granted for treatment of thymoma or thymic carcinoma with failure of one previous chemotherapy regimen.

F. Thyroid Carcinoma

Authorization of 12 months may be granted for treatment of progressive and/or symptomatic radioiodine refractory papillary, Hurthle cell, or follicular thyroid carcinoma.

G. Medullary Thyroid Carcinoma

Authorization of 12 months may be granted for treatment of metastatic medullary thyroid carcinoma when either of the following criteria are met:

1. Member has a contraindication or intolerance to vandetanib (Caprelsa) AND cabozantinib (Cometriq); OR
2. Disease progression occurred while on vandetanib (Caprelsa) OR cabozantinib (Cometriq)

H. Meningioma

Authorization of 12 months may be granted for treatment of surgically inaccessible recurrent or progressive meningioma for which radiation is not possible.

Reference number
2022-A

I. Chordoma

Authorization of 12 months may be granted for treatment of recurrent chordoma as single-agent therapy.

III. CONTINUATION OF THERAPY

- A. Authorization of 12 months may be granted for continued treatment in members requesting reauthorization who have not experienced disease progression or an unacceptable toxicity for the specified indications below:
 1. Relapsed or metastatic renal cell carcinoma
 2. Soft tissue sarcoma
 3. Gastrointestinal stromal tumor
 4. Pancreatic neuroendocrine tumor
 5. Thymoma and thymic carcinoma
 6. Thyroid carcinoma
 7. Medullary thyroid carcinoma
 8. Meningioma
 9. Chordoma
- B. Authorization of up to 54 weeks total may be granted for continued treatment in members requesting reauthorization for adjuvant treatment of renal cell carcinoma when the following criteria are met:
 1. Disease is not recurrent; AND
 2. Member has not exceeded a maximum of nine 6 week cycles.

IV. REFERENCES

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4. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Soft Tissue Sarcoma. Version 2.2019. Accessed May 13, 2019. https://www.nccn.org/professionals/physician_gls/pdf/sarcoma.pdf.
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SPECIALTY GUIDELINE MANAGEMENT

SYLATRON (peginterferon alfa-2b)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

1. Sylatron is indicated for the adjuvant treatment of melanoma with microscopic or gross nodal involvement within 84 days of definitive surgical resection including complete lymphadenectomy.

B. Compendial Uses

1. Low-risk myelofibrosis
2. Polycythemia vera
3. Essential thrombocythemia
4. Systemic mastocytosis

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Melanoma**

Authorization of 12 months may be granted for the treatment of melanoma.

B. **Myelofibrosis**

Authorization of 12 months may be granted for the treatment of myelofibrosis.

C. **Polycythemia Vera**

Authorization of 12 months may be granted for the treatment of polycythemia vera.

D. **Essential Thrombocythemia**

Authorization of 12 months may be granted for the treatment of essential thrombocythemia.

E. **Systemic Mastocytosis**

Authorization of 12 months may be granted for the treatment of systemic mastocytosis.

III. CONTINUATION OF THERAPY

A. **Systemic mastocytosis**

Authorization of 12 months may be granted if the patient is experiencing benefit from therapy as evidenced by improvement in symptoms and/or disease markers (e.g., reduction in serum and urine metabolites of mast cell activation, improvement in cutaneous lesions, skeletal disease, bone marrow mast cell burden, etc.)

B. All Other Indications

Authorization of 12 months may be granted for continuation of therapy for an indication outlined in section II when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Sylatron [package insert]. Whitehouse Station, NJ: Schering Corporation; May 2018.
2. The NCCN Drugs & Biologics Compendium 2018 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed May 14, 2019.
3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology™ Systemic Mastocytosis (Version 2.2019). <http://www.nccn.org>. Accessed May 22, 2019.

SPECIALTY GUIDELINE MANAGEMENT

SYLVANT (siltuximab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Sylvant is indicated for the treatment of patients with multicentric Castleman's disease who are human immunodeficiency virus (HIV) negative and human herpesvirus-8 (HHV-8) negative.

B. Compendial Use

Relapsed/refractory unicentric Castleman's disease

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Multicentric Castleman's disease or relapsed/refractory unicentric Castleman's disease.

Authorization of 12 months may be granted for treatment of active multicentric Castleman's disease with no organ failure or relapsed/refractory unicentric Castleman's disease when both of the following criteria are met:

- A. Member is human immunodeficiency virus (HIV) negative and human herpesvirus-8 (HHV-8) negative.
- B. Sylvant is used as a single agent.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced disease progression or an unacceptable toxicity.

IV. REFERENCES

1. Sylvant [package insert]. Horsham, PA: Janssen Biotech, Inc.; May 2018.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed September 12, 2019.

SPECIALTY GUIDELINE MANAGEMENT

SYMDEKO (tezacaftor/ivacaftor)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Symdeko is indicated for the treatment of patients with cystic fibrosis (CF) aged 6 years and older who are homozygous for the *F508del* mutation or who have at least one mutation in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene that is responsive to tezacaftor/ivacaftor based on *in vitro* data and/or clinical evidence. If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of *CFTR* mutation followed by verification with bi-directional sequencing when recommended by the mutation test instructions for use.

All other indications are considered experimental/investigational and are not medically necessary.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review: genetic testing report confirming the presence of the appropriate *CFTR* gene mutation.

III. CRITERIA FOR INITIAL APPROVAL

Cystic Fibrosis

Authorization of 12 months may be granted for treatment of cystic fibrosis when all of the following criteria are met:

- A. Genetic testing was conducted to detect a mutation in the *CFTR* gene.
- B. The member has one of the following mutations in the *CFTR* gene: A455E, A1067T, D110E, D110H, D579G, D1152H, D1270N, E56K, E193K, E831X, F1052V, F1074L, K1060T, L206W, P67L, R74W, R117C, R347H, R352Q, R1070W, S945L, S977F, 711+3A→G, 2789+5G→A, 3272-26A→G, 3849+10kbC→T, or the member is homozygous for the *F508del* mutation.
- C. The member is at least 6 years of age.
- D. Symdeko will not be used in combination with Kalydeco or Orkambi.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who are experiencing benefit from therapy as evidenced by disease stability or disease improvement (e.g., improvement in FEV1 from baseline).

Reference number(s)
2516-A

V. REFERENCES

1. Symdeko [package insert]. Boston, MA: Vertex Pharmaceuticals Inc.; June 2019.
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3. Taylor-Cousar JL, Munck A, McKone EF, et al. Tezacaftor–ivacaftor in patients with cystic fibrosis homozygous for Phe508del *N Engl J Med* 2017; 377:2013-2023

Reference number
1988-A

SPECIALTY GUIDELINE MANAGEMENT

SYNAGIS (palivizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Synagis is indicated for the prevention of serious lower respiratory tract disease caused by respiratory syncytial virus (RSV) in pediatric patients:

- with a history of premature birth (less than or equal to 35 weeks gestational age) and who are 6 months of age or younger at the beginning of RSV season,
- with bronchopulmonary dysplasia (BPD) that required medical treatment within the previous 6 months and who are 24 months of age or younger at the beginning of RSV season,
- with hemodynamically significant congenital heart disease (CHD) and who are 24 months of age or younger at the beginning of RSV season

Limitations of Use:

The safety and efficacy of Synagis have not been established for treatment of RSV disease.

B. Compendial Uses

1. RSV prophylaxis in infants with congenital abnormalities of the airway or neuromuscular disease that compromise handling of respiratory secretions
2. RSV prophylaxis in immunocompromised pediatric patients
3. RSV prophylaxis in pediatric patients with cystic fibrosis who have evidence of chronic lung disease or nutritional compromise in the first year of life

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of up to 5 doses per RSV season may be granted for the prevention of serious lower respiratory tract disease caused by RSV when a member has any of the following diagnoses and meets the criteria pertaining to the diagnosis:

1. Prematurity
2. Chronic lung disease (CLD) of prematurity
3. Congenital heart disease (CHD) (See Appendix B)
4. Congenital airway abnormality
5. Neuromuscular condition
6. Immunocompromised children
7. Cystic fibrosis

A. Prematurity

Reference number
1988-A

All of the following criteria are met:

1. Member's gestational age is < 29 weeks, 0 days.
2. Member's chronological age at the start of RSV season is < 12 months.

B. CLD of prematurity

ALL of the following criteria must be met:

1. Member's gestational age is < 32 weeks, 0 days.
2. Requirement for > 21% oxygen for at least the first 28 days after birth.
3. Member meets either of the following criteria:
 - i. Member's chronological age at the start of their first RSV season is < 12 months.
 - ii. Member's chronological age at the start of the subsequent RSV season is < 24 months and the member continues to require medical support (e.g., chronic corticosteroids, diuretic therapy, supplemental oxygen) during the 6-month period prior to the start of the RSV season.

C. CHD

All of the following criteria are met:

1. CHD is hemodynamically significant.
2. Member meets either of the following criteria:
 - i. Member's chronological age at the start of RSV season is < 12 months.
 - ii. Member's chronological age at the start of RSV season is between 12 to 24 months and the member will be undergoing cardiac transplantation during the RSV season.

D. Congenital airway abnormality

All of the following criteria must be met:

1. The condition compromises handling of respiratory secretions.
2. Member's chronological age at the start of RSV season is < 12 months.

E. Neuromuscular condition

All of the following criteria must be met:

1. The condition compromises handling of respiratory secretions.
2. Member's chronological age at the start of RSV season is < 12 months.

F. Immunocompromised children

All of the following criteria must be met:

1. Member is profoundly immunocompromised during the RSV season (e.g., SCID, stem cell transplant, bone marrow transplant)
2. Member's chronological age at the start of the RSV season is <24 months

G. Cystic Fibrosis

Either of the following criteria must be met:

1. Member's chronological age at the start of the RSV season is < 12 months and the member has evidence of CLD or nutritional compromise
2. Member's chronological age at the start of RSV season is between 12 to 24 months and the member has manifestations of lung disease (e.g., hospitalizations for pulmonary exacerbations) or weight less than the 10th percentile

III. OTHER

For all off-season Synagis requests, authorization of 1 dose per request, up to a maximum of 5 doses per RSV season, may be granted if the RSV activity for the requested region is $\geq 10\%$ within 2 weeks of the intended dose according to the CDC National Respiratory and Enteric Virus Surveillance System (NREVSS). The local

Reference number
1988-A

health department or the CDC NREVSS will be consulted to assess the RSV activity for that region (<http://www.cdc.gov/surveillance/nrevss/rsv/index.html>). Other Specialty Guideline Management criteria apply.

CVS Caremark PBM Synagis Season for 2019-2020 will be November 1, 2019 to March 31, 2020. Other health plans may differ.

IV. APPENDIX

Appendix A: Recommended Use of Synagis for Prevention of RSV Infection

Recommendations from the American Academy of Pediatrics for the prevention of RSV infection with Synagis are summarized in Table below. Synagis should be administered intramuscularly at a dose of 15 mg/kg once per month beginning prior to the onset of the RSV season, which typically occurs in November. Because 5 monthly doses of Synagis will provide more than 6 months of serum Synagis concentrations above the desired serum concentration for most infants, administration of more than 5 monthly doses is not recommended within the continental United States.

Table. Recommended Use of Synagis for Prevention of RSV Infection

Prematurity	<ul style="list-style-type: none"> • Preterm infants born < 29 weeks, 0 days of gestation who are younger than 12 months at the start of the RSV season
Congenital Heart Disease	<ul style="list-style-type: none"> • Infants and children < 12 months of age with hemodynamically significant CHD • Those most likely to benefit from prophylaxis include: <ul style="list-style-type: none"> ○ Infants with acyanotic heart disease who are receiving medication to control congestive heart failure and will require cardiac surgical procedures ○ Infants with moderate to severe pulmonary hypertension • Infants and children < 24 months of age who undergo cardiac transplantation during the RSV season
Chronic Lung Disease of Prematurity	<ul style="list-style-type: none"> • For the first RSV season during the first year of life: Preterm infants who develop CLD of prematurity defined as: <ul style="list-style-type: none"> ○ Gestational age < 32 weeks, 0 days <u>AND</u> ○ Requirement for > 21% oxygen for at least the first 28 days after birth • For the second RSV season during the second year of life: Preterm infants who: <ul style="list-style-type: none"> ○ Satisfy the above definition of CLD of prematurity <u>AND</u> ○ Continue to require medical support* for CLD during the 6-month period prior to the start of the second RSV season
Congenital Abnormality of the Airway/ Neuromuscular Condition	<ul style="list-style-type: none"> • Infants who have either a significant congenital abnormality of the airway or a neuromuscular condition that compromises handling of respiratory secretions for the first year of life

Reference number
1988-A

Immunocompromised children	<ul style="list-style-type: none"> Children younger than 24 months of age who are profoundly immunocompromised during the RSV season
Cystic Fibrosis	<ul style="list-style-type: none"> For the first year of life, children with clinical evidence of CLD and/or nutritional compromise For the second year of life, children with manifestations of severe lung disease (previous hospitalization for pulmonary exacerbation in the first year of life or abnormalities on chest radiography or chest computed tomography that persist when stable) OR weight for length less than the 10th percentile.

Abbreviations: CHD = congenital heart disease; CLD = chronic lung disease (formerly bronchopulmonary dysplasia); RSV = respiratory syncytial virus.

* Medical support includes supplemental oxygen, diuretic therapy, or chronic corticosteroid therapy.

Appendix B: Examples of Congenital Heart Anomalies*

- Atrial or ventricular septal defect
- Coarctation of aorta
- Tetralogy of Fallot
- Pulmonary or aortic valve stenosis
- Tricuspid atresia
- Ebstein's anomaly
- Pulmonary atresia
- Transposition of great arteries
- Truncus arteriosus
- Hypoplastic left/right ventricle
- Single ventricle
- Double-outlet right ventricle
- Total anomalous pulmonary venous return

*Must be hemodynamically significant. See Table above for examples of infants and children who are most likely to benefit from Synagis.

V. REFERENCES

1. Synagis [package insert]. Gaithersburg, MD: MedImmune, LLC; May 2017.
2. American Academy of Pediatrics. Updated guidance for palivizumab prophylaxis among infants and young children at increased risk of hospitalization for respiratory syncytial virus infection. *Pediatrics*. 2014;134(2):415-20.
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Reference number(s)
2174-A

SPECIALTY GUIDELINE MANAGEMENT

SYNRIBO (omacetaxine mepesuccinate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Adult patients with chronic or accelerated phase chronic myeloid leukemia (CML) with resistance and/or intolerance to two or more tyrosine kinase inhibitors (TKIs)

B. Compendial Use

1. Primary treatment of advanced phase CML for patients with disease progression to accelerated phase
2. Follow-up therapy for CML patients after hematopoietic stem cell transplant (HSCT)
3. Patients with a T315I mutation or disease that is resistant and/or intolerant to two or more tyrosine kinase inhibitors (TKIs)

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review:

- A. Prior to initiation of therapy: results of cytogenetic and/or molecular testing for detection of the Ph chromosome or the BCR-ABL gene
- B. For members requesting initiation of Synribo therapy for treatment of T315I-positive CML: results of T315I mutation testing

III. CRITERIA FOR INITIAL APPROVAL

Chronic Myeloid Leukemia (CML)

Authorization of 6 months may be granted for treatment of chronic or accelerated phase CML confirmed by detection of the BCR-ABL gene by cytogenetic and/or molecular testing when any of the following criteria are met:

- A. Member has a T315I mutation
- B. Member has experienced resistance, toxicity, or intolerance to prior therapy with two or more TKIs (e.g., imatinib, bosutinib, dasatinib, nilotinib, ponatinib)
- C. Disease has progressed to accelerated phase
- D. Member has received HSCT for CML

Reference number(s)
2174-A

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment of CML that has been confirmed by detection of Ph chromosome or BCR-ABL gene by cytogenetic and/ or molecular testing when either of the following criteria are met:

- A. Member has not experienced disease progression or an unacceptable toxicity
- B. Member has received HSCT

V. REFERENCES

1. Synribo [package insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; June 2017.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed April 23, 2019.
3. NCCN Clinical Practice Guidelines in Oncology® Chronic Myeloid Leukemia (Version 1.2019). © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed April 16, 2019.

SPECIALTY GUIDELINE MANAGEMENT

Adcirca (tadalafil) tadalafil tablets (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Indicated for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group 1) to improve exercise ability. Studies establishing effectiveness included predominately patients with NYHA Functional Class II – III symptoms and etiologies of idiopathic or heritable PAH (61%) or PAH associated with connective tissue diseases (23%).

B. Compendial Use

Secondary Raynaud's phenomenon

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Pulmonary Arterial Hypertension**

Authorization of 12 months may be granted for treatment of PAH when ALL of the following criteria are met:

1. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
2. PAH was confirmed by either criterion (1) or criterion (2) below:
 - i. Pretreatment right heart catheterization with all of the following results:
 - a. mPAP \geq 25 mmHg
 - b. PCWP \leq 15 mmHg
 - c. PVR $>$ 3 Wood units
 - ii. For infants less than one year of age with any of the following conditions, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed:
 - a. Post cardiac surgery
 - b. Chronic heart disease
 - c. Chronic lung disease associated with prematurity
 - d. Congenital diaphragmatic hernia

B. **Secondary Raynaud 's Phenomenon**

Authorization of 12 months may be granted for treatment of secondary Raynaud's phenomenon when the patient has had an inadequate response to one of the following medications:

1. Calcium channel blockers
2. Angiotensin receptor blockers
3. Selective serotonin reuptake inhibitors
4. Alpha blockers

5. Topical nitrates

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with an indication listed in Section II who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

IV. APPENDIX

WHO Classification of Pulmonary Hypertension

1 PAH

- 1.1 Idiopathic (PAH)
- 1.2 Heritable PAH
- 1.3 Drug- and toxin-induced PAH
- 1.4. PAH associated with:
 - 1.4.1 Connective tissue diseases
 - 1.4.2 HIV infection
 - 1.4.3 Portal hypertension
 - 1.4.4 Congenital heart diseases
 - 1.4.5 Schistosomiasis
- 1.5 PAH long-term responders to calcium channel blockers
- 1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement
- 1.7 Persistent PH of the newborn syndrome

2 PH due to left heart disease

- 2.1 PH due to heart failure with preserved LVEF
- 2.2 PH due to heart failure with reduced LVEF
- 2.3 Valvular heart disease
- 2.4 Congenital/acquired cardiovascular conditions leading to post-capillary PH

3 PH due to lung diseases and/or hypoxia

- 3.1 Obstructive lung disease
- 3.2 Restrictive lung disease
- 3.3 Other lung disease with mixed restrictive/obstructive pattern
- 3.4 Hypoxia without lung disease
- 3.5 Developmental lung disorders

4 PH due to pulmonary artery obstruction

- 4.1 Chronic thromboembolic PH
- 4.2 Other pulmonary artery obstructions
 - 4.2.1 Sarcoma (high or intermediate grade) or angiosarcoma
 - 4.2.2 Other malignant tumors
 - Renal carcinoma
 - Uterine carcinoma
 - Germ cell tumours of the testis
 - Other tumours
 - 4.2.3 Non-malignant tumours
 - Uterine leiomyoma
 - 4.2.4 Arteritis without connective tissue disease
 - 4.2.5 Congenital pulmonary artery stenosis
 - 4.2.6 Parasites

Hydatidosis

5 PH with unclear and/or multifactorial mechanisms

5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders

5.2 Systemic and metabolic disorders: Pulmonary Langerhans cell histiocytosis, Gaucher disease, glycogen storage disease, neurofibromatosis, sarcoidosis

5.3 Others: chronic renal failure with or without hemodialysis, fibrosing mediastinitis

5.4 Complex congenital heart disease

V. REFERENCES

1. Adcirca [package insert]. Indianapolis, IN: Eli Lilly and Company; August 2017.
2. Tadalafil [package insert]. Morgantown, WV: Mylan Pharmaceuticals Inc.; August 2018.
3. IBM Micromedex® DRUGDEX® (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: [https:// www.micromedexsolutions.com](https://www.micromedexsolutions.com) (cited: 06/17/2019).
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7. Simonneau G, Robbins IM, Beghetti M, et al. Updated clinical classification of pulmonary hypertension. *J Am Coll Cardiol*. 2013;62:D34-S41.
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9. Barst RJ, Gibbs SR, Ghofrani HA, et al. Updated evidence-based treatment algorithm in pulmonary arterial hypertension. *J Am Coll Cardiol*. 2009;54:S78-S84.
10. Taichman DB, Ornelas J, Chung L, et al. Pharmacologic therapy for pulmonary arterial hypertension in adults. CHEST guideline and expert panel report. *Chest*. 2014;46(2):449-475.
11. Abman, SH, Hansmann G, Archer SL, et al. Pediatric pulmonary hypertension: guidelines from the American Heart Association and American Thoracic Society. *Circulation*. 2015;132(21):2037-99.
12. Klinger, JR., Elliott, CG, Levine, DJ, et al. Therapy for Pulmonary Arterial Hypertension in Adults: Update of the CHEST Guidelines and Expert Panel Report. *Chest*. 2019;155(3): 565-586.
13. Galie, N., McLaughlin, VV, Rubin, LJ, Simonneau, G. An overview of the 6th World Symposium on Pulmonary Hypertension. *Eur Respir J* 2019; 53: 1802148; DOI: 10.1183/13993003.02148-2018. Published 24 January 2019.

SPECIALTY GUIDELINE MANAGEMENT

TAFINLAR (dabrafenib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Tafinlar is indicated as a single agent for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E mutation as detected by an FDA-approved test.
2. Tafinlar is indicated, in combination with trametinib, for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test.
3. Tafinlar is indicated, in combination with trametinib, for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) with BRAF V600E mutation as detected by an FDA-approved test.
4. Tafinlar is indicated, in combination with trametinib, for the adjuvant treatment of patients with melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test, and involvement of lymph node(s), following complete resection.
5. Tafinlar is indicated, in combination with trametinib, for the treatment of patients with locally advanced or metastatic anaplastic thyroid cancer (ATC) with BRAF V600E mutation and no satisfactory locoregional treatment options.

B. Compendial Uses

1. Melanoma, BRAF V600 activating mutation-positive
2. Brain metastases from melanoma
3. NSCLC, BRAF V600E
4. Glioma, BRAF V600 activating mutation-positive
5. Meningioma, BRAF V600 activating mutation-positive
6. Astrocytoma, BRAF V600 activating mutation-positive
7. Papillary, follicular, Hürthle cell thyroid carcinoma
8. Colorectal cancer, BRAF V600E activating mutation-positive

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of BRAF mutation documentation is necessary to initiate prior authorization review.

III. CRITERIA FOR INITIAL APPROVAL

A. **Melanoma**

1. Authorization of 12 months may be granted for treatment of unresectable or metastatic cutaneous melanoma with a BRAF V600 activating mutation as a single agent or in combination with trametinib (Mekinist).

Reference number(s)
1683-A

2. Authorization of 12 months may be granted for treatment of brain metastases from melanoma with a BRAF V600 activating mutation in combination with trametinib (Mekinist).
3. Authorization of 12 months may be granted for adjuvant treatment of cutaneous melanoma with a BRAF V600 activating mutation in combination with trametinib (Mekinist).

B. Non-Small Cell Lung Cancer (NSCLC)

Authorization of 12 months may be granted for treatment of BRAF V600E mutation-positive NSCLC as a single agent or in combination with trametinib (Mekinist).

C. Anaplastic Thyroid Cancer (ATC)

Authorization of 12 months may be granted for treatment of metastatic BRAF V600E mutation-positive ATC in combination with trametinib (Mekinist).

D. Central Nervous System Cancer

Authorization of 12 months may be granted for treatment of BRAF V600 mutation-positive gliomas, meningiomas, or astrocytomas.

E. Thyroid carcinoma

Authorization of 12 months may be granted for treatment of progressive and/or symptomatic radioiodine-refractory BRAF-activating mutation positive follicular, Hurthle cell, or papillary thyroid carcinoma.

F. Colorectal Cancer

Authorization of 12 months may be granted for treatment of unresectable advanced or metastatic colorectal cancer when the following criteria are met:

1. Tafinlar is used in combination with trametinib (Mekinist) and either cetuximab or panitumumab
2. Tumor is positive for BRAF V600E mutation.
3. Will be used as subsequent therapy

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy for an indication outlined in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen. For patients using Tafinlar for adjuvant treatment of cutaneous melanoma, only 12 months of therapy total will be approved.

V. REFERENCES

1. Tafinlar [package insert]. East Hanover, NJ: Novartis Pharmaceutical Corporation; May 2018.
2. The NCCN Drugs & Biologics Compendium 2018 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed July 30, 2019.
3. The NCCN Clinical Practice Guidelines in Oncology Central Nervous System Cancers (Version 1.2018). 2018 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed November 19, 2018.
4. The NCCN Clinical Practice Guidelines in Oncology Non-Small Cell Lung Cancer (Version 1.2019). 2018 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed November 19, 2018.
5. The NCCN Clinical Practice Guidelines in Oncology Cutaneous Melanoma (Version 1.2019). 2018 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed November 19, 2018.
6. The NCCN Clinical Practice Guidelines in Oncology Thyroid Carcinoma (Version 1.2018). 2018 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed November 19, 2018.
7. Usabalieva A, Pierson CR, Kavran CA, et al. Primary Meningeal Pleomorphic Xanthoastrocytoma With Anaplastic Features: A Report of 2 Cases, One With *BRAFV600E* Mutation and Clinical Response to the *BRAF* Inhibitor Dabrafenib. *Journal of neuropathology and experimental neurology*. 2015;74(10):960-969. doi:10.1097/NEN.0000000000000240.

Reference number(s)
1683-A

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10. Meletah SK, Pavlick D, Brennan T, et al. Personalized Treatment for a Patient with a BRAF V600E Mutation using Dabrafenib and a Tumor Treatment Fields Device in a High-Grade Glioma Arising from Ganglioglioma. *Journal of the National Comprehensive Cancer Network*. 2016; 14(11): 1345-1350.

SPECIALTY GUIDELINE MANAGEMENT

TAGRISSO (osimertinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications¹

1. Tagrisso is indicated for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test.
2. Tagrisso is indicated for the treatment of patients with metastatic epidermal growth factor receptor (EGFR) T790M mutation-positive non-small cell lung cancer (NSCLC), as detected by an FDA-approved test, who have progressed on or after EGFR tyrosine kinase inhibitor (TKI) therapy.

B. Compendial Uses²⁻⁴

1. EGFR mutation-positive recurrent, advanced or metastatic NSCLC.
2. Brain metastases from sensitizing EGFR mutation-positive NSCLC.
3. Brain metastases from EGFR T790M mutation-positive NSCLC.

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: EGFR mutation testing results.

III. CRITERIA FOR INITIAL APPROVAL

Non-small cell lung cancer (NSCLC)¹⁻⁴

Authorization of 12 months may be granted for treatment of recurrent, advanced, or metastatic NSCLC (including brain metastases from NSCLC) in members with sensitizing EGFR mutation-positive disease

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced an unacceptable toxicity.

V. REFERENCES

1. Tagrisso [package insert]. Wilmington, DE: AstraZeneca; August 2018.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed March 5, 2019.
3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology® Non-Small Cell Lung Cancer (Version 3.2019). © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed March 5, 2019.

Reference number(s)
1663-A

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ENHANCED SPECIALTY GUIDELINE MANAGEMENT

TAKHZYRO (lanadelumab-flyo)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Prophylaxis to prevent attacks of hereditary angioedema (HAE) in patients 12 years of age and older

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

- A. C4 levels and C1 inhibitor functional and antigenic protein levels
- B. F12, angiopoietin-1 or plasminogen gene mutation testing, if applicable
- C. Chart notes confirming family history of angioedema, if applicable

III. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for prevention of hereditary angioedema attacks when the requested medication will not be used in combination with Cinryze or Haegarda and either of the following criteria is met:

- A. Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing:
 - 1. C1 inhibitor (C1-INH) antigenic level is below the lower limit of normal as defined by the laboratory performing the test or
 - 2. Normal C1-INH antigenic level and a low C1-INH functional level (functional C1-INH less than 50% or C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test).
- B. Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
 - 1. Member has an F12, angiopoietin-1, or plasminogen gene mutation as confirmed by genetic testing, or
 - 2. Member has a documented family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine (e.g., cetirizine) for at least one month.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy when all of the following criteria are met:

- A. Member meets the criteria for initial approval.
- B. Member has experienced reduction in frequency, severity, and/or duration of attacks since starting treatment.

V. REFERENCES

1. Takhzyro [package insert]. Lexington, MA: Dyax Corp.; August 2018.
2. Maurer M, Magerl M, Ansotegui I, et al. The international WAO/EAACI guideline for the management of hereditary angioedema – the 2017 revision and update. *Allergy*. 2018;00:1-22.
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SPECIALTY GUIDELINE MANAGEMENT

TALTZ (ixekizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

1. Moderate to severe plaque psoriasis
2. Active psoriatic arthritis
3. Active ankylosing spondylitis

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Moderate to severe plaque psoriasis

1. Authorization of 12 months may be granted for members who have previously received Otezla or a biologic indicated for the treatment of moderate to severe plaque psoriasis.
2. Authorization of 12 months may be granted for treatment of moderate to severe plaque psoriasis in members when all of the following criteria are met:
 - a. At least 3% of body surface area (BSA) is affected OR crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
 - b. Member meets any of the following criteria:
 - i. Member has had an inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) or pharmacologic treatment with methotrexate, cyclosporine or acitretin.
 - ii. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine and acitretin (see Appendix).
 - iii. Member has severe psoriasis that warrants a biologic DMARD as first-line therapy (i.e. at least 10% of the body surface area (BSA) or crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected).

B. Active psoriatic arthritis (PsA)

Authorization of 12 months may be granted for treatment of active psoriatic arthritis.

C. Active ankylosing spondylitis (AS)

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for active ankylosing spondylitis.
2. Authorization of 12 months may be granted for treatment of active ankylosing spondylitis when either of the following criteria is met:
 - a. Member has experienced an inadequate response to at least two non-steroidal anti-inflammatory drugs (NSAIDs).

- b. Member has an intolerance or contraindication to two or more NSAIDs.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who are using Taltz for an indication outlined in section II achieve or maintain positive clinical response with Taltz as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

For all indications: Member has had a documented negative TB test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic DMARDs or targeted synthetic DMARDs (e.g., Xeljanz), and repeated yearly for members with risk factors** for TB that are continuing therapy with biologics.

* If the screening testing for TB is positive, there must be documentation of further testing to confirm there is no active disease. Do not administer ixekizumab to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of ixekizumab.

** Risk factors for TB include: Persons with close contact to people with infectious TB disease; persons who have recently immigrated from areas of the world with high rates of TB (e.g., Africa, Asia, Eastern Europe, Latin America, Russia); children less than 5 years of age who have a positive TB test; groups with high rates of TB transmission (e.g., homeless persons, injection drug users, persons with HIV infection); persons who work or reside with people who are at an increased risk for active TB (e.g., hospitals, long-term care facilities, correctional facilities, homeless shelters).

For all indications: Member cannot use Taltz concomitantly with any other biologic DMARD or targeted synthetic DMARD.

V. APPENDIX

Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine or Acitretin

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Cannot be used due to risk of treatment-related toxicity
4. Drug interaction
5. Pregnancy or planning pregnancy
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

VI. REFERENCES

1. Taltz [package insert]. Indianapolis, IN: Eli Lilly and Company; August 2019.
2. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 6: Guidelines of care for the treatment of psoriasis and psoriatic arthritis: case-based presentations and evidence-based conclusions. *J Am Acad Dermatol*. 2011;65(1):137-174.
3. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 4: Guidelines of care for the management and treatment of psoriasis with traditional systemic agents. *J Am Acad Dermatol*. 2009;61:451-485.

4. Griffiths CE, Reich K, Lebwohl M, et al. Comparison of ixekizumab with etanercept or placebo in moderate-to-severe psoriasis (UNCOVER-2 and UNCOVER-3): results from two phase 3 randomised trials. *Lancet*. 2015;386(9993):541-51.
5. Gossec L, Smolen JS, Ramiro S, et al. European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies: 2015 update. *Ann Rheum Dis*. 2016;75(3):499-510.
6. McInnes IB, Mease PJ, Kirkham B, et al. Secukinumab, a human anti-interleukin-17A monoclonal antibody, in patients with psoriatic arthritis (FUTURE 2): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet*. 2015;386(9999):1137-46.
7. Menter A, Strober BE, Kaplan DH, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. *J Am Acad Dermatol*. 2019;80(4):1029-1072.
8. Tuberculosis (TB). TB risk factors. Centers for Disease Control and Prevention. Retrieved on 21 June 2019 from: <https://www.cdc.gov/tb/topic/basics/risk.htm>.
9. Braun J, van den Berg R, Baraliakos X, et al. 2010 update of the ASAS/EULAR recommendations for the management of ankylosing spondylitis. *Ann Rheum Dis* 2011;70:896–904.
10. Ward MM, Deodhar A, Akl EA, et al. American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network 2015 recommendations for the treatment of ankylosing spondylitis and nonradiographic axial spondyloarthritis. *Arthritis Rheumatol*. 2015: 10.1002/art.39298.

SPECIALTY GUIDELINE MANAGEMENT

TALZENNA (talazoparib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Talzenna is indicated for the treatment of adult patients with deleterious or suspected deleterious germline breast cancer susceptibility gene (BRCA)-mutated (*gBRCAm*) human epidermal growth factor receptor 2 (HER2)-negative locally advanced or metastatic breast cancer. Select patients for therapy based on an FDA-approved companion diagnostic for Talzenna.

B. Compendial Uses

Single agent therapy for recurrent or stage IV (M1) human epidermal growth factor receptor 2 (HER2)-negative, BRCA 1/2-germline mutated breast cancer

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: HER2 status, BRCA mutation testing results.

III. CRITERIA FOR INITIAL APPROVAL

Breast cancer

Authorization of 12 months may be granted for the treatment of human epidermal growth factor receptor 2 (HER2)-negative locally advanced, recurrent or metastatic breast cancer when the following criteria are met:

1. Member has documented deleterious or suspected deleterious germline BRCA mutated disease; and
2. Talzenna will be used as a single agent.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for breast cancer who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES

1. Talzenna [package insert]. New York, NY: Pfizer Inc.; October 2018.
2. The NCCN Drugs & Biologics Compendium 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed August 14, 2019.

Reference number(s)
2782-A

3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Breast Cancer. Version 3.2018. https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed January 26, 2019.

SPECIALTY GUIDELINE MANAGEMENT

TARCEVA (erlotinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Non-Small Cell Lung Cancer (NSCLC)

Tarceva is indicated for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test receiving first-line, maintenance, or second or greater line treatment after progression following at least one prior chemotherapy regimen.

Limitations of use:

- a. Safety and efficacy of Tarceva have not been established in patients with NSCLC whose tumors have other EGFR mutations.
- b. Tarceva is not recommended for use in combination with platinum-based chemotherapy.

2. Pancreatic cancer

Tarceva in combination with gemcitabine is indicated for the first-line treatment of patients with locally advanced, unresectable or metastatic pancreatic cancer.

B. Compendial Uses

1. NSCLC, recurrent, advanced or metastatic sensitizing EGFR mutation-positive
2. Recurrent bone cancer – recurrent chordoma
3. Renal cell carcinoma, relapsed or stage IV disease with non-clear cell histology
4. Recurrent brain metastases from EGFR sensitizing mutation-positive NSCLC
5. Vulvar cancer

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: EGFR mutation testing results (where applicable).

III. CRITERIA FOR INITIAL APPROVAL

A. Non-small cell lung cancer (NSCLC)

Reference number(s)
1664-A

Authorization of 12 months may be granted for treatment of recurrent, advanced or metastatic NSCLC (including brain metastases from NSCLC) when the member has sensitizing EGFR mutation-positive disease.

B. Pancreatic cancer

Authorization of 12 months may be granted for treatment of locally advanced, unresectable or metastatic pancreatic cancer.

C. Renal cell carcinoma (RCC)

Authorization of 12 months may be granted for treatment of relapsed or stage IV renal cell carcinoma with non-clear cell histology.

D. Chordoma

Authorization of 12 months may be granted for treatment of recurrent chordoma.

E. Vulvar cancer

Authorization of 12 months may be granted for treatment of vulvar cancer.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced an unacceptable toxicity.

V. REFERENCES

1. Tarceva [package insert]. South San Francisco, CA: Genentech USA, Inc.; October 2016.
2. The NCCN Drugs & Biologics Compendium 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 14, 2019.
3. The NCCN Clinical Practice Guidelines in Oncology Non-Small Cell Lung Cancer (Version 3.2019). 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 14, 2019.
4. The NCCN Clinical Practice Guidelines in Oncology Pancreatic Adenocarcinoma (Version 1.2019). 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 14, 2019.
5. The NCCN Clinical Practice Guidelines in Oncology Bone Cancer (Version 1.2019). 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 14, 2019.
6. The NCCN Clinical Practice Guidelines in Oncology Kidney Cancer (Version 3.2019). 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 14, 2019.
7. The NCCN Clinical Practice Guidelines in Oncology Central Nervous System Cancers (Version 1.2019). 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 14, 2019.
8. The NCCN Clinical Practice Guidelines in Oncology Vulvar Cancer (Squamous Cell Carcinoma) (Version 2.2019). 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 14, 2019.

SPECIALTY GUIDELINE MANAGEMENT

TASIGNA (nilotinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Adult patients and pediatric patients greater than or equal to 1 year of age with newly diagnosed Philadelphia chromosome positive chronic myeloid leukemia (Ph+ CML) in chronic phase
2. Adult patients with chronic phase and accelerated phase Ph+ CML resistant or intolerant to prior therapy that included imatinib
3. Pediatric patients greater than or equal to 1 year of age with chronic phase Ph+ CML with resistance or intolerance to prior tyrosine-kinase inhibitor (TKI) therapy.

B. Compendial Uses

1. Primary treatment of advanced phase CML (accelerated phase or blast phase)
2. Follow-up therapy for CML patients after hematopoietic stem cell transplant (HSCT)
3. CML patients resistant or intolerant to primary treatment with alternative tyrosine kinase inhibitors (TKIs)
4. Ph+ acute lymphoblastic leukemia (ALL)
5. Gastrointestinal stromal tumor (GIST) in patients with disease progression on imatinib, sunitinib or regorafenib

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review:

- A. Prior to initiation of therapy for treatment of CML or Ph+ ALL: results of cytogenetic and/or molecular testing for detection of the Ph chromosome or the BCR-ABL gene
- B. For members requesting initiation of Tasigna therapy for treatment of CML or ALL after experiencing resistance to prior tyrosine kinase inhibitor (TKI) therapy: results of T315I mutation testing

III. CRITERIA FOR INITIAL APPROVAL

A. **Chronic Myeloid Leukemia (CML)**

Authorization of 6 months may be granted for treatment of CML that has been confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing when any of the following criteria are met:

1. Member has not received prior therapy with a TKI (e.g., bosutinib, dasatinib, imatinib, ponatinib)
2. Member experienced toxicity or intolerance to prior therapy with a TKI

3. Member experienced resistance to prior therapy with a TKI and results of mutational testing are negative for T315I mutation
4. Member has received HSCT for CML

B. Ph+ Acute Lymphoblastic Leukemia (ALL)/Lymphoblastic Lymphoma (LL)

Authorization of 12 months may be granted for treatment of Ph+ ALL or LL that has been confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing when any of the following criteria are met:

1. Member has not received prior therapy with a TKI (e.g., bosutinib, dasatinib, imatinib, ponatinib)
2. Member experienced toxicity or intolerance to prior therapy with a TKI
3. Member experienced resistance to prior therapy with a TKI and results of mutational testing are negative for T315I mutation

C. Gastrointestinal stromal tumor (GIST)

Authorization of 12 months may be granted for treatment of GIST who have experienced disease progression on imatinib, sunitinib, or regorafenib.

IV. CONTINUATION OF THERAPY

A. CML

Authorization of 12 months may be granted for treatment of CML that has been confirmed by detection of Ph chromosome or BCR-ABL gene by cytogenetic and/ or molecular testing when any of the following criteria are met:

1. BCR-ABL1 \leq 10% for members who have been receiving Tasigna for \leq 12 months
2. No evidence of disease progression for members who have been receiving Tasigna for $>$ 12 months
3. Member has received HSCT

B. Ph+ ALL/LL

Authorization of 12 months may be granted for continued treatment of Ph+ ALL or LL that has been confirmed by detection of Ph chromosome or BCR-ABL gene by cytogenetic and/ or molecular testing in members who have not experienced disease progression or an unacceptable toxicity.

C. GIST

Authorization of 12 months may be granted for continued treatment of GIST in members who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES

1. Tasigna [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2018.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed April 19, 2019.
3. NCCN Clinical Practice Guidelines in Oncology® Chronic Myeloid Leukemia (Version 1.2019). © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed April 16, 2019.
4. NCCN Clinical Practice Guidelines in Oncology® Acute Lymphoblastic Leukemia (Version 1.2019). © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed April 17, 2019.
5. NCCN Clinical Practice Guidelines in Oncology® Soft Tissue Sarcoma (Version 2.2019). © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed April 18, 2019.

SPECIALTY GUIDELINE MANAGEMENT

TAVALISSE (fostamatinib disodium hexahydrate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Treatment of thrombocytopenia in adult patients with chronic immune thrombocytopenia (ITP) who have had an insufficient response to a previous treatment.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: pretreatment and current platelet counts

III. EXCLUSIONS

Coverage will not be provided for members with the following exclusion: concomitant use of Tavalisse with thrombopoietin receptor agonists (e.g., Promacta, Nplate, Doptelet, Mulpleta)

IV. CRITERIA FOR INITIAL APPROVAL

Chronic or persistent immune thrombocytopenia (ITP)

Authorization of 12 weeks may be granted to members 18 years of age or older with chronic or persistent ITP who meet all of the following criteria:

- A. Inadequate response or intolerance to prior therapy such as corticosteroids, immunoglobulins, splenectomy, or thrombopoietin receptor agonists.
- B. Untransfused platelet count prior to the initiation of ITP therapy is less than $30 \times 10^9/L$ OR $30 \times 10^9/L$ to $50 \times 10^9/L$ with symptomatic bleeding (e.g., significant mucous membrane bleeding, gastrointestinal bleeding or trauma) or risk factors for bleeding (see Section VI).

V. CONTINUATION OF THERAPY

Chronic or persistent immune thrombocytopenia (ITP)

- A. Authorization of 3 months may be granted to members 18 years of age or older with current platelet count less than $50 \times 10^9/L$ for whom the platelet count is not sufficient to prevent clinically important bleeding and who have not received a maximal Tavalisse dose for at least 8 weeks.

Reference number(s)
2560-A

- B. Authorization of 12 months may be granted to members 18 years of age or older with current platelet count less than $50 \times 10^9/L$ for whom the current platelet count is sufficient to prevent clinically important bleeding.
- C. Authorization of 12 months may be granted to members 18 years of age or older with current platelet count of $50 \times 10^9/L$ to $200 \times 10^9/L$.
- D. Authorization of 12 months may be granted to members 18 years of age or older with current platelet count greater than $200 \times 10^9/L$ to less than or equal to $400 \times 10^9/L$ for whom Tavalisse dosing will be adjusted to achieve a platelet count sufficient to avoid clinically important bleeding.

VI. APPENDIX

Examples of risk factors for bleeding (not all inclusive)

- Undergoing a medical or dental procedure where blood loss is anticipated
- Comorbidity (e.g., peptic ulcer disease, hypertension)
- Mandated anticoagulation therapy
- Profession (e.g., construction worker) or lifestyle (e.g., plays contact sports) that predisposes patient to trauma

VII. REFERENCES

1. Tavalisse [package insert]. South San Francisco, CA: Rigel Pharmaceuticals, Inc.; April 2018.
2. Neunert C, Lim W, Crowther M, et al. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. *Blood*. 2011;117(16):4190-4207.
3. Provan D, Stasi R, Newland AC, et al. International consensus report on the investigation and management of primary immune thrombocytopenia. *Blood*. 2010;115(2):168-186.
4. Rodeghiero F, Stasi R, Gernsheimer T, et al. Standardization of terminology, definitions and outcome criteria in immune thrombocytopenic purpura of adults and children: report from an international working group. *Blood*. 2009;113(11):2386-2393.
5. Bussel J, Arnold DM, Grossbard E, et al. Fostamatinib for the treatment of adult chronic and persistent immune thrombocytopenia: Results of two, phase III, randomized placebo-controlled trials. *Am J Hematol*. 2018; published online: <https://doi.org/10.1002/ajh.25125>.

Specialty Guideline Management

TAZVERIK (tazemetostat)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Tazverik is indicated for the treatment of adults and pediatric patients aged 16 years and older with metastatic or locally advanced epithelioid sarcoma not eligible for complete resection.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Epithelioid Sarcoma

Authorization of 12 months may be granted for the treatment of metastatic or locally advanced epithelioid sarcoma when all of the following criteria are met:

- A. The disease is not eligible for complete resection
- B. The member is 16 years of age or older

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Tazverik [package insert]. Cambridge, MA: Epizyme, Inc.; January 2020.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME (generic)	TAZVERIK (tazemetostat)
<div style="display: flex; justify-content: space-between;"> <div> Status: CVS Caremark Criteria Type: Initial Prior Authorization </div> <div style="text-align: right;"> MDC Ref # 3503-A </div> </div>	

FDA-APPROVED INDICATIONS¹

Tazverik is indicated for the treatment of adults and pediatric patients aged 16 years and older with metastatic or locally advanced epithelioid sarcoma not eligible for complete resection.

<u>CRITERIA FOR APPROVAL</u>			
1	Does the patient have a diagnosis of epithelioid sarcoma? [If no, no further questions.]	Yes	No
2	Is the patient's disease metastatic or locally advanced? [If no, no further questions.]	Yes	No
3	Is the disease eligible for complete resection? [If yes, no further questions.]	Yes	No
4	Is the patient 16 years of age or older?	Yes	No

Guidelines for Approval	
Duration of Approval	12 Months
Set 1	
Yes to question(s)	No to question(s)
1	3
2	
4	

Mapping Instructions	
	Yes
	No
1.	Go to 2
2.	Go to 3
3.	Deny
4.	Approve, 12 months

RATIONALE

These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to ensure that patients follow selection elements noted in labeling and/or practice guidelines in order to decrease the potential for inappropriate utilization.

REFERENCES

1. Tazverik [package insert]. Cambridge, MA: Epizyme, Inc.; January 2020.

DOCUMENT HISTORY

Created: Specialty Clinical Development (JL) 01/2020
Revised:
Reviewed: CDPR / JG 01/2020
External Review: 02/2020

SPECIALTY GUIDELINE MANAGEMENT

TECENTRIQ (atezolizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Locally advanced or metastatic urothelial carcinoma
Indicated for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma who:
 - i. Are not eligible for cisplatin-containing chemotherapy, and whose tumors express PD-L1 (PD-L1 stained tumor-infiltrating immune cells [IC] covering $\geq 5\%$ of the tumor area), as determined by an FDA-approved test, or
 - ii. Are not eligible for any platinum-containing chemotherapy regardless of PD-L1 status, or
 - iii. Have disease progression during or following any platinum-containing chemotherapy, or within 12 months of neoadjuvant or adjuvant chemotherapy.
2. Metastatic non-small cell lung cancer (NSCLC)
 - i. Indicated in combination with bevacizumab, paclitaxel, and carboplatin, for the first-line treatment, of adult patients with metastatic non-squamous NSCLC with no EGFR or ALK genomic tumor aberrations.
 - ii. Indicated in combination with paclitaxel protein-bound and carboplatin for the first-line treatment of adult patients with metastatic non-squamous NSCLC with no EGFR or ALK genomic tumor aberrations.
 - iii. Indicated as a single agent for the treatment of adult patients with metastatic NSCLC who have disease progression during or following platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for NSCLC harboring these aberrations prior to receiving the requested medication.
3. Unresectable locally advanced or metastatic triple-negative breast cancer (TNBC)
Indicated in combination with paclitaxel protein-bound for the treatment of adult patients with unresectable locally advanced or metastatic TNBC whose tumors express PD-L1 (PD-L1 stained tumor-infiltrating immune cells (IC) of any intensity covering $\geq 1\%$ of the tumor area), as determined by an FDA approved test.
4. Small cell lung cancer (SCLC)
Indicated in combination with carboplatin and etoposide, for the first-line treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC).

B. Compendial Uses

1. Stage II or Stage IIIa bladder cancer
2. Bladder cancer with metastatic or local recurrence post-cystectomy
3. Subsequent therapy for urothelial carcinoma
4. Subsequent therapy or continued maintenance therapy for non-small cell lung cancer

5. Recurrent triple-negative breast cancer

All other indications are considered experimental/investigational and are not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

- A. Test results confirming PD-L1 tumor expression (where applicable)
- B. Test results confirming that the cancer cells are negative for the following receptors (where applicable):
 1. human epidermal growth factor receptor 2 (HER-2)
 2. estrogen
 3. progesterone

III. EXCLUSIONS

Coverage will not be provided for members who have experienced disease progression while on PD-1 or PD-L1 inhibitor therapy

IV. CRITERIA FOR INITIAL APPROVAL

A. Urothelial Carcinoma - Bladder Cancer

Authorization of 6 months may be granted for treatment as a single agent for bladder cancer when any of the following criteria are met:

1. The requested medication is used as first line therapy in cisplatin ineligible persons whose tumors express PD-L1 (defined as PD-L1 stained tumor-infiltrating immune cells [IC] covering greater than or equal to 5% of the tumor area) or in persons who are not eligible for any platinum containing chemotherapy regardless of PD-L1 expression for any of the following:
 - i. Stage II or Stage IIIa disease if tumor is present following reassessment of tumor status 2-3 months after primary treatment with concurrent chemoradiotherapy
 - ii. locally advanced or metastatic disease
 - iii. metastatic or local recurrence post-cystectomy
2. The requested medication is used as subsequent systemic therapy following platinum containing chemotherapy for either of the following:
 - i. locally advanced or metastatic disease
 - ii. metastatic or local recurrence post-cystectomy

B. Urothelial Carcinoma - Primary Carcinoma of the Urethra

Authorization of 6 months may be granted for treatment as a single agent for primary carcinoma of the urethra when any of the following criteria are met:

1. The requested medication is used as first line therapy for recurrent, locally advanced or metastatic disease in cisplatin ineligible persons whose tumors express PD-L1 (defined as PD-L1 stained tumor-infiltrating immune cells [IC] covering greater than or equal to 5% of the tumor area) or in persons who are not eligible for any platinum containing chemotherapy regardless of PD-L1 expression.
2. The requested medication is used as subsequent therapy for recurrent, locally advanced or metastatic disease following platinum-containing chemotherapy.

C. Urothelial Carcinoma - Upper Genitourinary Tract Tumors or Urothelial Carcinoma of the Prostate

Authorization of 6 months may be granted for treatment as a single agent for upper genitourinary tract tumors or urothelial carcinoma of the prostate when any of the following criteria are met:

1. The requested medication is used as first line therapy for locally advanced or metastatic disease in cisplatin ineligible persons whose tumors express PD-L1 (defined as PD-L1 stained tumor-infiltrating immune cells [IC] covering greater than or equal to 5% of the tumor area) or in persons who are not eligible for any platinum containing chemotherapy regardless of PD-L1 expression
2. The requested medication is used as subsequent therapy for locally advanced or metastatic disease following platinum-containing chemotherapy

D. Non-Small Cell Lung Cancer (NSCLC)

Authorization of 6 months may be granted for treatment of NSCLC when any of the following criteria are met:

1. The requested medication is used as treatment for recurrent, advanced or metastatic nonsquamous NSCLC in combination with carboplatin, paclitaxel and bevacizumab (if EGFR or ALK positive, will be used following EGFR or ALK therapy)
2. The requested medication is used as treatment for recurrent, advanced or metastatic nonsquamous NSCLC in combination with paclitaxel protein-bound and carboplatin (if EGFR or ALK positive, will be used following EGFR or ALK therapy)
3. The requested medication is used as continuation maintenance therapy as a single agent or in combination with bevacizumab for recurrent, advanced or metastatic nonsquamous NSCLC following atezolizumab/carboplatin/paclitaxel/bevacizumab therapy when tumor response or stable disease is achieved
4. The requested medication is used as continuation maintenance therapy for recurrent, advanced or metastatic nonsquamous NSCLC following atezolizumab/carboplatin/paclitaxel protein-bound therapy when tumor response or stable disease is achieved
5. The requested medication is used as subsequent therapy as a single agent for recurrent, advanced, or metastatic disease

E. Breast Cancer

Authorization of 6 months may be granted for treatment of unresectable locally advanced, recurrent, or metastatic breast cancer when all of the following criteria are met:

1. The diagnosis of breast cancer is confirmed by the cancer cells testing negative for ALL of the following receptors:
 - i. human epidermal growth factor receptor 2 (HER-2)
 - ii. estrogen
 - iii. progesterone
2. Tumors must express programmed death ligand 1 (PD-L1) (i.e., PD-L1 stained tumor-infiltrating immune cells [IC] of any intensity covering greater than or equal to 1 percent of the tumor area).
3. The requested medication will be used in combination with protein-bound paclitaxel (Abraxane).

F. Small Cell Lung Cancer (SCLC)

Authorization of 6 months may be granted for treatment of small cell lung cancer when the requested medication will be used as initial treatment in combination with etoposide and carboplatin (followed by single agent maintenance) for extensive-stage disease.

V. CONTINUATION OF THERAPY

Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section IV who have not experienced disease progression or an unacceptable toxicity.

VI. REFERENCE

1. Tecentriq [package insert]. South San Francisco, CA: Genentech, Inc.; December 2019.

Reference number(s)
1766-A

2. The NCCN Drugs & Biologics Compendium™ © 2019 National Comprehensive Cancer Network, Inc.
<https://www.nccn.org>. Accessed December 30, 2019.

SPECIALTY GUIDELINE MANAGEMENT

TECFIDERA (dimethyl fumarate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Tecfidera is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease and active secondary progressive disease, in adults.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Relapsing forms of multiple sclerosis

Authorization of 12 months may be granted to members who have been diagnosed with a relapsing form of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse).

B. Clinically isolated syndrome

Authorization of 12 months may be granted to members for the treatment of clinically isolated syndrome.

III. CONTINUATION OF THERAPY

For all indications: Authorization of 12 months may be granted for members who are experiencing disease stability or improvement while receiving Tecfidera.

IV. OTHER CRITERIA

Members will not use Tecfidera concomitantly with other medications used for the treatment of multiple sclerosis, excluding Ampyra.

V. REFERENCE

1. Tecfidera [package insert]. Cambridge, MA: Biogen Inc.; July 2019.

SPECIALTY GUIDELINE MANAGEMENT

TECHNIVIE (ombitasvir/paritaprevir/ritonavir)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Technivie is indicated in combination with ribavirin for the treatment of patients with genotype 4 chronic hepatitis C virus (HCV) infection without cirrhosis or with compensated cirrhosis.

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

Coverage will not be provided for members with decompensated cirrhosis/moderate or severe hepatic impairment (Child Turcotte Pugh Class B or C)

Note: When the requested drug is being used in a combination therapy regimen, exclusions to the other antiviral drugs also apply.

III. CRITERIA FOR APPROVAL

A. Chronic hepatitis C virus infection, in combination with ribavirin (RBV) Genotype 4 infection

Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who are either of the following:

1. Treatment-naïve
2. Failed prior treatment with peginterferon alfa and RBV

B. Chronic hepatitis C virus infection, without RBV Genotype 4 infection

Authorization of up to 12 weeks total may be granted for members without cirrhosis who meet all of the following criteria:

1. Treatment-naïve
2. Member has intolerance to RBV, has documented anemia (baseline hemoglobin below 10 g/dL) or RBV ineligibility (see Section V for ribavirin ineligibility)

C. HCV and HIV coinfection

Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in Section A or B above are met.

IV. CONTINUATION OF THERAPY

Reference number(s)
2142-A, 2681-A

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. APPENDIX: RIBAVIRIN INELIGIBILITY

RBV ineligibility is defined as one or more of the below:

- Pregnant female or male whose female partner is pregnant
- Hemoglobinopathy
- Coadministration with didanosine
- History of significant or unstable cardiac disease

VI. REFERENCES

1. Technivie [package insert]. North Chicago, IL: AbbVie Inc.; July 2018.
2. AASLD/IDSA/IAS–USA. Recommendations for testing, managing, and treating hepatitis C. <http://www.hcvguidelines.org>. Last changes made May 24, 2018. Accessed August 03, 2018.

SPECIALTY GUIDELINE MANAGEMENT

TEGSEDI (inotersen)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Tegsedi is indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults.

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

- A. Testing or analysis confirming a mutation of the TTR gene
- B. Medical record documentation confirming the member demonstrates signs and symptoms of polyneuropathy and an improvement in these signs and symptoms since starting therapy for continuation

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a neurologist, geneticist, or physician specializing in the treatment of amyloidosis.

IV. CRITERIA FOR INITIAL APPROVAL

Polyneuropathy of Hereditary Transthyretin-mediated Amyloidosis

Authorization of 12 months may be granted for treatment of polyneuropathy of hereditary transthyretin-mediated amyloidosis (also called transthyretin-type familial amyloid polyneuropathy [ATTR-FAP]) when all of the following criteria are met:

- A. The diagnosis is confirmed by detection of a mutation of the TTR gene.
- B. Member exhibits clinical manifestations of ATTR-FAP (e.g., amyloid deposition in biopsy specimens, TTR protein variants in serum, progressive peripheral sensory-motor polyneuropathy).
- C. The member is not a liver transplant recipient.
- D. The requested medication will not be used in combination with patisiran (Onpattro) or tafamidis.

V. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for the continued treatment of ATTR-FAP when all of the following criteria are met:

- A. The member must have met all initial authorization criteria.
- B. The member must have demonstrated a beneficial response to treatment with Tegsedi therapy compared to baseline (e.g., improvement of neuropathy severity and rate of disease progression as demonstrated by the modified Neuropathy Impairment Scale+7 (mNIS+7) composite score, the Norfolk Quality of Life-Diabetic Neuropathy (QoL-DN) total score, polyneuropathy disability (PND) score, FAP disease stage, manual grip strength). Documentation from the medical record must be provided.

VI. REFERENCES

- 1. Tegsedi [package insert]. Boston, MA: Akcea Therapeutics, Inc. October 2018.
- 2. Benson MD, et. al., Inotersen Treatment for Patients with Hereditary Transthyretin Amyloidosis. N Engl J Med. 2018 Jul 5; 379(1):22-31.
- 3. Ando Y, Coelho T, Berk JL, Cruz MW, Ericzon BG, Ikeda S, Lewis WD, Obici L, Planté-Bordeneuve V, Rapezzi C, et al. Guideline of transthyretin-related hereditary amyloidosis for clinicians. Orphanet J Rare Dis. 2013;8:31.

SPECIALTY GUIDELINE MANAGEMENT

Temodar (temozolomide) temozolomide (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. **Newly Diagnosed Glioblastoma Multiforme**
Temodar is indicated for the treatment of adult patients with newly diagnosed glioblastoma multiforme concomitantly with radiotherapy and then as maintenance treatment.
2. **Refractory Anaplastic Astrocytoma**
Temodar is indicated for the treatment of adult patients with refractory anaplastic astrocytoma, i.e., patients who have experienced disease progression on a drug regimen containing nitrosourea and procarbazine.

B. Compendial Uses

1. Central nervous system (CNS) cancer
2. Ewing sarcoma
3. Neuroendocrine tumors of pancreas, gastrointestinal tract, lung, and thymus
4. Poorly differentiated (high grade) neuroendocrine tumors/large or small cell carcinoma
5. Pheochromocytoma/paraganglioma
6. Melanoma²
7. Mycosis fungoides/Sézary syndrome
8. Small cell lung cancer
9. Soft tissue sarcoma
10. Uterine sarcoma
11. Primary cutaneous anaplastic large cell lymphoma (ALCL)

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Central nervous system (CNS) cancer**

Authorization of 12 months may be granted for treatment of CNS cancers.

B. **Ewing sarcoma**

Authorization of 12 months may be granted for treatment of Ewing sarcoma.

C. **Neuroendocrine tumors of pancreas, gastrointestinal tract, lung, and thymus**

Reference number(s)
1665-A

Authorization of 12 months may be granted for treatment of neuroendocrine tumors of pancreas, gastrointestinal tract, lung, or thymus.

D. Poorly differentiated (high grade) neuroendocrine tumors/large or small cell carcinoma

Authorization of 12 months may be granted for treatment of poorly differentiated (high grade) neuroendocrine tumors or large or small cell carcinoma.

E. Pheochromocytoma/paraganglioma

Authorization of 12 months may be granted for treatment of pheochromocytoma or paraganglioma.

F. Melanoma

Authorization of 12 months may be granted for treatment of metastatic or unresectable melanoma.

G. Mycosis fungoides/Sezary syndrome

Authorization of 12 months may be granted for treatment of mycosis fungoides/Sezary syndrome.

H. Small cell lung cancer (SCLC)

Authorization of 12 months may be granted for treatment of SCLC.

I. Soft tissue sarcoma (STS)

Authorization of 12 months may be granted for treatment of STS.

J. Uterine sarcoma

Authorization of 12 months may be granted for treatment of uterine sarcoma.

K. Primary cutaneous anaplastic large cell lymphoma (ALCL)

Authorization of 12 months may be granted for treatment of primary cutaneous ALCL.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced disease progression or an unacceptable toxicity.

IV. REFERENCES

1. Temodar [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; October 2017.
2. The NCCN Drugs & Biologics Compendium® © 2018 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed September 28, 2018.
3. The NCCN Clinical Practice Guidelines in Oncology® Central Nervous System Cancers (Version 2.2018). © 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. January 29, 2019.
4. The NCCN Clinical Practice Guidelines in Oncology® Soft Tissue Sarcoma (Version 1.2019). © 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. January 29, 2019.
5. The NCCN Clinical Practice Guidelines in Oncology® Neuroendocrine and adrenal tumors (Version 4.2018). © 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed January 29, 2019.

SPECIALTY GUIDELINE MANAGEMENT

TEPEZZA (teprotumumab-trbw)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Tepezza is indicated for the treatment of thyroid eye disease.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Supporting chart notes or medical record indicating clinical activity score (CAS) and moderate-to-severe disease as applicable to Section V.

III. EXCLUSIONS

Coverage will not be provided for repeat series of Tepezza infusions.

IV. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with an ophthalmologist.

V. CRITERIA FOR INITIAL APPROVAL

Thyroid eye disease (TED)

Authorization of 6 months may be granted for treatment of TED when all of the following criteria are met:

- A. Member is 18 years of age or older
- B. Member has active disease with a CAS greater than or equal to 4 (see Appendix A)
- C. Member has moderate-to-severe disease (see Appendix B)

VI. APPENDICES

Appendix A: TED Activity Assessment – CAS Elements

Elements*	Score
Painful feeling behind the globe over last 4 weeks	1

Pain with eye movement during last 4 weeks	1
Redness of the eyelids	1
Redness of the conjunctiva	1
Swelling of the eyelids	1
Chemosis (edema of the conjunctiva)	1
Swollen caruncle (flesh body at medial angle of eye)	1

*A 7-point scale with 1-point given for each element present

Appendix B: Disease Severity Assessment

1. Mild disease, at least one of the following:
 - a. Minor lid retraction (<2 mm)
 - b. Mild soft-tissue involvement
 - c. Exophthalmos <3 mm above normal for race and gender
 - d. No or intermittent diplopia
 - e. Corneal exposure responsive to lubricants
2. Moderate-to-severe disease, at least one of the following:
 - a. Lid retraction ≥ 2 mm
 - b. Moderate or severe soft-tissue involvement
 - c. Exophthalmos ≥ 3 mm above normal for race and gender
 - d. Inconstant or constant diplopia
3. Sight-threatening disease, at least one of the following:
 - a. Dysthyroid optic neuropathy (DON)
 - b. Corneal breakdown

VII. REFERENCES

1. Tepezza [package insert]. Dublin, Ireland: Horizon Therapeutics Ireland DAC; January 2020.
2. Bartalena L, Baldeschi L, Kostas B, et al. The 2016 European Thyroid Association/European Group on Graves' Orbitopathy guidelines for the management of Graves' orbitopathy. *Eur Thyroid*. 2016;5(1):9-26.
3. Ross DS, Burch HB, Cooper DS, et al. 2016 American Thyroid Association guidelines for diagnosis and management of hyperthyroidism and other causes of thyrotoxicosis. *Thyroid*. 2016;26(10):1343-1421.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME (generic)	TEPEZZA (teprotumumab-trbw)	
Status: CVS Caremark Criteria		MDC
Type: Initial Prior Authorization		Ref # 3523-A

FDA-APPROVED INDICATION¹

Tepezza is indicated for the treatment of thyroid eye disease.

Compendial Uses

None

B vs D CRITERIA FOR DETERMINATION

1	Is the requested drug being supplied from the physician and/or office stock supply and billed as part of a physician service (i.e., the drug is being furnished "incident to a physician's service")? [If yes, no further questions.]	Yes	No
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CRITERIA FOR APPROVAL

2	Does the patient have a diagnosis of thyroid eye disease?	Yes	No
---	---	-----	----

Continue to Clinical Questions if:

Guidelines for Determination	
Process through Medicare Part D	
Set 1	
Yes to question(s)	No to question(s)
None	1

For any other scenarios other than the Set above, close PA, drug is not covered as Part D.

Approve if:

Guidelines for Approval	
Duration of Approval	6 Months
Set 1: Thyroid eye disease	
Yes to question(s)	No to question(s)
2	None

Mapping Instructions	
	No
1. Close PA, drug is not covered as Part D	Go to 2
2. Approve, 6 months	Deny

RATIONALE

These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to:

1. Determine if the medication should be processed through Medicare Part D.
2. Ensure that patients follow selection elements noted in labeling and/or practice guidelines in order to decrease the potential for inappropriate utilization.

REFERENCES

1. Tepezza [package insert]. Dublin, Ireland: Horizon Therapeutics Ireland DAC; January 2020.

DOCUMENT HISTORY

Created: Specialty Clinical Development (SP) 01/2020
Revised:
Reviewed: CDPR / MMF 02/2020
External Review: 02/2020

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS **TESTOSTERONE PRODUCTS - INJECTABLE**

BRAND NAME*
(generic)

DEPO-TESTOSTERONE
(testosterone cypionate injection)

Status: CVS Caremark Criteria

Type: Initial Prior Authorization

Ref # 1371-A

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Depo-Testosterone Injection is indicated for replacement therapy in the male in conditions associated with symptoms of deficiency or absence of endogenous testosterone:

Primary hypogonadism (congenital or acquired) - testicular failure due to conditions such as cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, or orchiectomy.

Hypogonadotropic hypogonadism (congenital or acquired) - gonadotropin or LHRH deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation.

Safety and efficacy of Depo-Testosterone in men with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for primary or hypogonadotropic hypogonadism [Note: Safety and efficacy of testosterone products in patients with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.]

AND

- Before the start of testosterone therapy, the patient has at least two confirmed low testosterone levels according to current practice guidelines or your standard lab reference values **OR**
- For continuation of testosterone therapy: before the patient started testosterone therapy, the patient had a confirmed low testosterone level according to current practice guidelines or your standard lab reference values

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Depo-Testosterone (testosterone cypionate) is indicated for replacement therapy in males in conditions associated with symptoms of deficiency or absence of endogenous testosterone: congenital or acquired primary hypogonadism (testicular failure due to conditions such as cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, or orchiectomy), or congenital or acquired hypogonadotropic hypogonadism (gonadotropin or luteinizing hormone-releasing hormone [LHRH] deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation). Safety and efficacy of Depo-Testosterone in men with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.¹⁻³

A testosterone determination, in conjunction with a free testosterone or sex hormone-binding globulin level, is the threshold test in the evaluation of suspected male hypogonadism (serum total testosterone levels less than 300 ng/dL). Testosterone levels should be determined in the morning, and studies should be repeated in patients with subnormal

levels. The normative ranges for total and free testosterone levels in healthy young men vary among laboratories and assays. In some laboratories, the lower limit of the normal range for total testosterone level in healthy young men is 280-300 ng/dL and for serum free testosterone level is 5–9 pg/mL. The clinicians should use the lower limit of normal range for healthy young men established in their laboratory.^{4,5} For initial therapy, testosterone will be approved for patients with at least two confirmed low testosterone levels according to current practice guidelines or standard lab reference values. If the patient is already on testosterone therapy and did not get a repeat testosterone level before starting therapy, it would be inappropriate for the patient to stop treatment to get a repeat testosterone level. For continuation of therapy, one low testosterone level is required before the patient started testosterone therapy.

REFERENCES

1. Depo-Testosterone [package insert]. New York, NY: Pharmacia and Upjohn Company; August 2018.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed October 2018.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed October 2018.
4. Petak S, Nankin H, Spark R, et al. American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice for the Evaluation and Treatment of Hypogonadism in Adult Male Patients – 2002 update. *Endocrine Practice* 2002;8(6):439-456.
5. Bhasin S, Brito J, Cunningham G, et al. Testosterone Therapy in Adult Men with Androgen Deficiency Syndromes: An Endocrine Society Clinical Practice Guideline. *Journal of Clinical Endocrinology & Metabolism* 2018 103(5):1715-1744.

Written by: UM Development (MG)
 Date: 05/2003
 Revised: (NB) 01/2005, (MG) 02/2006; (NB) 02/2007(2); (AM) 01/2008, 12/2008; (MS) 11/2009, 11/2010, (TM) 11/2011, 10/2012 (extended duration); (PL) 11/2012, (SE) 04/2013 (created separate Med-D depo-testosterone document), (PL) 11/2013,(SE) 04/2014 (rephrased diagnosis question); (CF/JH) 11/2014, 02/2015 (updated testosterone level question), (LN) 04/2015 (added denial reasons); (CF/JH) 11/2015; (JH) 05/2016 (removed TGC coverage); (CF/JH) 11/2016; (KC) 11/2017 (no clinical changes), 10/2018 (no clinical changes), 08/2019 (removed "male" from lab questions)
 Reviewed: CDPR/Medical Affairs (MM): 01/2005, 02/2006; (WF): 02/2007, 01/2008, 12/2008, 11/2009; (KP) 11/2010, 11/2011, 03/2012, 10/2012; (DNC) 11/2012; (LCB) 11/2013; (SES) 11/2014; (KRU) 02/2015; (LCB) 11/2015; (ME) 05/2016; (MC) 12/2016; (ME) 02/2017; (EPA) 08/2019
 External Review: 08/2005, 04/2006, 06/2007, 04/2008, 04/2009, 02/2010, 02/2011, 03/2012, 02/2013, 02/2014, 02/2015, 02/2016, 06/2016, 02/2017, 02/2018, 02/2019, 10/2019 (FYI)

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for primary or hypogonadotropic hypogonadism? [Note: Safety and efficacy of testosterone products in patients with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established.]	Yes	No
2	Is this request for a continuation of testosterone therapy? [If no, then skip to question 4.]	Yes	No
3	Before the patient started testosterone therapy, did the patient have a confirmed low testosterone level according to current practice guidelines or your standard lab reference values? [No further questions.]	Yes	No
4	Does the patient have at least two confirmed low testosterone levels according to current practice guidelines or your standard lab reference values?	Yes	No

Mapping Instructions			
	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have primary or hypogonadotropic hypogonadism. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
2.	Go to 3	Go to 4	
3.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have had a test that showed low testosterone levels before you started testosterone therapy. Your request has been denied based on the information we have. [Short Description: No confirmation of diagnosis (tests, labs, etc.)]
4.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have had two tests that showed low testosterone levels. Your request has been denied based on the information we have. [Short Description: No confirmation of diagnosis (tests, labs, etc.)]

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS TESTOSTERONE PRODUCTS - INJECTABLE

BRAND NAME*
(generic)

DEPO-TESTOSTERONE
(testosterone cypionate injection)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

MDC-2
Ref # 976-A

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Depo-Testosterone Injection is indicated for replacement therapy in the male in conditions associated with symptoms of deficiency or absence of endogenous testosterone:

Primary hypogonadism (congenital or acquired) - testicular failure due to conditions such as cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, or orchiectomy.

Hypogonadotropic hypogonadism (congenital or acquired) - gonadotropin or LHRH deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation.

Limitations of Use

Safety and efficacy of Depo-Testosterone in men with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established.

Compendial Uses

Gender Dysphoria in transgender male patients ^{2-3, 6-9}

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for primary or hypogonadotropic hypogonadism [Note: Safety and efficacy of testosterone products in patients with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established.]

AND

- Before the start of testosterone therapy, the patient has at least two confirmed low testosterone levels according to current practice guidelines or your standard lab reference values **OR**
- For continuation of testosterone therapy: before the patient started testosterone therapy, the patient had a confirmed low testosterone level according to current practice guidelines or your standard lab reference values

OR

- The requested drug is being prescribed for gender dysphoria in a patient who is able to make an informed decision to engage in hormone therapy

RATIONALE

These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Depo-Testosterone is indicated for replacement therapy in males in conditions associated with symptoms of deficiency or absence of endogenous testosterone: congenital or acquired primary hypogonadism (testicular failure due to conditions such as cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, or orchiectomy), or congenital or acquired hypogonadotropic hypogonadism (gonadotropin or luteinizing hormone-releasing hormone [LHRH] deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation). Safety and efficacy of Depo-Testosterone in men with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.¹⁻³

A testosterone determination, in conjunction with a free testosterone or sex hormone-binding globulin level, is the threshold test in the evaluation of suspected male hypogonadism (serum total testosterone levels less than 300 ng/dL [nanograms per deciliter]). Testosterone levels should be determined in the morning, and studies should be repeated in patients with subnormal levels. The normative ranges for total and free testosterone levels in healthy young men vary among laboratories and assays. In some laboratories, the lower limit of the normal range for total testosterone level in healthy young men is 280-300 ng/dL and for serum free testosterone level is 5–9 pg/mL (picograms per milliliter). Clinicians should use the lower limit of normal range for healthy young men established in their laboratory.^{4,5} For initial therapy, testosterone will be approved for patients with at least two confirmed low testosterone levels according to current practice guidelines or standard lab reference values. If the patient is already on testosterone therapy and did not get a repeat testosterone level before starting therapy, it would be inappropriate for the patient to stop treatment to get a repeat testosterone level. For continuation of therapy, one low testosterone level is required before the patient started testosterone therapy.

Depo-Testosterone (testosterone cypionate) has a compendial use for gender dysphoria in transgender male (female-to-male) patients.^{2-3, 6-9}

Transgender persons seeking to develop the physical characteristics of the desired gender require a safe, effective hormone regimen that will suppress endogenous hormone secretion determined by the person's genetic/biologic sex and maintain sex hormone levels within the normal range for the person's desired gender. The two major goals of hormonal therapy are to reduce endogenous hormone levels and, thereby, the secondary sex characteristics of the individual's biological/genetic sex and to replace endogenous sex hormone levels with those of the reassigned sex. The Endocrine Society suggests that pubertal development of the desired opposite sex be initiated at about the age of 16 years, using a gradually increasing dose schedule of cross-sex steroids. However, the Endocrine Society Guidelines also state that identifying an age at which pubertal development is initiated can be difficult and may depend on several factors (such as the age when pubertal suppression was begun, medications used to initiate pubertal suppression, and relative risks of prolonged pubertal suppression), and the goal is to start the process at a time when the individual will be able to make informed, mature decisions to engage in the therapy. Some patients may advance to Tanner stage 2 of pubertal development at an early age (such as 9 or 10) and using pubertal suppression therapy for 6 or 7 years may be deemed inappropriate. Medical professionals involved in the patient's care should be involved in assessing whether the patient is ready to make the decision to begin hormone therapy and pubertal development.⁶ Therefore, individuals who are able to make an informed decision to engage in hormone therapy will be approved.

For transgender male persons, regimens to change secondary sex characteristics follow the general principle of hormone replacement treatment of male hypogonadism. Either parenteral or transdermal preparations can be used to achieve testosterone values in the normal male range (320-1000 ng/dL).⁶ The agent primarily used for endocrine treatment of transgender male patients is testosterone. When determining the appropriate method of testosterone delivery, many considerations should be taken into account. The most well-described formulation of testosterone therapy used to treat transgender male patients is intramuscular injection of testosterone esters (cypionate or enanthate).⁷

REFERENCES

1. Depo-Testosterone [package insert]. New York, NY: Pharmacia and Upjohn Company; August 2018.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed February 2019.

3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed February 2019.
4. Petak S, Nankin H, Spark R, et al. American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice for the Evaluation and Treatment of Hypogonadism in Adult Male Patients – 2002 update. *Endocrine Practice* 2002;8(6):439-456.
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Written by: UM Development (MG)

Date: 05/2003

Revised:(NB) 01/2005, (MG) 02/2006; (NB) 02/2007(2); (AM) 01/2008, 12/2008; (MS) 11/2009, 11/2010, (TM) 11/2011, 10/2012 (extended duration); (PL) 11/2012, (SE) 04/2013 (created separate Med-D depo-testosterone document), (PL) 11/2013,(SE) 04/2014 (rephrased diagnosis question); (CF/JH) 11/2014, 02/2015 (updated testosterone level question), (LN) 04/2015 (added denial reasons); (CF/JH) 11/2015, (SE) 06/2016 (created separate Med D); (CF/JH) 02/2017; (KC) 02/2018, 02/2019 (no clinical changes), 06/2019 (updated questions)

Reviewed: CDPR/Medical Affairs (MM): 01/2005, 02/2006; (WF): 02/2007, 01/2008, 12/2008, 11/2009; (KP) 11/2010, 11/2011, 03/2012, 10/2012; (DNC) 11/2012; (LCB) 11/2013; (SES) 11/2014; (KRU) 02/2015; (LCB) 11/2015; (ME) 02/2017; (AN) 02/2018; (ME) 07/2019

External Review: 08/2005, 04/2006, 06/2007, 04/2008, 04/2009, 02/2010, 02/2011, 03/2012, 02/2013, 02/2014, 02/2015, 02/2016, 06/2016, 06/2017, 06/2018, 06/2019

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for primary or hypogonadotropic hypogonadism? [Note: Safety and efficacy of testosterone products in patients with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.] [If no, then skip to question 5.]	Yes	No
2	Is this request for a continuation of testosterone therapy? [If no, then skip to question 4.]	Yes	No
3	Before the patient started testosterone therapy, did the patient have a confirmed low testosterone level according to current practice guidelines or your standard lab reference values? [No further questions.]	Yes	No
4	Does the patient have at least two confirmed low testosterone levels according to current practice guidelines or your standard lab reference values? [No further questions.]	Yes	No
5	Is the requested drug being prescribed for gender dysphoria in a patient who is able to make an informed decision to engage in hormone therapy?	Yes	No

Mapping Instructions			
	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Go to 5	
2.	Go to 3	Go to 4	
3.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have had a test that showed low testosterone levels before you started testosterone therapy. Your request has been denied based on the information we have. [Short Description: No confirmation of diagnosis (tests, labs, etc.)]
4.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have had two tests that showed low testosterone levels. Your request has been denied based on the information we have. [Short Description: No confirmation of diagnosis (tests, labs, etc.)]
5.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet one of these conditions: <ul style="list-style-type: none"> - You have primary or hypogonadotropic hypogonadism - You have gender dysphoria and you can make an informed decision to use this drug Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS TESTOSTERONE PRODUCTS – ORAL

BRAND NAME*
(generic)

JATENZO
(testosterone undecanoate oral)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

Ref # 3059-A

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Jatenzo is an androgen indicated for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone:

Primary hypogonadism (congenital or acquired) - testicular failure due to conditions such as cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy, Klinefelter Syndrome, chemotherapy, or toxic damage from alcohol or heavy metals. These men usually have low serum testosterone concentrations and gonadotropins (FSH, LH) above the normal range.

Hypogonadotropic hypogonadism (congenital or acquired) - gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation. These men have low testosterone serum concentrations but have gonadotropins in the normal or low range.

Limitations of Use

Safety and efficacy of Jatenzo in males less than 18 years old have not been established.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for primary or hypogonadotropic hypogonadism [Note: Safety and efficacy of testosterone products in patients with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.]

AND

- Before the start of testosterone therapy, the patient has at least two confirmed low testosterone levels according to current practice guidelines or your standard lab reference values **OR**
- For continuation of testosterone therapy: before the patient started testosterone therapy, the patient had a confirmed low testosterone level according to current practice guidelines or your standard lab reference values

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Jatenzo is indicated for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone: congenital or acquired primary hypogonadism (testicular failure due to conditions such as cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy, Klinefelter Syndrome, chemotherapy, or toxic damage from alcohol or heavy metals), congenital or acquired hypogonadotropic hypogonadism (gonadotropin or luteinizing hormone-releasing hormone [LHRH] deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation). Safety and efficacy of topical, buccal, and nasal testosterone products in men with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.

The safety and efficacy of Jatenzo was evaluated in 166 adult hypogonadal males in an open-label study of approximately 4 months duration. The primary endpoint was the percentage of patients with mean plasma total testosterone concentration over 24 hours within the normal eugonadal range on the final pharmacokinetics visit of the study. 145 (87%) of the 166 hypogonadal men who received Jatenzo had a mean total testosterone concentration within the normal eugonadal range at the end of treatment.

A testosterone determination, in conjunction with a free testosterone or sex hormone-binding globulin level, is the threshold test in the evaluation of suspected male hypogonadism (serum total testosterone levels less than 300 ng/dL [nanograms per deciliter]). Testosterone levels should be determined in the morning, and studies should be repeated in patients with subnormal levels. The normative ranges for total and free testosterone levels in healthy young men vary among laboratories and assays. In some laboratories, the lower limit of the normal range for total testosterone level in healthy young men is 280-300 ng/dL and for serum free testosterone level is 5–9 pg/mL (picograms per milliliter). Clinicians should use the lower limit of normal range for healthy young men established in their laboratory.^{4,5} For initial therapy, testosterone will be approved for patients with at least two confirmed low testosterone levels according to current practice guidelines or standard lab reference values. If the patient is already on testosterone therapy and did not get a repeat testosterone level before starting therapy, it would be inappropriate for the patient to stop treatment to get a repeat testosterone level. For continuation of therapy, one low testosterone level is required before the patient started testosterone therapy.

REFERENCES

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3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed February 2019.
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5. Bhasin S, Cunningham G, Hayes F, et al. Testosterone Therapy in Adult Men with Androgen Deficiency Syndromes: An Endocrine Society Clinical Practice Guideline. *Journal of Clinical Endocrinology & Metabolism* 2018 103(5):1715-1744.

Written by: UM Development (KC)
 Date Written: 04/2019
 Revised:
 Reviewed: Medical Affairs: (GAD) 05/2019
 External Review: 06/2019

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for primary or hypogonadotropic hypogonadism? [Note: Safety and efficacy of testosterone products in patients with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.]	Yes	No
2	Is this request for a continuation of testosterone therapy? [If no, then skip to question 4.]	Yes	No
3	Before the patient started testosterone therapy, did the patient have a confirmed low testosterone level according to current practice guidelines or your standard lab reference values? [No further questions.]	Yes	No

- | | | | |
|---|---|-----|----|
| 4 | Does the patient have at least two confirmed low testosterone levels according to current practice guidelines or your standard lab reference values?
[No further questions.] | Yes | No |
|---|---|-----|----|

Mapping Instructions

DENIAL REASONS – DO NOT USE FOR MEDICARE PART D			
	Yes	No	
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have primary or hypogonadotropic hypogonadism. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
2.	Go to 3	Go to 4	
3.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have had a test that showed low testosterone levels before you started testosterone therapy. Your request has been denied based on the information we have. [Short Description: No confirmation of diagnosis (tests, labs, etc.)]
4.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have had two tests that showed low testosterone levels. Your request has been denied based on the information we have. [Short Description: No confirmation of diagnosis (tests, labs, etc.)]

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS TESTOSTERONE PRODUCTS – ORAL

BRAND NAME*
(generic)

JATENZO
(testosterone undecanoate oral)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

Ref # 3060-A

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Jatenzo is an androgen indicated for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone:

Primary hypogonadism (congenital or acquired) - testicular failure due to conditions such as cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy, Klinefelter Syndrome, chemotherapy, or toxic damage from alcohol or heavy metals. These men usually have low serum testosterone concentrations and gonadotropins (FSH, LH) above the normal range.

Hypogonadotropic hypogonadism (congenital or acquired) - gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation. These men have low testosterone serum concentrations but have gonadotropins in the normal or low range.

Limitations of Use

Safety and efficacy of Jatenzo in males less than 18 years old have not been established.

Compendial Uses

Gender Dysphoria^{3,6-9}

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for primary or hypogonadotropic hypogonadism [Note: Safety and efficacy of testosterone products in patients with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.]

AND

- Before the start of testosterone therapy, the patient has at least two confirmed low testosterone levels according to current practice guidelines or your standard lab reference values **OR**
- For continuation of testosterone therapy: before the patient started testosterone therapy, the patient had a confirmed low testosterone level according to current practice guidelines or your standard lab reference values

OR

- The requested drug is being prescribed for gender dysphoria in a patient who is able to make an informed decision to engage in hormone therapy

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Jatenzo is indicated for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone: congenital or

acquired primary hypogonadism (testicular failure due to conditions such as cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy, Klinefelter Syndrome, chemotherapy, or toxic damage from alcohol or heavy metals), congenital or acquired hypogonadotropic hypogonadism (gonadotropin or luteinizing hormone-releasing hormone [LHRH] deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation). Safety and efficacy of topical, buccal, and nasal testosterone products in men with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.

The safety and efficacy of Jatenzo was evaluated in 166 adult hypogonadal males in an open-label study of approximately 4 months duration. The primary endpoint was the percentage of patients with mean plasma total testosterone concentration over 24 hours within the normal eugonadal range on the final pharmacokinetics visit of the study. 145 (87%) of the 166 hypogonadal men who received Jatenzo had a mean total testosterone concentration within the normal eugonadal range at the end of treatment.

A testosterone determination, in conjunction with a free testosterone or sex hormone-binding globulin level, is the threshold test in the evaluation of suspected male hypogonadism (serum total testosterone levels less than 300 ng/dL [nanograms per deciliter]). Testosterone levels should be determined in the morning, and studies should be repeated in patients with subnormal levels. The normative ranges for total and free testosterone levels in healthy young men vary among laboratories and assays. In some laboratories, the lower limit of the normal range for total testosterone level in healthy young men is 280-300 ng/dL and for serum free testosterone level is 5–9 pg/mL (picograms per milliliter). Clinicians should use the lower limit of normal range for healthy young men established in their laboratory.^{4,5} For initial therapy, testosterone will be approved for patients with at least two confirmed low testosterone levels according to current practice guidelines or standard lab reference values. If the patient is already on testosterone therapy and did not get a repeat testosterone level before starting therapy, it would be inappropriate for the patient to stop treatment to get a repeat testosterone level. For continuation of therapy, one low testosterone level is required before the patient started testosterone therapy.

Jatenzo has a compendial use for gender dysphoria in transgender male (female-to-male) patients.⁶⁻⁹

Transgender persons seeking to develop the physical characteristics of the desired gender require a safe, effective hormone regimen that will suppress endogenous hormone secretion determined by the person's genetic/biologic sex and maintain sex hormone levels within the normal range for the person's desired gender. The two major goals of hormonal therapy are to reduce endogenous hormone levels and, thereby, the secondary sex characteristics of the individual's biological/genetic sex and to replace endogenous sex hormone levels with those of the reassigned sex. The Endocrine Society suggests that pubertal development of the desired opposite sex be initiated at about the age of 16 years, using a gradually increasing dose schedule of cross-sex steroids. However, the Endocrine Society Guidelines also state that identifying an age at which pubertal development is initiated can be difficult and may depend on several factors (such as the age when pubertal suppression was begun, medications used to initiate pubertal suppression, and relative risks of prolonged pubertal suppression), and the goal is to start the process at a time when the individual will be able to make informed, mature decisions to engage in the therapy. Some patients may advance to Tanner stage 2 of pubertal development at an early age (such as 9 or 10) and using pubertal suppression therapy for 6 or 7 years may be deemed inappropriate. Medical professionals involved in the patient's care should be involved in assessing whether the patient is ready to make the decision to begin hormone therapy and pubertal development.⁶ Therefore, individuals who are able to make an informed decision to engage in hormone therapy will be approved.

For transgender male (female-to-male) persons, regimens to change secondary sex characteristics follow the general principle of hormone replacement treatment of male hypogonadism. Testosterone generally can be given orally, transdermally, or parenterally (IM) to achieve testosterone values in the normal male range (320-1000 ng/dL).^{6,8} The agent primarily used for endocrine treatment of transgender male patients is testosterone. When determining the appropriate method of testosterone delivery, many considerations should be taken into account. The most well-described formulation of testosterone therapy used to treat transgender male patients is intramuscular injection of testosterone esters (cypionate or enanthate).⁷ Because intramuscular testosterone cypionate or enanthate is often administered every 2-4 weeks, some patients may notice a cyclic variation in effects as well as more time outside the normal physiologic levels.⁸ Transdermal testosterone has been shown to provide less variation in serum testosterone levels compared with injectable preparations. Testosterone administered transdermally more closely mimics physiologic testosterone levels. However, transdermal preparations achieve low-normal ranges of testosterone levels in hypogonadal men, which may translate to a lessened change in physical appearance and virilization in the transgender male patient.⁷ Oral

testosterone undecanoate formulations available outside the United States result in lower serum testosterone levels than nonoral preparations.⁸ However, studies for Jatenzo indicate that it achieves normal serum testosterone levels in hypogonadal patients, indicating that normal levels can be achieved for transgender patients.

REFERENCES

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5. Bhasin S, Cunningham G, Hayes F, et al. Testosterone Therapy in Adult Men with Androgen Deficiency Syndromes: An Endocrine Society Clinical Practice Guideline. *Journal of Clinical Endocrinology & Metabolism* 2018 103(5):1715-1744.
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Written by: UM Development (KC)
 Date Written: 04/2019
 Revised: (KC) 06/2019 (updated gender dysphoria question)
 Reviewed: Medical Affairs: (GAD) 05/2019; (ME) 07/2019
 External Review: 06/2019

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for primary or hypogonadotropic hypogonadism? [Note: Safety and efficacy of testosterone products in patients with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.] [If no, then skip to question 5.]	Yes	No
2	Is this request for a continuation of testosterone therapy? [If no, then skip to question 4.]	Yes	No
3	Before the patient started testosterone therapy, did the patient have a confirmed low testosterone level according to current practice guidelines or your standard lab reference values? [No further questions.]	Yes	No
4	Does the patient have at least two confirmed low testosterone levels according to current practice guidelines or your standard lab reference values? [No further questions.]	Yes	No

5	Is the requested drug being prescribed for gender dysphoria in a patient who is able to make an informed decision to engage in hormone therapy?	Yes	No
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Mapping Instructions

	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Go to 5	
2.	Go to 3	Go to 4	
3.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have had a test that showed low testosterone levels before you started testosterone therapy. Your request has been denied based on the information we have. [Short Description: No confirmation of diagnosis (tests, labs, etc.)]
4.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have had two tests that showed low testosterone levels. Your request has been denied based on the information we have. [Short Description: No confirmation of diagnosis (tests, labs, etc.)]
5.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet one of these conditions: <ul style="list-style-type: none"> - You have primary or hypogonadotropic hypogonadism - You have gender dysphoria and you can make an informed decision to use this drug Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	TESTOSTERONE PRODUCTS – ORAL
BRAND NAME* (generic)	<p>ANDROID (methyltestosterone oral capsule)</p> <p>ANDROXY (fluoxymesterone oral tablet)</p> <p>METHITEST (methyltestosterone oral tablet)</p> <p>TESTRED (methyltestosterone oral capsule)</p>
Status: CVS Caremark Criteria	REG
Type: Initial Prior Authorization	Ref # 2817-A

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Males

Androgens are indicated for replacement therapy in conditions associated with deficiency or absence of endogenous testosterone:

Primary hypogonadism (congenital or acquired) - testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, or orchiectomy.

Hypogonadotropic hypogonadism (congenital or acquired) - gonadotropin or LHRH deficiency, or pituitary-hypothalamic injury from tumors, trauma, or radiation. (Appropriate adrenal cortical and thyroid hormone replacement therapy are still necessary, however, and are actually of primary importance.)

If the above conditions occur prior to puberty, androgen replacement therapy will be needed during the adolescent years for development of secondary sexual characteristics. Prolonged androgen treatment will be required to maintain sexual characteristics in these and other males who develop testosterone deficiency after puberty.

Safety and efficacy of oral testosterone in men with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.

Androgens may be used to stimulate puberty in carefully selected males with clearly delayed puberty. These patients usually have a familial pattern of delayed puberty that is not secondary to a pathological disorder; puberty is expected to occur spontaneously at a relatively late date. Brief treatment with conservative doses may occasionally be justified in these patients if they do not respond to psychological support. The potential adverse effect on bone maturation should be discussed with the patient and parents prior to androgen administration. An X-ray of the hand and wrist to determine bone age should be obtained every 6 months to assess the effect of treatment on the epiphyseal centers.

Females

Androgens may be used secondarily in women with advancing inoperable metastatic (skeletal) mammary cancer who are 1 to 5 years postmenopausal. Primary goals of therapy in these women include ablation of the ovaries. Other methods of counteracting estrogen activity are adrenalectomy, hypophysectomy, and/or anti-estrogen therapy. This treatment has also been used in premenopausal women with breast cancer who have benefited from oophorectomy and are considered

to have a hormone-responsive tumor. Judgment concerning androgen therapy should be made by an oncologist with expertise in this field.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for primary or hypogonadotropic hypogonadism [Note: Safety and efficacy of testosterone products in patients with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.]
AND
 - Before the start of testosterone therapy, the patient has at least two confirmed low testosterone levels according to current practice guidelines or your standard lab reference values **OR**
 - For continuation of testosterone therapy: before the patient started testosterone therapy, the patient had a confirmed low testosterone level according to current practice guidelines or your standard lab reference values
- OR**
- The requested drug is being prescribed for inoperable metastatic breast cancer in a patient who is 1 to 5 years postmenopausal
- OR**
- The requested drug is being prescribed for a premenopausal patient with breast cancer who has benefited from oophorectomy and is considered to have a hormone-responsive tumor
- OR**
- The requested drug is being prescribed for delayed puberty

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. In males, oral androgens are indicated for replacement therapy in conditions associated with a deficiency or absence of endogenous testosterone: primary hypogonadism (testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, or orchiectomy), hypogonadotropic hypogonadism (gonadotropin or luteinizing hormone-releasing hormone [LHRH] deficiency, or pituitary-hypothalamic injury from tumors, trauma, or radiation), and delayed puberty. Safety and efficacy of oral testosterone in men with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.¹⁻⁶

A testosterone determination, in conjunction with a free testosterone or sex hormone-binding globulin level, is the threshold test in the evaluation of suspected male hypogonadism (serum total testosterone levels less than 300 ng/dL). Testosterone levels should be determined in the morning, and studies should be repeated in patients with subnormal levels. The normative ranges for total and free testosterone levels in healthy young men vary among laboratories and assays. In some laboratories, the lower limit of the normal range for total testosterone level in healthy young men is 280-300 ng/dL and for serum free testosterone level is 5–9 pg/mL. The clinicians should use the lower limit of normal range for healthy young men established in their laboratory.^{7,8} For initial therapy, testosterone will be approved for patients with at least two confirmed low testosterone levels according to current practice guidelines or standard lab reference values. If the patient is already on testosterone therapy and did not get a repeat testosterone level before starting therapy, it would be inappropriate for the patient to stop treatment to get a repeat testosterone level. For continuation of therapy, one low testosterone level is required before the patient started testosterone therapy.

Oral androgens may be used secondarily in women with advancing inoperable metastatic (skeletal) mammary cancer who are one to five years postmenopausal. Primary goals of therapy in these women include ablation of the ovaries. Other methods of counteracting estrogen activity are adrenalectomy, hypophysectomy, and/or anti-estrogen therapy.¹⁻⁶

This treatment has also been used in premenopausal women with breast cancer who have benefited from oophorectomy and are considered to have a hormone-responsive tumor. Judgment concerning androgen therapy should be made by an oncologist with expertise in this field.¹⁻⁶

Oral androgens may be used to stimulate puberty in carefully selected males with clearly delayed puberty. Brief treatment with conservative doses may occasionally be justified in these patients if they do not respond to psychological support.¹⁻⁵

REFERENCES

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2. Androxy [package insert]. Maple Grove, MN: Upsher-Smith Laboratories, Inc.; September 2017.
3. Methitest [package insert]. Philadelphia, PA: Global Pharmaceutical Corporation; February 2017.
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5. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed December 2018.
6. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed December 2018.
7. Petak S, Nankin H, Spark R, et al. American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice for the Evaluation and Treatment of Hypogonadism in Adult Male Patients – 2002 update. *Endocrine Practice* 2002;8(6):439-456.
8. Bhasin S, Cunningham G, Hayes F, et al. Testosterone Therapy in Adult Men with Androgen Deficiency Syndromes: An Endocrine Society Clinical Practice Guideline. *Journal of Clinical Endocrinology & Metabolism* 2018 103(5):1715-1744.

Written by: UM Development (KC)
 Date: 12/2018 (created REG version of 878-A)
 Revised: (KC) 08/2019 (removed "male" from lab questions)
 Reviewed: CDPR/Medical Affairs: (ME) 12/2018; (EPA) 08/2019
 External Review: 02/2019 (FYI), 10/2019 (FYI)

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for primary or hypogonadotropic hypogonadism? [Note: Safety and efficacy of testosterone products in patients with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established.] [If no, then skip to question 5.]	Yes	No
2	Is this request for a continuation of testosterone therapy? [If no, then skip to question 4.]	Yes	No
3	Before the patient started testosterone therapy, did the patient have a confirmed low testosterone level according to current practice guidelines or your standard lab reference values? [No further questions.]	Yes	No
4	Does the patient have at least two confirmed low testosterone levels according to current practice guidelines or your standard lab reference values? [No further questions.]	Yes	No
5	Is the requested drug being prescribed for inoperable metastatic breast cancer in a patient who is 1 to 5 years postmenopausal? [If yes, then no further questions.]	Yes	No
6	Is the requested drug being prescribed for a premenopausal patient with breast cancer who has benefited from oophorectomy and is considered to have a hormone-responsive tumor?	Yes	No

[If yes, then no further questions.]

7 Is the requested drug being prescribed for delayed puberty?

Yes

No

Mapping Instructions

DENIAL REASONS – DO NOT USE FOR MEDICARE PART D

	Yes	No	
1.	Go to 2	Go to 5	
2.	Go to 3	Go to 4	
3.	Approve, 36 Months	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions:</p> <ul style="list-style-type: none"> - You have primary or hypogonadotropic hypogonadism - Before starting testosterone therapy, you had a test that showed low testosterone levels <p>Your request has been denied based on the information we have. [Short Description: No confirmation of diagnosis (tests, labs, etc.)]</p>
4.	Approve, 36 Months	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions:</p> <ul style="list-style-type: none"> - You have primary or hypogonadotropic hypogonadism - You have had 2 tests that showed low testosterone levels <p>Your request has been denied based on the information we have. [Short Description: No confirmation of diagnosis (tests, labs, etc.)]</p>
5.	Approve, 36 months	Go to 6	
6.	Approve, 36 months	Go to 7	
7.	Approve, 36 Months	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you meet one of these conditions:</p> <ul style="list-style-type: none"> - You have primary or hypogonadotropic hypogonadism - You are postmenopausal with metastatic breast cancer and surgery is not possible - You are premenopausal with breast cancer, have a hormone-responsive tumor, and had your ovaries removed - You have delayed puberty <p>Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]</p>

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	TESTOSTERONE PRODUCTS – INJECTABLE
BRAND NAME* (generic)	DELATESTRYL (testosterone enanthate injection) XYOSTED (testosterone enanthate injection)
Status: CVS Caremark Criteria	MDC-2
Type: Initial Prior Authorization	Ref # 906-A

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Delatestryl

Males

Delatestryl (Testosterone Enanthate Injection) is indicated for replacement therapy in conditions associated with a deficiency or absence of endogenous testosterone.

Primary hypogonadism (congenital or acquired) - testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, or orchiectomy.

Hypogonadotropic hypogonadism (congenital or acquired) - gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency, or pituitary-hypothalamic injury from tumors, trauma, or radiation. (Appropriate adrenal cortical and thyroid hormone replacement therapy are still necessary, however, and are actually of primary importance).

If the above conditions occur prior to puberty, androgen replacement therapy will be needed during the adolescent years for development of secondary sexual characteristics. Prolonged androgen treatment will be required to maintain sexual characteristics in these and other males who develop testosterone deficiency after puberty.

Safety and efficacy of Delatestryl in men with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.

Delayed puberty - Delatestryl (Testosterone Enanthate Injection) may be used to stimulate puberty in carefully selected males with clearly delayed puberty. These patients usually have a familial pattern of delayed puberty that is not secondary to a pathological disorder; puberty is expected to occur spontaneously at a relatively late date. Brief treatment with conservative doses may occasionally be justified in these patients if they do not respond to psychological support. The potential adverse effect on bone maturation should be discussed with the patient and parents prior to androgen administration. An X-ray of the hand and wrist to determine bone age should be obtained every six months to assess the effect of treatment on the epiphyseal centers.

Females

Metastatic Mammary Cancer - Delatestryl (Testosterone Enanthate Injection) may be used secondarily in women with advancing inoperable metastatic (skeletal) mammary cancer who are one to five years postmenopausal. Primary goals of therapy in these women include ablation of the ovaries. Other methods of counteracting estrogen activity are adrenalectomy, hypophysectomy, and/or anti-estrogen therapy. This treatment has also been used in pre-menopausal women with breast cancer who have benefited from oophorectomy and are considered to have a hormone-responsive tumor. Judgment concerning androgen therapy should be made by an oncologist with expertise in this field.

Xyosted

Xyosted (testosterone enanthate) injection is an androgen indicated for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone:

- Primary hypogonadism (congenital or acquired): testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy, Klinefelter's syndrome, chemotherapy, or toxic damage from alcohol or heavy meals. These men usually have low serum testosterone concentrations and gonadotropins (follicle-stimulating hormone [FSH], luteinizing hormone [LH]) above the normal range.
- Hypogonadotropic hypogonadism (congenital or acquired): gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation. These men have low testosterone serum concentrations but have gonadotropins in the low or normal range.

Limitations of Use

- Safety and efficacy of Xyosted in adult males with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established.
- Safety and efficacy of Xyosted in males less than 18 years of age have not been established.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for primary or hypogonadotropic hypogonadism [Note: Safety and efficacy of testosterone products in patients with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established.]
AND
 - Before the start of testosterone therapy, the patient has at least two confirmed low testosterone levels according to current practice guidelines or your standard lab reference values **OR**
 - For continuation of testosterone therapy: before the patient started testosterone therapy, the patient had a confirmed low testosterone level according to current practice guidelines or your standard lab reference values
- OR**
- Testosterone enanthate injection (generic Delatestryl) is being prescribed for inoperable metastatic breast cancer in a patient who is 1 to 5 years postmenopausal **AND** the patient had an incomplete response to other therapy for metastatic breast cancer
OR
- Testosterone enanthate injection (generic Delatestryl) is being prescribed for a premenopausal patient with breast cancer who has benefited from oophorectomy and is considered to have a hormone-responsive tumor
OR
- Testosterone enanthate injection (generic Delatestryl) is being prescribed for delayed puberty

RATIONALE

These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. In males, Delatestryl and Xyosted are indicated for replacement therapy in conditions associated with a deficiency or absence of endogenous testosterone: primary hypogonadism (testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, or orchiectomy) or hypogonadotropic hypogonadism (gonadotropin or luteinizing hormone-releasing hormone [LHRH] deficiency, or pituitary-hypothalamic injury from tumors, trauma, or radiation). Delatestryl is also indicated for delayed puberty. Safety and efficacy of Delatestryl and Xyosted in men with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established.¹⁻⁴

A testosterone determination, in conjunction with a free testosterone or sex hormone-binding globulin level, is the threshold test in the evaluation of suspected male hypogonadism (serum total testosterone levels less than 300 ng/dL). Testosterone levels should be determined in the morning, and studies should be repeated in patients with subnormal levels. The normative ranges for total and free testosterone levels in healthy young men vary among laboratories and assays. In some laboratories, the lower limit of the normal range for total testosterone level in healthy young men is 280-

300 ng/dL and for serum free testosterone level is 5–9 pg/mL. The clinicians should use the lower limit of normal range for healthy young men established in their laboratory.^{5,6} For initial therapy, testosterone will be approved for patients with at least two confirmed low testosterone levels according to current practice guidelines or standard lab reference values. If the patient is already on testosterone therapy and did not get a repeat testosterone level before starting therapy, it would be inappropriate for the patient to stop treatment to get a repeat testosterone level. For continuation of therapy, one low testosterone level is required before the patient started testosterone therapy.

Delatestryl may be used secondarily in women with advancing inoperable metastatic (skeletal) mammary cancer who are one to five years postmenopausal. Primary goals of therapy in these women include ablation of the ovaries. Other methods of counteracting estrogen activity are adrenalectomy, hypophysectomy, and/or anti-estrogen therapy.^{1, 3-4} Since testosterone is not a first-line drug for breast cancer, the patient must have had an incomplete response to other breast cancer therapy before using testosterone.

This treatment has also been used in premenopausal women with breast cancer who have benefited from oophorectomy and are considered to have a hormone-responsive tumor. Judgment concerning androgen therapy should be made by an oncologist with expertise in this field.^{1, 3-4}

Delatestryl may be used to stimulate puberty in carefully selected males with clearly delayed puberty. Brief treatment with conservative doses may occasionally be justified in these patients if they do not respond to psychological support.^{1, 3-4}

REFERENCES

1. Delatestryl [package insert]. Malvern, PA: Endo Pharmaceuticals Solutions Inc.; October 2016.
2. Xyosted [package insert]. Ewing, NJ: Antares Pharma, Inc; September 2018.
3. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed October 2018.
4. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed October 2018.
5. Petak S, Nankin H, Spark R, et al. American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice for the Evaluation and Treatment of Hypogonadism in Adult Male Patients – 2002 update. *Endocrine Practice* 2002;8(6):439-456.
6. Bhasin S, Cunningham G, Hayes F, et al. Testosterone Therapy in Adult Men with Androgen Deficiency Syndromes: An Endocrine Society Clinical Practice Guideline. *Journal of Clinical Endocrinology & Metabolism* 2018 103(5):1715-1744.

Written by: UM Development (AP)
Date: 02/2002

Revised: (MG) 02/2003; (NB) 01/2005; (MG) 02/2006; (NB) 02/2007(2); (AM) 01/2008, 12/2008; (MS) 11/2009, 11/2010, (TM) 11/2011, 10/2012 (extended duration); (PL) 11/2012, (PL) 11/2013, (SE) 04/2014 (rephrased diagnosis question); (CF/JH) 11/2014, 02/2015 (updated testosterone level question), (LN) 04/2015 (added denial reasons); (CF/JH) 11/2015, (SE) 06/2016 (created separate Med D); (CF/JH) 11/2016; (KC) 11/2017, 10/2018 (added Xyosted), 10/2018, 08/2019 (removed "male" from lab questions)
Reviewed: CDPR/Medical Affairs (MM): 01/2005, 02/2006; (WF): 02/2007, 01/2008, 12/2008, 11/2009; (KP) 11/2010, 11/2011, 03/2012, 10/2012; (DNC) 11/2012; (LCB) 11/2013; (SES) 11/2014; (KRU) 02/2015; (LCB) 11/2015; (ME) 11/2016; (ME) 02/2017; (ME) 11/2017; (ME) 10/2018; (EPA) 08/2019
External Review: 08/2005, 04/2006, 06/2007, 04/2008, 04/2009, 02/2010, 02/2011, 03/2012, 02/2013, 02/2014, 02/2015, 02/2016, 02/2017, 02/2018, 02/2019, 10/2019 (FYI)

CRITERIA FOR APPROVAL

- | | | | |
|---|--|-----|----|
| 1 | Is the requested drug being prescribed for primary or hypogonadotropic hypogonadism?
[Note: Safety and efficacy of testosterone products in patients with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established.]
[If no, then skip to question 5.] | Yes | No |
|---|--|-----|----|

2	Is this request for a continuation of testosterone therapy? [If no, then skip to question 4.]	Yes	No
3	Before the patient started testosterone therapy, did the patient have a confirmed low testosterone level according to current practice guidelines or your standard lab reference values? [No further questions.]	Yes	No
4	Does the patient have at least two confirmed low testosterone levels according to current practice guidelines or your standard lab reference values? [No further questions.]	Yes	No
5	Is testosterone enanthate injection (generic Delatestryl) being prescribed for inoperable metastatic breast cancer in a patient who is 1 to 5 years postmenopausal AND has the patient had an incomplete response to other therapy for metastatic breast cancer? [If yes, then no further questions.]	Yes	No
6	Is testosterone enanthate injection (generic Delatestryl) being prescribed for a premenopausal patient with breast cancer who has benefited from oophorectomy and is considered to have a hormone-responsive tumor? [If yes, then no further questions.]	Yes	No
7	Is testosterone enanthate injection (generic Delatestryl) being prescribed for delayed puberty?	Yes	No

Guidelines for Approval					
Duration of Approval			12 Months		
Set 1		Set 2		Set 3	
Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)
1	None	1	2	5	1
2		4			
3					
Set 4		Set 5			
Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)		
6	1	7	1		
	5		5		
			6		

Mapping Instructions			
	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Go to 5	
2.	Go to 3	Go to 4	
3.	Approve, 12 Months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have had a test that showed low testosterone levels before you started testosterone therapy. Your request has been denied based on the information we have. [Short Description: No confirmation of diagnosis (tests, labs, etc.)]
4.	Approve, 12 Months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have had two tests that showed low testosterone levels. Your request has been denied based on the information we have.

			[Short Description: No confirmation of diagnosis (tests, labs, etc.)]
5.	Approve, 12 Months	Go to 6	
6.	Approve, 12 Months	Go to 7	
7.	Approve, 12 Months	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you meet one of these conditions:</p> <ul style="list-style-type: none"> - You have primary or hypogonadotropic hypogonadism - For testosterone enanthate injection (generic Delatestryl), you are a postmenopausal patient with metastatic breast cancer, surgery is not possible, and other drugs for your cancer did not work for you - For testosterone enanthate injection (generic Delatestryl), you are a premenopausal patient with breast cancer, have a hormone-responsive tumor, and had your ovaries removed - Testosterone enanthate injection (generic Delatestryl) is being prescribed for delayed puberty <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No approvable diagnosis]</p>

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS TESTOSTERONE PRODUCTS – INJECTABLE

BRAND NAME*
(generic)

DELATESTRYL
(testosterone enanthate injection)

XYOSTED
(testosterone enanthate injection)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

Ref # 1368-A

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Delatestryl

Males

Delatestryl (Testosterone Enanthate Injection) is indicated for replacement therapy in conditions associated with a deficiency or absence of endogenous testosterone.

Primary hypogonadism (congenital or acquired) - testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, or orchiectomy.

Hypogonadotropic hypogonadism (congenital or acquired) - gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency, or pituitary-hypothalamic injury from tumors, trauma, or radiation. (Appropriate adrenal cortical and thyroid hormone replacement therapy are still necessary, however, and are actually of primary importance).

If the above conditions occur prior to puberty, androgen replacement therapy will be needed during the adolescent years for development of secondary sexual characteristics. Prolonged androgen treatment will be required to maintain sexual characteristics in these and other males who develop testosterone deficiency after puberty.

Safety and efficacy of Delatestryl in men with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.

Delayed puberty - Delatestryl (Testosterone Enanthate Injection) may be used to stimulate puberty in carefully selected males with clearly delayed puberty. These patients usually have a familial pattern of delayed puberty that is not secondary to a pathological disorder; puberty is expected to occur spontaneously at a relatively late date. Brief treatment with conservative doses may occasionally be justified in these patients if they do not respond to psychological support. The potential adverse effect on bone maturation should be discussed with the patient and parents prior to androgen administration. An X-ray of the hand and wrist to determine bone age should be obtained every six months to assess the effect of treatment on the epiphyseal centers.

Females

Metastatic Mammary Cancer - Delatestryl (Testosterone Enanthate Injection) may be used secondarily in women with advancing inoperable metastatic (skeletal) mammary cancer who are one to five years postmenopausal. Primary goals of therapy in these women include ablation of the ovaries. Other methods of counteracting estrogen activity are adrenalectomy, hypophysectomy, and/or anti-estrogen therapy. This treatment has also been used in pre-menopausal women with breast cancer who have benefited from oophorectomy and are considered to have a hormone-responsive tumor. Judgment concerning androgen therapy should be made by an oncologist with expertise in this field.

Xyosted

Xyosted (testosterone enanthate) injection is an androgen indicated for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone:

- Primary hypogonadism (congenital or acquired): testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy, Klinefelter's syndrome, chemotherapy, or toxic damage from alcohol or heavy meals. These men usually have low serum testosterone concentrations and gonadotropins (follicle-stimulating hormone [FSH], luteinizing hormone [LH]) above the normal range.
- Hypogonadotropic hypogonadism (congenital or acquired): gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation. These men have low testosterone serum concentrations but have gonadotropins in the low or normal range.

Limitations of Use

- Safety and efficacy of Xyosted in adult males with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established.
- Safety and efficacy of Xyosted in males less than 18 years of age have not been established.

Compindial Uses

Gender Dysphoria in transgender male patients^{4,7-10}

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for primary or hypogonadotropic hypogonadism [Note: Safety and efficacy of testosterone products in patients with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established.]

AND

- Before the start of testosterone therapy, the patient has at least two confirmed low testosterone levels according to current practice guidelines or your standard lab reference values **OR**
- For continuation of testosterone therapy: before the patient started testosterone therapy, the patient had a confirmed low testosterone level according to current practice guidelines or your standard lab reference values

OR

- The requested drug is being prescribed for gender dysphoria in a patient who is able to make an informed decision to engage in hormone therapy

OR

- Testosterone enanthate injection (generic Delatestryl) is being prescribed for delayed puberty

OR

- Testosterone enanthate injection (generic Delatestryl) is being prescribed for inoperable metastatic breast cancer in a patient who is 1 to 5 years postmenopausal AND the patient had an incomplete response to other therapy for metastatic breast cancer

OR

- Testosterone enanthate injection (generic Delatestryl) is being prescribed for a pre-menopausal patient with breast cancer who has benefited from oophorectomy and is considered to have a hormone-responsive tumor

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. In males, Delatestryl is indicated for replacement therapy in conditions associated with a deficiency or absence of endogenous testosterone: primary hypogonadism (testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, or orchiectomy) or hypogonadotropic hypogonadism (gonadotropin or luteinizing hormone-releasing hormone [LHRH] deficiency, or pituitary-hypothalamic injury from tumors, trauma, or radiation). Delatestryl is also indicated for delayed puberty. Safety and efficacy of Delatestryl and Xyosted in men with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established.¹⁻⁴

A testosterone determination, in conjunction with a free testosterone or sex hormone-binding globulin level, is the threshold test in the evaluation of suspected male hypogonadism (serum total testosterone levels less than 300 ng/dL [nanograms per deciliter]). Testosterone levels should be determined in the morning, and studies should be repeated in

patients with subnormal levels. The normative ranges for total and free testosterone levels in healthy young men vary among laboratories and assays. In some laboratories, the lower limit of the normal range for total testosterone level in healthy young men is 280-300 ng/dL and for serum free testosterone level is 5–9 pg/mL (picograms per milliliter). Clinicians should use the lower limit of normal range for healthy young men established in their laboratory.^{5,6} For initial therapy, testosterone will be approved for patients with at least two confirmed low testosterone levels according to current practice guidelines or standard lab reference values. If the patient is already on testosterone therapy and did not get a repeat testosterone level before starting therapy, it would be inappropriate for the patient to stop treatment to get a repeat testosterone level. For continuation of therapy, one low testosterone level is required before the patient started testosterone therapy.

Delatestryl may be used secondarily in women with advancing inoperable metastatic (skeletal) mammary cancer who are one to five years postmenopausal. Primary goals of therapy in these women include ablation of the ovaries. Other methods of counteracting estrogen activity are adrenalectomy, hypophysectomy, and/or anti-estrogen therapy.^{1,3,4} Since testosterone is not a first-line drug for breast cancer, the patient must have had an incomplete response to other breast cancer therapy before using testosterone.

This treatment has also been used in pre-menopausal women with breast cancer who have benefited from oophorectomy and are considered to have a hormone-responsive tumor. Judgment concerning androgen therapy should be made by an oncologist with expertise in this field.^{1,3,4}

Delatestryl may be used to stimulate puberty in carefully selected males with clearly delayed puberty. Brief treatment with conservative doses may occasionally be justified in these patients if they do not respond to psychological support.^{1,3,4}

Testosterone enanthate injection has a compendial use for gender dysphoria in transgender male (female-to-male) patients.⁷⁻¹⁰

Transgender persons seeking to develop the physical characteristics of the desired gender require a safe, effective hormone regimen that will suppress endogenous hormone secretion determined by the person's genetic/biologic sex and maintain sex hormone levels within the normal range for the person's desired gender. The two major goals of hormonal therapy are to reduce endogenous hormone levels and, thereby, the secondary sex characteristics of the individual's biological/genetic sex and to replace endogenous sex hormone levels with those of the reassigned sex. The Endocrine Society suggests that pubertal development of the desired opposite sex be initiated at about the age of 16 years, using a gradually increasing dose schedule of cross-sex steroids. However, the Endocrine Society Guidelines also state that identifying an age at which pubertal development is initiated can be difficult and may depend on several factors (such as the age when pubertal suppression was begun, medications used to initiate pubertal suppression, and relative risks of prolonged pubertal suppression), and the goal is to start the process at a time when the individual will be able to make informed, mature decisions to engage in the therapy. Some patients may advance to Tanner stage 2 of pubertal development at an early age (such as 9 or 10) and using pubertal suppression therapy for 6 or 7 years may be deemed inappropriate. Medical professionals involved in the patient's care should be involved in assessing whether the patient is ready to make the decision to begin hormone therapy and pubertal development.⁷ Therefore, individuals who are able to make an informed decision to engage in hormone therapy will be approved.

For transgender male persons, regimens to change secondary sex characteristics follow the general principle of hormone replacement treatment of male hypogonadism. Either parenteral or transdermal preparations can be used to achieve testosterone values in the normal male range (320-1000 ng/dL).⁷ The agent primarily used for endocrine treatment of transgender male patients is testosterone. When determining the appropriate method of testosterone delivery, many considerations should be taken into account. The most well-described formulation of testosterone therapy used to treat transgender male patients is intramuscular injection of testosterone esters (cypionate or enanthate).⁸ Because intramuscular testosterone cypionate or enanthate is often administered every 2-4 weeks, some patients may notice a cyclic variation in effects as well as more time outside the normal physiologic levels.⁹ Due to this cyclic variation, other preparations such as weekly subcutaneous testosterone enanthate injection may be considered.

REFERENCES

1. Delatestryl [package insert]. Malvern, PA: Endo Pharmaceuticals Solutions Inc.; October 2016.

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10. American Psychiatric Association. The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V). 2013. Available at <http://dsm.psychiatryonline.org/book.aspx?bookid=556>.

Written by: UM Development (JH)

Date: 05/2016

Revised: (CF/JH) 11/2016, 02/2017; (KC) 02/2018, 10/2018 (added Xyosted), 02/2019 (no clinical changes), 06/2019 (updated questions)

Reviewed: CDPR/Medical Affairs: (ME) 05/2016, 11/2016, 02/2017; (AN) 02/2018; (ME) 10/2018, 07/2019

External Review: 06/2016, 06/2017, 06/2018, 12/2018, 06/2019

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for primary or hypogonadotropic hypogonadism? [Note: Safety and efficacy of testosterone products in patients with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.] [If no, then skip to question 5.]	Yes	No
2	Is this request for a continuation of testosterone therapy? [If no, then skip to question 4.]	Yes	No
3	Before the patient started testosterone therapy, did the patient have a confirmed low testosterone level according to current practice guidelines or your standard lab reference values? [No further questions.]	Yes	No
4	Does the patient have at least two confirmed low testosterone levels according to current practice guidelines or your standard lab reference values? [No further questions.]	Yes	No
5	Is the requested drug being prescribed for gender dysphoria in a patient who is able to make an informed decision to engage in hormone therapy? [If yes, then no further questions.]	Yes	No

6	Is testosterone enanthate injection (generic Delatestryl) being prescribed for delayed puberty? [If yes, then no further questions.]	Yes	No
7	Is testosterone enanthate injection (generic Delatestryl) being prescribed for inoperable metastatic breast cancer in a patient who is 1 to 5 years postmenopausal AND has the patient had an incomplete response to other therapy for metastatic breast cancer? [If yes, then no further questions.]	Yes	No
8	Is testosterone enanthate injection (generic Delatestryl) being prescribed for a premenopausal patient with breast cancer who has benefited from oophorectomy and is considered to have a hormone-responsive tumor?	Yes	No

Mapping Instructions			
	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Go to 5	
2.	Go to 3	Go to 4	
3.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have had a test that showed low testosterone levels before you started testosterone therapy. Your request has been denied based on the information we have. [Short Description: No confirmation of diagnosis (tests, labs, etc.)]
4.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have had two tests that showed low testosterone levels. Your request has been denied based on the information we have. [Short Description: No confirmation of diagnosis (tests, labs, etc.)]
5.	Approve, 12 months	Go to 6	
6.	Approve, 12 months	Go to 7	
7.	Approve, 12 months	Go to 8	
8.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet one of these conditions: <ul style="list-style-type: none"> - You have primary or hypogonadotropic hypogonadism - You have gender dysphoria and you can make an informed decision to use this drug - Testosterone enanthate injection (generic Delatestryl) is being prescribed for delayed puberty - For testosterone enanthate injection (generic Delatestryl), you are a postmenopausal patient with metastatic breast cancer, surgery is not possible, and other drugs for your cancer did not work for you - For testosterone enanthate injection (generic Delatestryl), you are a premenopausal patient with breast cancer, have a hormone-responsive tumor, and had your ovaries removed Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	TESTOSTERONE PRODUCTS – TOPICAL/BUCCAL/NASAL
BRAND NAME* (generic)	<p>ANDRODERM (testosterone transdermal patch)</p> <p>ANDROGEL (testosterone topical gel)</p> <p>AXIRON (testosterone topical solution)</p> <p>FORTESTA (testosterone topical gel)</p> <p>NATESTO (testosterone nasal gel)</p> <p>STRIANT (testosterone mucoadhesive buccal system)</p> <p>TESTIM (testosterone topical gel)</p> <p>VOGELXO (testosterone topical gel)</p>
<p>Status: CVS Caremark Criteria Type: Initial Prior Authorization</p>	
<p>MDC-2 Ref # 229-A</p>	

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Topical, buccal, and nasal testosterone products are indicated for replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone.

Primary hypogonadism (congenital or acquired) - testicular failure due to conditions such as cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy, Klinefelter Syndrome, chemotherapy, or toxic damage from alcohol or heavy metals. These men usually have low serum testosterone concentrations and gonadotropins (FSH, LH) above the normal range.

Hypogonadotropic hypogonadism (congenital or acquired) - gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation. These men have low testosterone serum concentrations but have gonadotropins in the normal or low range.

Limitations of Use

Testosterone - Topical, Buccal, Nasal Non-TGC MDC-2 229-A 10-2018.doc

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Safety and efficacy of topical, buccal, and nasal testosterone products in men with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.

Safety and efficacy of topical, buccal, and nasal testosterone products in males less than 18 years old have not been established.

Topical testosterone products may have different doses, strengths or application instructions that may result in different systemic exposure.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for primary or hypogonadotropic hypogonadism [Note: Safety and efficacy of testosterone products in patients with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.]
AND
 - Before the start of testosterone therapy, the patient has at least two confirmed low testosterone levels according to current practice guidelines or your standard lab reference values **OR**
 - For continuation of testosterone therapy: before the patient started testosterone therapy, the patient had a confirmed low testosterone level according to current practice guidelines or your standard lab reference values

RATIONALE

These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Topical, buccal, and nasal testosterone products are indicated for replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone: congenital or acquired primary hypogonadism (testicular failure due to conditions such as cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy, Klinefelter Syndrome, chemotherapy, or toxic damage from alcohol or heavy metals), congenital or acquired hypogonadotropic hypogonadism (gonadotropin or luteinizing hormone-releasing hormone [LHRH] deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation). Safety and efficacy of topical, buccal, and nasal testosterone products in men with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.¹⁻¹¹

A testosterone determination, in conjunction with a free testosterone or sex hormone-binding globulin level, is the threshold test in the evaluation of suspected male hypogonadism (serum total testosterone levels less than 300 ng/dL). Testosterone levels should be determined in the morning, and studies should be repeated in patients with subnormal levels. The normative ranges for total and free testosterone levels in healthy young men vary among laboratories and assays. In some laboratories, the lower limit of the normal range for total testosterone level in healthy young men is 280-300 ng/dL and for serum free testosterone level is 5–9 pg/mL. The clinicians should use the lower limit of normal range for healthy young men established in their laboratory.^{12,13} For initial therapy, testosterone will be approved for patients with at least two confirmed low testosterone levels according to current practice guidelines or standard lab reference values. If the patient is already on testosterone therapy and did not get a repeat testosterone level before starting therapy, it would be inappropriate for the patient to stop treatment to get a repeat testosterone level. For continuation of therapy, one low testosterone level is required before the patient started testosterone therapy.

REFERENCES

1. Androderm [package insert]. Madison, NJ: Allergan USA, Inc.; June 2018.
2. Androgel 1.62% [package insert]. North Chicago, IL: Abbvie Inc; November 2017.
3. Androgel 1% [package insert]. North Chicago, IL: Abbvie Inc; November 2017.
4. Axiron [package insert]. Indianapolis, IN: Lilly USA, LLC; July 2018.

5. Fortesta [package insert]. Malvern, PA: Endo Pharmaceuticals Inc.; July 2017.
6. Striant [package insert]. Malvern, PA: Endo Pharmaceuticals.; October 2016.
7. Testim [package insert]. Malvern, PA: Endo Pharmaceuticals; April 2018.
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Written by: UM Development (AH)
Date: 07/2003

Revised: (NB) 01/2005, (MG) 02/2006; (NB) 02/2007(2); (AM) 01/2008, 12/2008; (MS) 11/2009, 12/2010, (TM) 11/2011; (PL) 10/2012 (created MDC-2 due to extended commercial duration), 11/2012; (CS) 08/2013; (PL) 11/2013; (SE) 04/2014 (rephrased diagnosis question); (RP) 06/2014 (Add Natesto), (PL) 06/2014 (Add Vogelxo); (CF/JH) 11/2014, 02/2015 (updated testosterone level question), (LN) 04/2015 (added denial reasons); (CF/JH) 11/2015, (SE) 06/2016 (created separate Med D); (CF/JH) 11/2016; (KC) 11/2017, 10/2018 (no clinical changes), 08/2019 (removed "male" from lab questions)

Reviewed: CDPR/Medical Affairs (MM): 01/2005, 02/2006; (WF): 02/2007, 01/2008, 12/2008, 11/2009; (KP) 11/2010, 11/2011, 03/2012, 10/2012; (DNC) 11/2012; (LCB) 11/2013; (SES) 11/2014; (KRU) 02/2015; (LCB) 11/2015; (MC) 12/2016; (DNC) 02/2017; (ME) 11/2017; (EPA) 08/2019
External Review: 08/2005, 04/2006, 06/2007, 04/2008, 04/2009, 02/2010, 02/2011, 03/2012, 02/2013, 08/2013, 02/2014, 06/2014, 02/2015, 02/2016, 02/2017, 02/2018, 02/2019, 10/2019 (FYI)

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for primary or hypogonadotropic hypogonadism? [Note: Safety and efficacy of testosterone products in patients with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established.]	Yes	No
2	Is this request for a continuation of testosterone therapy? [If no, then skip to question 4.]	Yes	No
3	Before the patient started testosterone therapy, did the patient have a confirmed low testosterone level according to current practice guidelines or your standard lab reference values? [No further questions.]	Yes	No
4	Does the patient have at least two confirmed low testosterone levels according to current practice guidelines or your standard lab reference values?	Yes	No

Guidelines for Approval

Duration of Approval		12 Months	
Set 1		Set 2	
Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)
1	None	1	2
2		4	

3			
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Mapping Instructions			
	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have primary or hypogonadotropic hypogonadism. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
2.	Go to 3	Go to 4	
3.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have had a test that showed low testosterone levels before you started testosterone therapy. Your request has been denied based on the information we have. [Short Description: No confirmation of diagnosis (tests, labs, etc.)]
4.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have had two tests that showed low testosterone levels. Your request has been denied based on the information we have. [Short Description: No confirmation of diagnosis (tests, labs, etc.)]

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	TESTOSTERONE PRODUCTS – TOPICAL/BUCCAL/NASAL
BRAND NAME* (generic)	<p>ANDRODERM (testosterone transdermal patch)</p> <p>ANDROGEL (testosterone topical gel)</p> <p>AXIRON (testosterone topical solution)</p> <p>FORTESTA (testosterone topical gel)</p> <p>NATESTO (testosterone nasal gel)</p> <p>STRIANT (testosterone mucoadhesive buccal system)</p> <p>TESTIM (testosterone topical gel)</p> <p>VOGELXO (testosterone topical gel)</p>
<p>Status: CVS Caremark Criteria Type: Initial Prior Authorization</p>	
Ref # 1370-A	

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Topical, buccal, and nasal testosterone products are indicated for replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone.

Primary hypogonadism (congenital or acquired) - testicular failure due to conditions such as cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy, Klinefelter Syndrome, chemotherapy, or toxic damage from alcohol or heavy metals. These men usually have low serum testosterone concentrations and gonadotropins (FSH, LH) above the normal range.

Hypogonadotropic hypogonadism (congenital or acquired) - gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation. These men have low testosterone serum concentrations but have gonadotropins in the normal or low range.

Limitations of Use

Safety and efficacy of topical, buccal, and nasal testosterone products in men with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.

Safety and efficacy of topical, buccal, and nasal testosterone products in males less than 18 years old have not been established.

Topical testosterone products may have different doses, strengths or application instructions that may result in different systemic exposure.

Compendial Uses

Gender Dysphoria in transgender male patients^{11,14-17}

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for primary or hypogonadotropic hypogonadism [Note: Safety and efficacy of testosterone products in patients with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.]
AND
 - Before the start of testosterone therapy, the patient has at least two confirmed low testosterone levels according to current practice guidelines or your standard lab reference values **OR**
 - For continuation of testosterone therapy: before the patient started testosterone therapy, the patient had a confirmed low testosterone level according to current practice guidelines or your standard lab reference values
- OR**
 - The requested drug is being prescribed for gender dysphoria in a patient who is able to make an informed decision to engage in hormone therapy

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Topical, buccal, and nasal testosterone products are indicated for replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone: congenital or acquired primary hypogonadism (testicular failure due to conditions such as cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy, Klinefelter Syndrome, chemotherapy, or toxic damage from alcohol or heavy metals), congenital or acquired hypogonadotropic hypogonadism (gonadotropin or luteinizing hormone-releasing hormone [LHRH] deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation). Safety and efficacy of topical, buccal, and nasal testosterone products in men with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.¹⁻¹¹

A testosterone determination, in conjunction with a free testosterone or sex hormone-binding globulin level, is the threshold test in the evaluation of suspected male hypogonadism (serum total testosterone levels less than 300 ng/dL [nanograms per deciliter]). Testosterone levels should be determined in the morning, and studies should be repeated in patients with subnormal levels. The normative ranges for total and free testosterone levels in healthy young men vary among laboratories and assays. In some laboratories, the lower limit of the normal range for total testosterone level in healthy young men is 280-300 ng/dL and for serum free testosterone level is 5–9 pg/mL (picograms per milliliter). Clinicians should use the lower limit of normal range for healthy young men established in their laboratory.^{12,13} For initial therapy, testosterone will be approved for patients with at least two confirmed low testosterone levels according to current practice guidelines or standard lab reference values. If the patient is already on testosterone therapy and did not get a repeat testosterone level before starting therapy, it would be inappropriate for the patient to stop treatment to get a repeat testosterone level. For continuation of therapy, one low testosterone level is required before the patient started testosterone therapy.

Topical, buccal, and nasal testosterone products have a compendial use for gender dysphoria in transgender male (female-to-male) patients.¹⁴⁻¹⁷

Transgender persons seeking to develop the physical characteristics of the desired gender require a safe, effective hormone regimen that will suppress endogenous hormone secretion determined by the person's genetic/biologic sex and maintain sex hormone levels within the normal range for the person's desired gender. The two major goals of hormonal therapy are to reduce endogenous hormone levels and, thereby, the secondary sex characteristics of the individual's biological/genetic sex and to replace endogenous sex hormone levels with those of the reassigned sex. The Endocrine Society suggests that pubertal development of the desired opposite sex be initiated at about the age of 16 years, using a gradually increasing dose schedule of cross-sex steroids. However, the Endocrine Society Guidelines also state that identifying an age at which pubertal development is initiated can be difficult and may depend on several factors (such as the age when pubertal suppression was begun, medications used to initiate pubertal suppression, and relative risks of prolonged pubertal suppression), and the goal is to start the process at a time when the individual will be able to make informed, mature decisions to engage in the therapy. Some patients may advance to Tanner stage 2 of pubertal development at an early age (such as 9 or 10) and using pubertal suppression therapy for 6 or 7 years may be deemed inappropriate. Medical professionals involved in the patient's care should be involved in assessing whether the patient is ready to make the decision to begin hormone therapy and pubertal development.¹⁴ Therefore, individuals who are able to make an informed decision to engage in hormone therapy will be approved.

For transgender male (female-to-male) persons, regimens to change secondary sex characteristics follow the general principle of hormone replacement treatment of male hypogonadism. Either parenteral or transdermal preparations can be used to achieve testosterone values in the normal male range (320-1000 ng/dL).¹⁴ The agent primarily used for endocrine treatment of transgender male patients is testosterone. When determining the appropriate method of testosterone delivery, many considerations should be taken into account. The most well-described formulation of testosterone therapy used to treat transgender male patients is intramuscular injection of testosterone esters (cypionate or enanthate).¹⁵ Because intramuscular testosterone cypionate or enanthate is often administered every 2-4 weeks, some patients may notice a cyclic variation in effects as well as more time outside the normal physiologic levels.¹⁶ Transdermal testosterone has been shown to provide less variation in serum testosterone levels compared with injectable preparations. Testosterone administered transdermally more closely mimics physiologic testosterone levels. However, transdermal preparations achieve low-normal ranges of testosterone levels in hypogonadal men, which may translate to a lessened change in physical appearance and virilization in the transgender male patient.¹⁵

REFERENCES

1. Androderm [package insert]. Madison, NJ: Allergan USA, Inc.; June 2018.
2. Androgel 1% [package insert]. North Chicago, IL: Abbvie Inc; December 2018.
3. Androgel 1.62% [package insert]. North Chicago, IL: Abbvie Inc; December 2018.
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17. American Psychiatric Association. The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V). 2013. Available at <http://dsm.psychiatryonline.org/book.aspx?bookid=556>.

Written by: UM Development (JH)
 Date: 05/2016
 Revised: (CF/JH) 02/2017; (KC) 02/2018, 02/2019 (no clinical changes), 06/2019 (updated questions)
 Reviewed: CDPR/Medical Affairs: (ME) 05/2016, 02/2017; (AN) 02/2018; (ME) 07/2019
 External Review: 06/2016, 06/2017, 06/2018, 06/2019

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for primary or hypogonadotropic hypogonadism? [Note: Safety and efficacy of testosterone products in patients with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.] [If no, then skip to question 5.]	Yes	No
2	Is this request for a continuation of testosterone therapy? [If no, then skip to question 4.]	Yes	No
3	Before the patient started testosterone therapy, did the patient have a confirmed low testosterone level according to current practice guidelines or your standard lab reference values? [No further questions.]	Yes	No
4	Does the patient have at least two confirmed low testosterone levels according to current practice guidelines or your standard lab reference values? [No further questions.]	Yes	No
5	Is the requested drug being prescribed for gender dysphoria in a patient who is able to make an informed decision to engage in hormone therapy?	Yes	No

Mapping Instructions

	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Go to 5	
2.	Go to 3	Go to 4	
3.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have had a test that showed low testosterone levels before you started testosterone therapy. Your request has been denied based on the information we have. [Short Description: no confirmation of diagnosis (tests, labs, etc.)]
4.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have had two tests that showed low testosterone levels. Your request has been denied based on the information we have. [Short Description: no confirmation of diagnosis (tests, labs, etc.)]
5.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet one of these conditions: - You have primary or hypogonadotropic hypogonadism - You have gender dysphoria and you can make an informed decision to use this drug

			Your request has been denied based on the information we have. [Short Description: no approvable diagnosis]
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SPECIALTY GUIDELINE MANAGEMENT

XENAZINE (tetrabenazine) tetrabenazine (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Treatment of chorea associated with Huntington's disease

B. Compendial Uses

1. Tic disorders
2. Tardive dyskinesia
3. Hemiballismus
4. Chorea not associated with Huntington's disease

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Documentation of score of items 1 to 7 of the Abnormal Involuntary Movement Scale (AIMS) for tardive dyskinesia

III. CRITERIA FOR INITIAL APPROVAL

A. **Chorea associated with Huntington's disease**

Authorization of 6 months may be granted for treatment of chorea associated with Huntington's disease when both of the following criteria are met:

1. Member demonstrates characteristic motor examination features
2. Member meets one of the following conditions:
 - i. Laboratory results indicate an expanded *HTT* CAG repeat sequence of at least 36
 - ii. Member has a positive family history for Huntington's disease

B. **Chorea not associated with Huntington's disease**

Authorization of 6 months may be granted for treatment of chorea not associated with Huntington's disease.

C. **Tic disorders**

Authorization of 6 months may be granted for treatment of tic disorders.

D. Tardive dyskinesia

Authorization of 6 months may be granted for the treatment of tardive dyskinesia when the baseline AIMS score for items 1 to 7 is obtained.

E. Hemiballismus

Authorization of 6 months may be granted for the treatment of hemiballismus.

IV. CONTINUATION OF THERAPY**A. Tardive dyskinesia**

Authorization of 12 months may be granted for treatment of tardive dyskinesia when the member's tardive dyskinesia symptoms have improved as indicated by a decreased AIMS score (items 1 to 7) from baseline.

B. Other indications

Authorization of 12 months may be granted for treatment of all other indications listed in Section III when the member has experienced improvement or stabilization.

V. REFERENCES

1. Xenazine [package insert]. Deerfield, IL: Lundbeck Inc.; September 2018.
2. Micromedex® (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. Available at: <http://www.micromedexsolutions.com>. Accessed August 06, 2019.
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5. Armstrong MJ, Miyasaki JM. Evidence-based guideline: pharmacologic treatment of chorea in Huntington disease: Report of the Guideline Development Subcommittee of the American Academy of Neurology. *Neurology*. 2012; 79(6):597-603.
6. Kenney C, Hunter C, Jankovic J. Long-term tolerability of tetrabenazine in the treatment of hyperkinetic movement disorders. *Movement Disorders*. 2007; 22(2): 193-7.
7. Tetrabenazine [package insert]. Baltimore, MD: Lupin Pharmaceuticals Inc.; April 2018.

SPECIALTY GUIDELINE MANAGEMENT

THALOMID (thalidomide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Thalomid in combination with dexamethasone is indicated for the treatment of patients with newly diagnosed multiple myeloma.
2. Erythema Nodosum Leprosum (ENL)
 - a. Acute treatment of the cutaneous manifestations of moderate to severe ENL
 - b. Maintenance therapy for prevention and suppression of the cutaneous manifestations of ENL recurrence

Limitations of Use: not indicated as monotherapy for ENL treatment in the presence of moderate to severe neuritis

B. Compendial Uses

1. Myelofibrosis-related anemia
2. Multicentric Castleman's disease
3. Recurrent aphthous stomatitis
4. Recurrent HIV-associated aphthous ulcers
5. Cachexia in patients with cancer or HIV-associated wasting syndrome
6. Diarrhea in patients with HIV infection
7. AIDS-Related Kaposi's sarcoma
8. Behcet's syndrome
9. Chronic graft-versus-host disease
10. Crohn's disease

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Multiple Myeloma**

Authorization of 12 months may be granted for treatment of multiple myeloma.

B. **Recurrent HIV-associated Aphthous Ulcers**

Authorization of 12 months may be granted for treatment of recurrent HIV-associated aphthous ulcers.

C. **Behcet's Syndrome**

Authorization of 12 months may be granted for treatment of Behcet's syndrome.

D. **Myelofibrosis-related Anemia**

Authorization of 12 months may be granted for treatment of myelofibrosis-related anemia when all of the following criteria are met:

1. The requested medication will be given as a single agent or in combination with prednisone
2. The member has serum erythropoietin levels of either of the following:
 - a. 500 mU/mL or greater
 - b. Less than 500 mU/mL and no response or loss of response to erythropoietic stimulating agents

E. Erythema Nodosum Leprosum

Authorization of 12 months may be granted for treatment of erythema nodosum leprosum.

F. Crohn's Disease

Authorization of 12 months may be granted for treatment of Crohn's disease.

G. AIDS-Related Kaposi's Sarcoma

Authorization of 12 months may be granted for treatment of AIDS-related Kaposi's sarcoma in combination with antiretroviral therapy.

H. Chronic Graft-versus-Host Disease

Authorization of 12 months may be granted for treatment of chronic graft-versus-host disease.

I. Multicentric Castleman's Disease

Authorization of 12 months may be granted for treatment of relapsed, refractory or progressive multicentric Castleman's disease.

J. Recurrent Aphthous Stomatitis

Authorization of 12 months may be granted for treatment of recurrent aphthous stomatitis.

K. Cachexia

Authorization of 12 months may be granted for treatment of cachexia caused by cancer or HIV-infection.

L. HIV-associated Diarrhea

Authorization of 12 months may be granted for treatment of HIV-associated diarrhea.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Thalomid [package insert]. Summit, NJ: Celgene Corporation; December 2017.
2. American Society of Health System Pharmacists. AHFS Drug Information. (Adult and Pediatric) Bethesda, MD. Electronic version, 2018. Available with subscription. URL: <http://online.lexi.com/lco>. Accessed March 25, 2019.
3. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 25, 2019.
4. DRUGDEX® System (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. Available at: <http://www.micromedexsolutions.com> (cited: 10/4/2018).
5. The NCCN Clinical Practice Guidelines in Oncology® Multiple Myeloma (Version 1.2018). © 2018 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed October 4, 2018.
6. The NCCN Clinical Practice Guidelines in Oncology® B-cell Lymphomas (Version 5.2018) © 2018 National Comprehensive Cancer Network, Inc. Available at: www.nccn.org. Accessed October 4, 2018.

SPECIALTY GUIDELINE MANAGEMENT

TIBSOVO (ivosidenib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. **Newly-Diagnosed Acute Myeloid Leukemia**
Tibsovo is indicated for the treatment of newly-diagnosed acute myeloid leukemia (AML) with a susceptible isocitrate dehydrogenase-1 (IDH1) mutation as detected by an FDA-approved test in adult patients who are ≥ 75 years old or who have comorbidities that preclude use of intensive induction chemotherapy.
2. **Relapsed or Refractory Acute Myeloid Leukemia**
Tibsovo is indicated for the treatment of adult patients with relapsed or refractory acute myeloid leukemia (AML) with a susceptible isocitrate dehydrogenase-1 (IDH1) mutation as detected by an FDA-approved test.

B. Compendial Uses

As a single agent in patients 60 years of age or older with IDH1-mutated AML in the following settings:

1. Treatment induction when not a candidate for intensive remission induction therapy or declines intensive therapy OR
2. Post-remission therapy following response to previous lower intensity therapy with the same regimen

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review (new starts only): medical record documentation of isocitrate dehydrogenase-1 (IDH1) mutation as detected by an FDA-approved test

III. CRITERIA FOR INITIAL APPROVAL

Acute Myeloid Leukemia (AML)

- A. Authorization of 12 months may be granted for treatment of newly diagnosed AML with a susceptible IDH1 mutation as a single-agent when any of the following criteria is met:
 1. Member is 75 years of age or older
 2. Member has comorbidities that preclude the use of intensive induction chemotherapy
 3. Member is 60 years of age or older and declines intensive induction chemotherapy

- B. Authorization of 12 months may be granted for post-remission therapy for AML with a susceptible IDH1 mutation when all of the following criteria is met:
1. The requested medication will be used as a single-agent
 2. Member is 60 years of age or older
 3. Member has experienced response to previous lower intensive therapy with the same requested regimen
- C. Authorization of 12 months may be granted for treatment of relapsed or refractory AML with a susceptible IDH1 mutation.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced an unacceptable toxicity.

V. REFERENCE

1. Tibsovo [package insert]. Cambridge, MA: Agios Pharmaceuticals, Inc; May 2019.
2. The NCCN Drugs & Biologics Compendium 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed July 11, 2019.

SPECIALTY GUIDELINE MANAGEMENT

tobramycin inhalation solution/TOBI TOBI Podhaler (tobramycin inhalation powder) Bethkis (tobramycin inhalation solution) Kitabis Pak (tobramycin inhalation solution)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Management of cystic fibrosis in patients with *Pseudomonas aeruginosa*

B. Compendial Uses

Pseudomonas aeruginosa lower respiratory tract infection in patients with non-cystic fibrosis bronchiectasis

All other indications are considered experimental/investigational and are not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Cystic Fibrosis**

Authorization of 12 months may be granted for members with cystic fibrosis when *Pseudomonas aeruginosa* is present in airway cultures OR the member has a history of *Pseudomonas aeruginosa* infection or colonization in the airways.

B. **Bronchiectasis (Non-Cystic Fibrosis)**

Authorization of 12 months may be granted for members with non-cystic fibrosis bronchiectasis when *Pseudomonas aeruginosa* is present in airway cultures OR the member has a history of *Pseudomonas aeruginosa* infection or colonization in the airways.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

IV. REFERENCES

1. Tobramycin inhalation solution [package insert]. Sellersville, PA: Teva Pharmaceuticals USA; January 2019.
2. TOBI [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; October 2015.
3. TOBI Podhaler [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; October 2015.
4. Bethkis [package insert]. Woodstock, IL: Chiesi USA, Inc.; July 2017.
5. Kitabis Pak [package insert]. Midlothian, VA: PARI Respiratory Equipment, Inc.; May 2016.

Reference number(s)
1887-A

6. Micromedex® (electronic version). IBM Watson Health, Greenwood Village, Colorado. Available at <https://www.micromedexsolutions.com> Accessed December 24, 2018.
7. Mogayzel PJ, Naureckas ET, Robinson KA, et al. Cystic fibrosis pulmonary guidelines. Chronic medications for maintenance of lung health. *Am J Respir Crit Care Med*. 2013;187:680-689.
8. Rosen, MJ. Chronic cough due to bronchiectasis: ACCP Evidence-Based Clinical Practice Guidelines. *Chest*. 2006;129:122S-131S.
9. Caremark Clinical Programs Review: Focus on Pulmonology; January 2008.

SPECIALTY GUIDELINE MANAGEMENT

tobramycin inhalation solution/TOBI TOBI Podhaler (tobramycin inhalation powder) Bethkis (tobramycin inhalation solution) Kitabis Pak (tobramycin inhalation solution)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Management of cystic fibrosis in patients with *Pseudomonas aeruginosa*

B. Compendial Uses

Pseudomonas aeruginosa lower respiratory tract infection in patients with non-cystic fibrosis bronchiectasis

All other indications are considered experimental/investigational and are not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Cystic Fibrosis**

Authorization of 12 months may be granted for members with cystic fibrosis when *Pseudomonas aeruginosa* is present in airway cultures OR the member has a history of *Pseudomonas aeruginosa* infection or colonization in the airways.

B. **Bronchiectasis (Non-Cystic Fibrosis)**

Authorization of 12 months may be granted for members with non-cystic fibrosis bronchiectasis when *Pseudomonas aeruginosa* is present in airway cultures OR the member has a history of *Pseudomonas aeruginosa* infection or colonization in the airways.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

IV. REFERENCES

1. Tobramycin inhalation solution [package insert]. Sellersville, PA: Teva Pharmaceuticals USA; January 2019.
2. TOBI [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; October 2015.
3. TOBI Podhaler [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; October 2015.
4. Bethkis [package insert]. Woodstock, IL: Chiesi USA, Inc.; July 2017.
5. Kitabis Pak [package insert]. Midlothian, VA: PARI Respiratory Equipment, Inc.; May 2016.

Reference number(s)
1887-A

6. Micromedex® (electronic version). IBM Watson Health, Greenwood Village, Colorado. Available at <https://www.micromedexsolutions.com> Accessed December 24, 2018.
7. Mogayzel PJ, Naureckas ET, Robinson KA, et al. Cystic fibrosis pulmonary guidelines. Chronic medications for maintenance of lung health. *Am J Respir Crit Care Med*. 2013;187:680-689.
8. Rosen, MJ. Chronic cough due to bronchiectasis: ACCP Evidence-Based Clinical Practice Guidelines. *Chest*. 2006;129:122S-131S.

Reference number
2081-A

SPECIALTY GUIDELINE MANAGEMENT

TORISEL (temsirolimus)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Advanced renal cell carcinoma

B. Compendial Uses

1. Relapsed or surgically unresectable stage IV kidney cancer
2. Endometrial carcinoma
3. Soft tissue sarcoma subtypes:
 - a. Perivascular epithelioid cell tumors (PEComa)
 - b. Recurrent angiomyolipoma
 - c. Lymphangioleiomyomatosis

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Renal Cell Carcinoma (RCC)**

Authorization of 12 months may be granted for treatment of relapsed, metastatic, or unresectable RCC.

B. **Endometrial Carcinoma**

Authorization of 12 months may be granted for single-agent treatment of endometrial carcinoma.

C. **Soft Tissue Sarcoma**

Authorization of 12 months may be granted for treatment of soft tissue sarcoma with any of the following subtypes: perivascular epithelioid cell tumor (PEComa), recurrent angiomyolipoma, or lymphangioleiomyomatosis.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy for an indication outlined in Section II when there is no evidence of unacceptable toxicity or disease progression on the current regimen.

IV. REFERENCES

1. Torisel [package insert]. Philadelphia, PA: Wyeth Pharmaceuticals Inc.; March 2018.

Reference number
2081-A

2. The NCCN Drugs & Biologics Compendium® © 2018 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed May 24, 2019.
3. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Kidney Cancer. Version 4.2019. Accessed May 24, 2019. https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf.
4. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Uterine Neoplasms. Version 3.2019. Accessed May 24, 2019. https://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf.
5. Oza AM, Elit L, Tsao MS, et al. Phase II study of temsirolimus in women with recurrent or metastatic endometrial cancer: a trial of the NCIC Clinical Trials Group. *J Clin Oncol*. 2011;29(24):3278-85.
6. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Soft Tissue Sarcoma. Version 2.2019. Accessed May 24, 2019. https://www.nccn.org/professionals/physician_gls/pdf/sarcoma.pdf.
7. Benson C, Vitfell-Rasmussen J, Maruzzo M, et al. A retrospective study of patients with malignant PEComa receiving treatment with sirolimus or temsirolimus: the Royal Marsden Hospital experience. *Anticancer Res* 2014;34:3663-8.

SPECIALTY GUIDELINE MANAGEMENT

TREANDA (bendamustine) BENDEKA (bendamustine) BELRAPZO (bendamustine)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Chronic lymphocytic leukemia (CLL)
2. Indolent B-cell non-Hodgkin lymphoma (NHL) that has progressed during or within six months of treatment with rituximab or a rituximab-containing regimen

B. Compendial Uses

1. Classical Hodgkin lymphoma (CHL)
2. Multiple myeloma (MM)
3. Non-Hodgkin lymphoma (NHL)
 - i. Adult T-cell leukemia/lymphoma (ATLL)
 - ii. Acquired immune deficiency syndrome (AIDS)-related B-cell lymphoma
 - iii. CLL/small lymphocytic lymphoma (SLL)
 - iv. Diffuse large B-cell lymphoma (DLBCL)
 - v. Histologic transformation of marginal zone lymphoma to diffuse large B-cell lymphoma
 - vi. Histologic transformation of follicular lymphoma to diffuse large B-cell lymphoma
 - vii. High grade B-cell lymphoma
 - viii. Follicular lymphoma
 - ix. Marginal zone lymphoma
 - a. Nodal marginal zone lymphoma
 - b. Gastric mucosa associated lymphoid tissue (MALT) lymphoma
 - c. Nongastric MALT lymphoma
 - d. Splenic marginal zone lymphoma
 - x. Mantle cell lymphoma (MCL)
 - xi. Mycosis fungoides (MF)/Sezary syndrome (SS)
 - xii. Peripheral T-cell lymphoma (PTCL)
 - xiii. Primary cutaneous B-cell lymphoma
 - xiv. Primary cutaneous CD30+ T-cell lymphoproliferative disorder: cutaneous anaplastic large cell lymphoma (ALCL)
 - xv. Post-transplant lymphoproliferative disorders
 - xvi. Hepatosplenic Gamma-Delta T-Cell lymphoma
4. Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma
5. Small cell lung cancer

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Non-Hodgkin lymphoma (NHL)

Authorization of 12 months may be granted for treatment of NHL with any of the following subtypes:

1. Follicular lymphoma
2. Chronic lymphocytic leukemia/small lymphocytic leukemia (CLL/SLL) without chromosome 17p deletion or TP53 mutation
3. High-grade B-cell lymphoma when both of following are met:
 - a. The requested agent is used as second-line or subsequent therapy, and
 - b. The patient is not a candidate for transplant.
4. Diffuse large B-cell lymphoma (DLBCL) when the both of the following are met:
 - a. The requested agent is used as second-line or subsequent therapy, and
 - b. The patient is not a candidate for transplant.
5. Histologic transformation of marginal zone lymphoma to diffuse large B-cell lymphoma when the patient has received at least two chemoimmunotherapy regimens.
6. Histologic transformation of follicular lymphoma to diffuse large B-cell lymphoma when the patient has received at least two chemoimmunotherapy regimens.
7. Adult T-cell leukemia/lymphoma (ATLL) when both of the following are met:
 - a. The requested agent is used as a single agent, and
 - b. The requested agent is used as second-line or subsequent therapy.
8. AIDS-related B-cell lymphoma when both of the following are met:
 - a. The requested agent is used as second-line or subsequent therapy, and
 - b. The patient is not a candidate for transplant.
9. Marginal zone lymphoma
 - a. Nodal marginal zone lymphoma when used in combination with rituximab or obinutuzumab.
 - b. Gastric MALT lymphoma when used in combination with rituximab or obinutuzumab.
 - c. Nongastric MALT lymphoma when used in combination with rituximab or obinutuzumab.
 - d. Splenic marginal zone lymphoma when used in combination with rituximab or obinutuzumab.
10. Mantle cell lymphoma (MCL) when either of the following are met:
 - a. The requested agent is used as a single agent, or
 - b. The requested agent is used in combination with rituximab.
11. Mycosis fungoides (MF)/Sezary syndrome (SS)
12. Peripheral T-cell lymphoma (PTCL) when both of the following are met:
 - a. The requested agent is used as a single agent, and
 - b. The requested agent is used as second-line or subsequent therapy.
13. Primary cutaneous B-cell lymphoma when both of the following are met:
 - a. The requested agent is used as second-line or subsequent therapy.
 - b. The patient is not a candidate for transplant.
14. Cutaneous anaplastic large cell lymphoma (ALCL) when both of the following are met:
 - a. The requested agent is used as a single agent, and
 - b. The requested agent is used for relapsed or refractory disease.
15. Post-transplant lymphoproliferative disorders when used as second-line or subsequent therapy.
16. Hepatosplenic gamma-delta T-Cell lymphoma when both of the following are met:
 - a. The requested agent is used as a single agent, and
 - b. The requested agent is used for refractory disease.

B. Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma

Authorization of 12 months may be granted for treatment of Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma when either of the following are met

1. The requested agent will be used in combination with rituximab, or

Reference number(s)
1705-A

2. The requested agent will be used as a single agent.

C. Multiple myeloma (MM)

Authorization of 12 months may be granted for treatment of MM when both of the following criteria are met:

1. The disease is relapsed or progressive, and
2. The requested agent will be used in any of the following regimens:
 - a. In combination with lenalidomide and dexamethasone, or
 - b. In combination with bortezomib and dexamethasone, or
 - c. As a single agent.

D. Classical Hodgkin lymphoma (CHL)

Authorization of 12 months may be granted for treatment of CHL when both of the following criteria are met:

1. The requested agent will be used as second line, subsequent therapy, or palliative therapy, and
2. The requested agent will be used in any of the following regimens:
 - a. In combination with brentuximab vedotin, or
 - b. In combination with gemcitabine and vinorelbine, or
 - c. As a single agent.

E. Small cell lung cancer (SCLC)

Authorization of 12 months may be granted for treatment of SCLC when both of the following criteria are met:

1. The requested agent is being used for subsequent therapy, and
2. The requested agent will be used as a single agent.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced disease progression or an unacceptable toxicity.

IV. REFERENCES

1. Treanda [package insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; December 2017.
2. Bendeka [package insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; September 2017.
3. Belrapzo [package insert]. Woodcliff, NJ; Eagle Pharmaceuticals, Inc; December 2018.
4. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed April 28, 2019.

SPECIALTY GUIDELINE MANAGEMENT

TRELSTAR (triptorelin pamoate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Palliative treatment of advanced prostate cancer

B. Compendial Uses

1. Prostate cancer
2. Gender dysphoria (also known as gender non-conforming or transgender persons)

NOTE: Some plans may opt-out of coverage for gender dysphoria.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Prostate cancer**

Authorization of 12 months may be granted for treatment of prostate cancer.

B. **Gender dysphoria**

1. Authorization of 12 months may be granted for pubertal suppression in preparation for gender reassignment in an adolescent member when all of the following criteria are met:
 - a. The member has a diagnosis of gender dysphoria.
 - b. The member has reached Tanner stage 2 of puberty.
2. Authorization of 12 months may be granted for gender reassignment in an adult member when all of the following criteria are met:
 - a. The member has a diagnosis of gender dysphoria.
 - b. The member will receive Trelstar concomitantly with cross sex hormones.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Trelstar [package insert]. Parsippany, NJ: Watson Pharma; January 2018.
2. The NCCN Drugs & Biologics Compendium® © 2018 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed October 11, 2018.

Reference number(s)
1968-A, 2085-A

3. National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology: prostate cancer. Version 4.2018. http://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed October 11, 2018.
4. Hembree WC, Cohen-Kettenis PT, Gooren L, et al. Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*. 2017;102(11):3869–3903.
5. Gender Identity Research and Education Society. Guidance for GPs and other clinicians on the treatment of gender variant people. UK Department of Health. Published March 10, 2008.
6. Standards of care for the health of transsexual, transgender, and gender-nonconforming people, 7th version. ©2012 World Professional Association for Transgender Health. Available at <http://www.wpath.org>.

Reference number
2156-A

SPECIALTY GUIDELINE MANAGEMENT

TREMFYA (guselkumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Treatment of adult patients with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Moderate to severe plaque psoriasis

- A. Authorization of 12 months may be granted for members who have previously received Otezla or a biologic indicated for the treatment of moderate to severe plaque psoriasis.
- B. Authorization of 12 months may be granted for treatment of moderate to severe plaque psoriasis for members when all of the following criteria are met:
 1. At least 3% of body surface area (BSA) is affected OR crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
 2. Member meets any of the following criteria:
 - a. Member has had an inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) or pharmacologic treatment with methotrexate, cyclosporine or acitretin.
 - b. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine and acitretin (see Appendix).
 - c. Member has severe psoriasis that warrants a biologic DMARD as first-line therapy (i.e. at least 10% of the body surface area (BSA) or crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected).

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who are using Tremfya for an indication outlined in section II and who achieve or maintain positive clinical response with Tremfya as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

For all indications: Member has had a documented negative TB test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons

who are naïve to biologic DMARDs or targeted synthetic DMARDs (e.g., Xeljanz), and repeated yearly for members with risk factors** for TB that are continuing therapy with biologics.

* If the screening testing for TB is positive, there must be documentation of further testing to confirm there is no active disease. Do not administer guselkumab to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of guselkumab.

** Risk factors for TB include: Persons with close contact to people with infectious TB disease; persons who have recently immigrated from areas of the world with high rates of TB (e.g., Africa, Asia, Eastern Europe, Latin America, Russia); children less than 5 years of age who have a positive TB test; groups with high rates of TB transmission (e.g., homeless persons, injection drug users, persons with HIV infection); persons who work or reside with people who are at an increased risk for active TB (e.g., hospitals, long-term care facilities, correctional facilities, homeless shelters).

For all indications: Member cannot use Tremfya concomitantly with any other biologic DMARD or targeted synthetic DMARD.

V. APPENDIX

Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine or Acitretin

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Cannot be used due to risk of treatment-related toxicity
4. Drug interaction
5. Pregnancy or planning pregnancy
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

VI. REFERENCES

1. Tremfya [package insert]. Horsham, PA: Janssen Biotech, Inc.; October 2017.
2. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 4: Guidelines of care for the management and treatment of psoriasis with traditional systemic agents. *J Am Acad Dermatol*. 2009;61:451-485.
3. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 6: Guidelines of care for the treatment of psoriasis and psoriatic arthritis: case-based presentations and evidence-based conclusions. *J Am Acad Dermatol*. 2011;65(1):137-174.
4. Reich K, Armstrong, AW, Foley P, et al. Efficacy and safety of guselkumab, an anti-interleukin-23 monoclonal antibody, compared with adalimumab for the treatment of patients with moderate to severe psoriasis with randomized withdrawal and retreatment: Results from the phase III, double-blind, placebo- and active comparator-controlled VOYAGE 2 trial. *Am J Clin Dermatol*. 2017;76(3):418-431.
5. Blauvelt A, Papp KA, Griffiths, CEM, et al. Efficacy and safety of guselkumab, an anti-interleukin-23 monoclonal antibody, compared with adalimumab for the continuous treatment of patients with moderate to severe psoriasis: Results from the phase III, double-blinded, placebo- and active comparator-controlled VOYAGE 1 trial. *Am J Clin Dermatol*. 2017;76(3):405-417.
6. Menter A, Strober BE, Kaplan DH, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. *J Am Acad Dermatol*. 2019;80(4):1029-1072.
7. Tuberculosis (TB). TB risk factors. Centers for Disease Control and Prevention. Retrieved on 21 June 2019 from: <https://www.cdc.gov/tb/topic/basics/risk.htm>.

SPECIALTY GUIDELINE MANAGEMENT

Remodulin injection (treprostinil injection) treprostinil injection (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

1. Pulmonary Arterial Hypertension

Remodulin is indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to diminish symptoms associated with exercise.

2. Pulmonary Arterial Hypertension in Patients Requiring Transition from Epoprostenol

In patients with PAH requiring transition from epoprostenol, Remodulin is indicated to diminish the rate of clinical deterioration. Consider the risks and benefits of each drug prior to transition.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Indefinite authorization may be granted for treatment of PAH when ALL of the following criteria are met:

- A. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
- B. PAH was confirmed by either criterion (1) or criterion (2) below:
 1. Pretreatment right heart catheterization with all of the following results:
 - i. mPAP \geq 25 mmHg
 - ii. PCWP \leq 15 mmHg
 - iii. PVR $>$ 3 Wood units
 2. For infants less than one year of age with any of the following conditions, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed:
 - i. Post cardiac surgery
 - ii. Chronic heart disease
 - iii. Chronic lung disease associated with prematurity
 - iv. Congenital diaphragmatic hernia

III. CONTINUATION OF THERAPY

Indefinite authorization may be granted for members with an indication listed in Section II who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

IV. APPENDIX

WHO Classification of Pulmonary Hypertension

1 PAH

- 1.1 Idiopathic (PAH)
- 1.2 Heritable PAH
- 1.3 Drug- and toxin-induced PAH
- 1.4. PAH associated with:
 - 1.4.1 Connective tissue diseases
 - 1.4.2 HIV infection
 - 1.4.3 Portal hypertension
 - 1.4.4 Congenital heart diseases
 - 1.4.5 Schistosomiasis
- 1.5 PAH long-term responders to calcium channel blockers
- 1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement
- 1.7 Persistent PH of the newborn syndrome

2 PH due to left heart disease

- 2.1 PH due to heart failure with preserved LVEF
- 2.2 PH due to heart failure with reduced LVEF
- 2.3 Valvular heart disease
- 2.4 Congenital/acquired cardiovascular conditions leading to post-capillary PH

3 PH due to lung diseases and/or hypoxia

- 3.1 Obstructive lung disease
- 3.2 Restrictive lung disease
- 3.3 Other lung disease with mixed restrictive/obstructive pattern
- 3.4 Hypoxia without lung disease
- 3.5 Developmental lung disorders

4 PH due to pulmonary artery obstruction

- 4.1 Chronic thromboembolic PH
- 4.2 Other pulmonary artery obstructions
 - 4.2.1 Sarcoma (high or intermediate grade) or angiosarcoma
 - 4.2.2 Other malignant tumors
 - Renal carcinoma
 - Uterine carcinoma
 - Germ cell tumours of the testis
 - Other tumours
 - 4.2.3 Non-malignant tumours
 - Uterine leiomyoma
 - 4.2.4 Arteritis without connective tissue disease
 - 4.2.5 Congenital pulmonary artery stenosis
 - 4.2.6 Parasites
 - Hydatidosis

5 PH with unclear and/or multifactorial mechanisms

- 5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders
- 5.2 Systemic and metabolic disorders: Pulmonary Langerhans cell histiocytosis, Gaucher disease, glycogen storage disease, neurofibromatosis, sarcoidosis
- 5.3 Others: chronic renal failure with or without hemodialysis, fibrosing mediastinitis
- 5.4 Complex congenital heart disease

V. REFERENCES

Reference number(s)
1644-A

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PRIOR AUTHORIZATION CRITERIA

DRUG CLASS*	RETINOIDS (ALL TOPICAL)
BRAND NAME (generic)	
	ALTRENO (tretinoin)
	ATRALIN (tretinoin)
	AVITA (tretinoin)
	RETIN-A (tretinoin)
	RETIN-A MICRO (tretinoin)
	TRETIN-X (tretinoin)
	VELTIN (clindamycin/tretinoin)
	ZIANA (clindamycin/tretinoin)
Status: CVS Caremark Criteria Type: Initial Prior Authorization	
Ref # 237-A Ref # 355-A	

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Atralin, Avita, Retin-A, Retin-A Micro, Tretin-X are indicated for topical application in the treatment of acne vulgaris. The safety and efficacy of these products in the treatment of other disorders have not been established.
Veltin and Ziana are indicated for the topical treatment of acne vulgaris in patients 12 years or older.
Altreno (tretinoin) lotion, 0.05% is indicated for the topical treatment of acne vulgaris in patients 9 years of age and older.

Compendial Use

Keratosis follicularis (Darier's disease, Darier-White disease) ^{12, 15, 16}

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has the diagnosis of acne vulgaris or keratosis follicularis (Darier's disease, Darier-White disease)

Tretinoins (Topical) 355-A, 237-A 06-2019.doc

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RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Tretinoin is indicated for the topical treatment of acne vulgaris. The safety and efficacy of these products in the treatment of other disorders have not been established. The criteria do not provide for cosmetic uses of these drugs.

The American Academy of Dermatology guidelines state that the topical therapy of acne vulgaris includes the usage of agents that are available over the counter or via prescription. Therapy choice may be influenced by age of the patient, site of involvement, extent and severity of disease, and patient preference. Topical therapies may be used as monotherapy, in combination with other topical agents or in combination with oral agents in both initial control and maintenance. Topical retinoids are important in addressing the development and maintenance of acne and are recommended as monotherapy in primarily comedonal acne, or in combination with topical or oral antimicrobials in patients with mixed or primarily inflammatory acne lesions. Commonly used topical acne therapies include benzoyl peroxide, salicylic acid, antibiotics, combination antibiotics with benzoyl peroxide, retinoids, retinoid with benzoyl peroxide, retinoid with antibiotic, azelaic acid, and sulfone agents.¹⁴

Topical tretinoin has been used for the treatment of keratosis follicularis.¹² Moisturizers with urea or lactic acid can help reduce scaling and thickening of the lesions, low to medium potency topical steroids are sometimes useful for reducing inflammation, and when bacterial growth is suspected, application of antiseptics can be helpful. Topical retinoids also may reduce hyperkeratosis within three months.^{15, 16}

Renova and Refissa are indicated as adjunctive agents for use in the mitigation of fine facial wrinkles in patients who use comprehensive skin care and sunlight avoidance programs.⁵⁻⁶ Since the treatment of these indications is considered cosmetic, these two tretinoin products are not included in the criteria.

REFERENCES

1. Altreno [package insert]. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; April 2019.
2. Atralin [package insert]. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; July 2016.
3. Avita Cream [package insert]. Morgantown, WV: Mylan Pharmaceuticals Inc; January 2018.
4. Avita Gel [package insert]. Morgantown, WV: Mylan Pharmaceuticals Inc.; November 2013.
5. Refissa [package insert]. Irvine, CA: ZO Skin Health, Inc.; June 2018.
6. Renova [package insert]. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; March 2017.
7. Retin-A [package insert]. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; June 2018.
8. Retin-A Micro [package insert]. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; October 2017.
9. Tretin-X [package insert]. Cumberland, RI: Onset Dermatologics, LLC; May 2013.
10. Veltin [package insert]. Exton, PA: Aqua Pharmaceuticals; March 2014.
11. Ziana [package insert]. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; March 2017.
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15. Darier disease. Office of Rare Disease Research. <https://rarediseases.info.nih.gov/gard/6243/darier-disease/resources/8>. Accessed June 2019.
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Written by: UM Development (GP)

Date Written: 08/1997

Revised: (LS) 12/1998; (MG) 12/2002, 12/2003; (TM) 11/2004; (NB) 09/2005, 05/2006 (Added Tretin-X), 09/2006; (CT) 11/2006 (Added Ziana); (AM) 08/2007; (MS) 08/2008; (AM) 09/2008; (SE) 09/2009; (CY) 08/2010; (MS) 08/2011, 08/2012, 10/2012 (extended duration), 06/2013, 06/2014; (RP) 06/2015, (SF) 06/2016 (no clinical changes); (RP) 06/2017 (no clinical changes), 06/2018 (no

clinical changes), 08/2018 (Added Altreno), 06/2019 (separated diagnoses questions; combined 237-A [removed MDC designation and applied compendial use to 237-A])

Reviewed:

CRC: 01/2004; Medical Affairs (MM) 10/2004, 09/2005, 11/2006; (WF) 08/2007, 08/2008, 09/2008, 09/2009; (KP) 09/2010, 08/2011, 08/2012; (LS) 06/2013; (DC) 06/2014, 06/2015, 09/2018, 06/2019

External Review: 02/2004, 12/2004, 12/2005, 12/2006, 02/2008, 04/2009, 12/2009, 02/2011, 02/2012, 12/2012, 10/2013, 10/2014, 10/2015, 10/2016, 10/2017, 10/2018, 10/2019

CRITERIA FOR APPROVAL

- | | | | |
|----|---|-----|----|
| 1. | Does the patient have the diagnosis of acne vulgaris?
[If yes, then no further questions.] | Yes | No |
| 2. | Does the patient have the diagnosis of keratosis follicularis (Darier's disease, Darier-White disease)? | Yes | No |

Mapping Instructions (355-A)

	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Approve, 36 Months	Go to 2	
2.	Approve, 36 Months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have any of these conditions: - Acne vulgaris - Keratosis follicularis (Darier's disease, Darier-White disease) Your request has been denied based on the information we have. [Short Description: No approvable diagnosis.]

Guidelines for Approval (237-A)

Duration of Approval 12 Months

Set 1		Set 2	
Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)
1	None	2	1

Mapping Instructions (237-A)

	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Approve, 12 Months	Go to 2	
2.	Approve, 12 Months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have any of these conditions: - Acne vulgaris - Keratosis follicularis (Darier's disease, Darier-White disease) Your request has been denied based on the information we have. [Short Description: No approvable diagnosis.]

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS*	RETINOIDS (ALL TOPICAL)
BRAND NAME (generic)	ALTRENO (tretinoin) ATRALIN (tretinoin) AVITA (tretinoin) RETIN-A (tretinoin) RETIN-A MICRO (tretinoin) TRETIN-X (tretinoin) VELTIN (clindamycin/tretinoin) ZIANA (clindamycin/tretinoin)
Status: CVS Caremark Criteria Type: Initial Prior Authorization	
MMT Ref # 904-A	

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Atralin, Avita, Retin-A, Retin-A Micro, Tretin-X are indicated for topical application in the treatment of acne vulgaris. The safety and efficacy of these products in the treatment of other disorders have not been established.
Veltin and Ziana are indicated for the topical treatment of acne vulgaris in patients 12 years or older.
Altreno (tretinoin) lotion, 0.05% is indicated for the topical treatment of acne vulgaris in patients 9 years of age and older.

Compendial Use

Keratosis follicularis (Darier's disease, Darier-White disease) ^{12, 15, 16}

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has the diagnosis of keratosis follicularis (Darier's disease, Darier-White disease)

Tretinoins (Topical) MMT 904-A 06-2019.doc

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OR

- The patient has the diagnosis of acne vulgaris AND experienced an inadequate treatment response, an intolerance, or contraindication to benzoyl peroxide

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Tretinoin is indicated for the topical treatment of acne vulgaris. The safety and efficacy of these products in the treatment of other disorders have not been established. The criteria do not provide for cosmetic uses of these drugs.

Benzoyl peroxide is a bactericidal agent that has proven effective in the treatment of acne vulgaris and is the most widely studied OTC medication. It is safe and may be used as a monotherapy or in combination with other topical medications for mild acne, and is part of the regimens of care applied to acne of all severities and types. Its use may also minimize the development of antibiotic-resistant *Propionibacterium acnes* when used in combination with systemic or topical antibiotics.¹² The American Academy of Dermatology guidelines state that the topical therapy of acne vulgaris includes the usage of agents that are available over the counter or via prescription. Therapy choice may be influenced by age of the patient, site of involvement, extent and severity of disease, and patient preference. Topical therapies may be used as monotherapy, in combination with other topical agents or in combination with oral agents in both initial control and maintenance. Commonly used topical acne therapies include benzoyl peroxide, salicylic acid, antibiotics, combination antibiotics with benzoyl peroxide, retinoids, retinoid with benzoyl peroxide, retinoid with antibiotic, azelaic acid, and sulfone agents.¹⁴

Topical tretinoin has been used for the treatment of keratosis follicularis.¹² Moisturizers with urea or lactic acid can help reduce scaling and thickening of the lesions, low to medium potency topical steroids are sometimes useful for reducing inflammation, and when bacterial growth is suspected, application of antiseptics can be helpful. Topical retinoids also may reduce hyperkeratosis within three months.^{15, 16}

Renova and Refissa are indicated as adjunctive agents for use in the mitigation of fine facial wrinkles in patients who use comprehensive skin care and sunlight avoidance programs.⁵⁻⁶ Since the treatment of these indications is considered cosmetic, these two tretinoin products are not included in the criteria.

REFERENCES

1. Altreno [package insert]. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; April 2019.
2. Atralin [package insert]. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; July 2016.
3. Avita Cream [package insert]. Morgantown, WV: Mylan Pharmaceuticals Inc; January 2018.
4. Avita Gel [package insert]. Morgantown, WV: Mylan Pharmaceuticals Inc.; November 2013.
5. Refissa [package insert]. Irvine, CA: ZO Skin Health, Inc.; June 2018.
6. Renova [package insert]. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; March 2017.
7. Retin-A [package insert]. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; June 2018.
8. Retin-A Micro [package insert]. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; October 2017.
9. Tretin-X [package insert]. Cumberland, RI: Onset Dermatologics, LLC; May 2013.
10. Veltin [package insert]. Exton, PA: Aqua Pharmaceuticals; March 2014.
11. Ziana [package insert]. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; March 2017.
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15. Darier disease. Office of Rare Disease Research. <https://rarediseases.info.nih.gov/gard/6243/darier-disease/resources/8>. Accessed June 2019.
16. Keratosis Follicularis National Organization for Rare Disorders. <https://rarediseases.org/rare-diseases/keratosis-follicularis/>. Accessed June 2019.

Written by: UM Development (GP)
Date Written: 08/1997
Revised: (LS) 12/1998; (MG) 12/2002, 12/2003; (TM) 11/2004; (NB) 09/2005, 05/2006 (Added Tretin-X), 09/2006; (CT) 11/2006 (Added Ziana); (AM) 08/2007; (MS) 08/2008; (AM) 09/2008; (SE) 09/2009; (CY) 08/2010; (MS) 08/2011, 10/2012 (extended duration); (JK) 12/2012 (shortened duration); (MS) 06/2013; (JK) 03/2014 (renamed with MMT); (MS) 06/2014, 10/2014, (LN) 04/2015 (added denial reasons); (RP) 06/2015, (SF) 06/2016 (no clinical changes); (RP) 06/2017 (no clinical changes), 06/2018 (no clinical changes; re-ordered questions), 08/2018 (Added Altreno), 06/2019 (no clinical changes)
Reviewed: CRC: 01/2004; Medical Affairs (MM) 10/2004, 09/2005, 11/2006; (WF) 08/2007, 08/2008, 09/2008, 09/2009; (KP) 09/2010, 08/2011, 10/2012; (LS) 06/2013; (DC) 06/2014; (LS) 10/2014; (DNC) 06/2015, 09/2018
External Review: 02/2004, 12/2004, 12/2005, 12/2006, 02/2008, 04/2009, 12/2009, 02/2011, 02/2012, 10/2013, 10/2014, 10/2015 10/2016, 10/2017, 10/2018, 10/2019

CRITERIA FOR APPROVAL

- | | | | |
|---|---|-----|----|
| 1 | Does the patient have the diagnosis of acne vulgaris?
[If no, then skip to question 3.] | Yes | No |
| 2 | Has the patient experienced an inadequate treatment response, an intolerance, or contraindication to benzoyl peroxide?
[No further questions.] | Yes | No |
| 3 | Does the patient have the diagnosis of keratosis follicularis (Darier's disease, Darier-White disease)? | Yes | No |

Mapping Instructions

	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Go to 3	
2.	Approve, 12 Months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have tried benzoyl peroxide and it did not work for you, or you cannot use it. Your request has been denied based on the information we have. [Short Description: No inadequate treatment response, an intolerance, or contraindication to benzoyl peroxide.]
3.	Approve, 12 Months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have any of these conditions: - Acne vulgaris - Keratosis follicularis (Darier's disease, Darier-White disease) Your request has been denied based on the information we have. [Short Description: No approvable diagnosis.]

Reference number(s)
2985-A

SPECIALTY GUIDELINE MANAGEMENT

TRETEN (coagulation Factor XIII A-Subunit [recombinant])

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Treten is indicated in patients with congenital factor XIII A-subunit deficiency for routine prophylaxis for bleeding.

Treten is not for use in patients with congenital factor XIII B-subunit deficiency

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Congenital Factor XIII A-Subunit Deficiency

Indefinite authorization may be granted for prophylactic treatment of congenital factor XIII A-subunit deficiency.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Tretten [package insert]. Plainsboro, NJ: Novo Nordisk Inc.; November 2016.
2. National Hemophilia Foundation. MASAC recommendations concerning products licensed for the treatment of hemophilia and other bleeding disorders. Revised April 2018. MASAC Document # 253. Accessed December 3, 2019.

SPECIALTY GUIDELINE MANAGEMENT

TRIKAFTA (elexacaftor/tezacaftor/ivacaftor)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Trikafta is indicated for the treatment of patients with cystic fibrosis (CF) aged 12 years and older who have at least one F508del mutation in the CFTR gene. If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to confirm the presence of at least one F508del mutation.

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review: genetic testing report confirming the presence of the appropriate *CFTR* gene mutation.

III. CRITERIA FOR INITIAL APPROVAL

Cystic Fibrosis ^[1]

Authorization of 12 months may be granted for treatment of cystic fibrosis when all of the following criteria are met:

- A. Genetic testing was conducted to detect a mutation in the CFTR gene.
- B. The member is positive for at least one F508del mutation in the CFTR gene.
- C. The member is at least 12 years of age.
- D. Trikafta will not be used in combination with other ivacaftor containing medications.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who are experiencing benefit from therapy as evidenced by disease stability or disease improvement (e.g., improvement in FEV1 from baseline).

V. REFERENCES

1. Trikafta [package insert]. Boston, MA: Vertex Pharmaceuticals Inc; October 2019.

SPECIALTY GUIDELINE MANAGEMENT

TRIKAFTA (elexacaftor/tezacaftor/ivacaftor)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Trikafta is indicated for the treatment of cystic fibrosis (CF) in patients aged 12 years and older who have at least one *F508del* mutation in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene.

If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to confirm the presence of at least one *F508del* mutation.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: genetic testing report confirming the presence of the appropriate *CFTR* gene mutation.

III. CRITERIA FOR INITIAL APPROVAL

Cystic Fibrosis

Authorization of 12 months may be granted for treatment of cystic fibrosis when all of the following criteria are met:

- A. Genetic testing was conducted to detect a mutation in the *CFTR* gene.
- B. The member is positive for at least one *F508del* mutation in the *CFTR* gene.
- C. The member is at least 12 years of age.
- D. Trikafta will not be used in combination with other medications containing ivacaftor.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who are experiencing benefit from therapy as evidenced by disease stability or disease improvement (e.g., improvement in FEV1 from baseline).

V. REFERENCES

1. Trikafta [package insert]. Boston, MA: Vertex Pharmaceuticals Inc; October 2019.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME (generic)	TRIKAFTA (elexacaftor/tezacaftor/ivacaftor)
Status: CVS Caremark Criteria Type: Initial Prior Authorization	MDC Ref # 3375-A

FDA-APPROVED INDICATIONS

Trikafta is a combination of ivacaftor, a CFTR potentiator, tezacaftor, and elexacaftor indicated for the treatment of cystic fibrosis (CF) in patients aged 12 years and older who have at least one F508del mutation in the CFTR gene. If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to confirm the presence of at least one F508del mutation.

CRITERIA FOR APPROVAL

1	Does the patient have a diagnosis of cystic fibrosis? [If no, no further questions.]	Yes	No
2	Was genetic testing performed to detect a mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene? [If no, no further questions.]	Yes	No
3	Is the patient positive for at least one F508del mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene? [If no, no further questions.]	Yes	No
4	Will the requested drug be used in combination with any other medications containing ivacaftor? [If yes, no further questions.]	Yes	No
5	Is the patient 12 years of age or older?	Yes	No

Guidelines for Approval	
Duration of Approval	12 months
Set 1: Cystic Fibrosis	
Yes to question(s)	No to question(s)
1	4
2	
3	
5	

Mapping Instructions		
	Yes	No
1.	Go to 2	Deny
2.	Go to 3	Deny
3.	Go to 4	Deny
4.	Deny	Go to 5
5.	Approve 12 months	Deny

RATIONALE

These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to ensure that patients follow selection elements noted in labeling and/or practice guidelines in order to decrease the potential for inappropriate utilization.

REFERENCES

1. Trikafta [package insert]. Boston, MA: Vertex Pharmaceuticals; October 2019.

DOCUMENT HISTORY

Created: Specialty Clinical Development (ST) 10/2019
Revised:
Reviewed: 10/2019
External Review: 11/2019

SPECIALTY GUIDELINE MANAGEMENT

TRIPTODUR (triptorelin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Triptodur is indicated for the treatment of pediatric patients 2 years of age and older with central precocious puberty (CPP).

B. Compendial Use

1. Gender dysphoria (also known as gender non-conforming or transgender persons)
NOTE: Some plans may opt-out of coverage for gender dysphoria.
2. Preservation of ovarian function
3. Prevention of recurrent menstrual related attacks in acute porphyria

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Central precocious puberty (CPP)**

1. Authorization up to age 12 may be granted for the treatment of CPP in a female member when all of the following criteria are met:
 - a. Intracranial tumor has been evaluated by appropriate lab tests and diagnostic imaging, such as computed tomography (CT scan), magnetic resonance imaging (MRI), or ultrasound.
 - b. The diagnosis of CPP has been confirmed by a pubertal response to a gonadotropin releasing hormone (GnRH) agonist test or a pubertal level of a third generation luteinizing hormone (LH) assay.
 - c. The assessment of bone age versus chronological age supports the diagnosis of CPP.
 - d. The member was less than 8 years of age at the onset of secondary sexual characteristics.
2. Authorization up to age 13 may be granted for the treatment of CPP in a male member when all of the following criteria are met:
 - a. Intracranial tumor has been evaluated by appropriate lab tests and diagnostic imaging, such as CT scan, MRI, or ultrasound.
 - b. The diagnosis of CPP has been confirmed by a pubertal response to a GnRH agonist test or a pubertal level of a third generation LH assay.
 - c. The assessment of bone age versus chronological age supports the diagnosis of CPP.
 - d. The member was less than 9 years of age at the onset of secondary sexual characteristics.

B. **Gender dysphoria**

1. Authorization of 12 months may be granted for pubertal suppression in preparation for gender reassignment in an adolescent member when all of the following criteria are met:
 - a. The member has a diagnosis of gender dysphoria.
 - b. The member has reached Tanner stage 2 of puberty.

2. Authorization of 12 months may be granted for gender reassignment in an adult member when all of the following criteria are met:
 - a. The member has a diagnosis of gender dysphoria.
 - b. The member will receive Triptodur concomitantly with cross sex hormones.

C. Preservation of ovarian function

Authorization of 3 months may be granted for preservation of ovarian function when the member is premenopausal and undergoing chemotherapy.

D. Prevention of recurrent menstrual related attacks in acute porphyria

Authorization of 12 months may be granted for prevention of recurrent menstrual related attacks in members with acute porphyria when the requested medication is prescribed by or in consultation with a physician experienced in the management of porphyrias.

III. CONTINUATION OF THERAPY

A. Central precocious puberty (CPP)

1. Authorization up to age 12 may be granted for continuation of therapy for CPP in a female member if the member is currently less than 12 years of age.
2. Authorization up to age 13 may be granted for continuation of therapy for CPP in a male member if the member is currently less than 13 years of age.

B. Gender Dysphoria

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

C. All other indications

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

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13. Bangalor Krishna K, Fuqua JS, Rogol AD, et al. Use of gonadotropin-releasing hormone analogs in children: Update by an international consortium. *Horm Res Paediatr*. 2019 Jul 18:1-16. doi: 10.1159/000501336. [Epub ahead of print]

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS BRAND NAME* (generic)	GLUCAGON-LIKE PEPTIDE 1 (GLP-1) RECEPTOR AGONIST
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TRULICITY
(dulaglutide)

Status: CVS Caremark Criteria

Type: Initial Prior Authorization with Quantity Limit

Ref # 1193-C

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Trulicity is indicated:

- as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
- to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus who have established cardiovascular disease or multiple cardiovascular risk factors.

Limitations of Use

- Trulicity has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.
- Trulicity should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis. Trulicity is not a substitute for insulin.
- Trulicity has not been studied in patients with severe gastrointestinal disease, including severe gastroparesis. The use of Trulicity is not recommended in patients with pre-existing severe gastrointestinal disease.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has been receiving GLP-1 Agonist therapy for at least 3 months
AND
 - The patient has demonstrated a reduction in A1c (hemoglobin A1c) since starting GLP-1 Agonist therapy [Note: Examples of GLP-1 Agonists are Adlyxin, Bydureon, Byetta, Ozempic, Tanzeum, Trulicity, Victoza]**OR**
 - The patient has established cardiovascular disease or multiple cardiovascular risk factors

OR

- The patient has a diagnosis of type 2 diabetes mellitus
AND
 - The patient has experienced an inadequate treatment response, intolerance or contraindication to metformin**OR**
 - The patient requires combination therapy AND has an A1c (hemoglobin A1c) of 7.5 percent or greater**OR**
 - The patient has established cardiovascular disease or multiple cardiovascular risk factors

Quantity Limits apply.

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Trulicity is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Trulicity is also indicated to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus who have established cardiovascular disease or multiple cardiovascular risk factors. Trulicity can be administered once every seven days. The dose can be administered at any time of day, with or without meals.¹⁻³

Clinical guidelines from the American Diabetes Association and the American Association of Clinical Endocrinologists and American College of Endocrinology for the management of hyperglycemia in type 2 diabetes indicate that metformin monotherapy should be started at diagnosis of type 2 diabetes unless there are contraindications. Metformin is effective and safe, is inexpensive, and may reduce risk of cardiovascular events and death. In patients with contraindications or intolerance of metformin, initial therapy should be based on patient factors; consider a drug from another class.⁴⁻⁵

The clinical guidelines also state that the A1c test is the major tool for assessing glycemic control and has strong predictive value for diabetes complications. Thus, A1c testing should be performed routinely in all patients with diabetes at initial assessment and as part of continuing care. The guidelines set goals for therapeutic effectiveness which must be evaluated frequently (e.g., every 3 months) until stable, using multiple criteria, including A1c. Less frequent monitoring is acceptable once targets are achieved.⁴⁻⁵ Therefore, continued use of any GLP-1 Agonist (e.g., Adlyxin, Byetta, Bydureon, Ozempic, Tanzeum, Trulicity, and Victoza) will be approved for patients who have demonstrated a reduction in A1c since starting GLP-1 Agonist therapy for at least three months.

If the A1c target is not achieved after approximately 3 months and patient does not have atherosclerotic cardiovascular disease (ASCVD) or chronic kidney disease (CKD), consider a combination of metformin and one of the preferred six treatment options: sulfonylurea, thiazolidinedione, dipeptidyl peptidase 4 (DPP-4) inhibitors, sodium-glucose cotransporter 2 (SGLT2) inhibitors, glucagon-like peptide 1 (GLP-1) receptor agonists, or basal insulin; the choice of which agent to add is based on drug-specific effects and patient factors. For patients in whom ASCVD, Heart Failure, or CKD predominates, the best choice for a second agent is a GLP-1 receptor agonist or SGLT2 inhibitor with demonstrated cardiovascular risk reduction, after consideration of drug-specific and patient factors.⁴⁻⁵

The REWIND trial compared the risk of Major Adverse Cardiovascular Events (MACE) outcome (which included CV death, non-fatal myocardial infarction (MI), and non-fatal stroke) between Trulicity 1.5 mg and placebo, both added to standard of care. During the trial, investigators were to modify antidiabetic and cardiovascular medications to achieve local standard of care treatment targets with respect to blood glucose, lipids, and blood pressure, and manage patients recovering from an acute coronary syndrome or stroke event per local treatment guidelines.¹ Therefore, Trulicity (dulaglutide) will be approved for initial therapy and continuation of therapy for patients have established cardiovascular disease or multiple cardiovascular risk factors.

In patients with an initial A1c of 7.5% or greater, or in patients who are unable to achieve their glycemic goals with monotherapy, combination therapy is recommended.⁴⁻⁵

The recommended dosage of Trulicity is 0.75 mg once weekly. The dosage may be increased to 1.5 mg once weekly for additional glycemic control. The maximum recommended dose is 1.5 mg once weekly. Trulicity is available in a 0.75 mg/0.5mL single-dose pen or prefilled syringe and a 1.5 mg/0.5mL single-dose pen or prefilled syringe.¹⁻³ A quantity limit is in place to aid proper utilization of Trulicity. At maximum approved dosing for Trulicity, four (4) pens or syringes will be allowed for a 28 day supply (12 pens or syringes per 84 day supply).

REFERENCES

1. Trulicity [package insert]. Indianapolis, IN: Eli Lilly and Company; February 2020.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed July 2019.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed July 2019.
4. American Diabetes Association (ADA) Standards of Medical Care in Diabetes-2019—*Diabetes Care*. 2019; 42(Supplement 1).

5. Garber AJ, et al. AACE/ACE Consensus Statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the Comprehensive Type 2 Diabetes Management Algorithm 2019, Endocr Pract. 2019; 25 (No 1); 69-100.

Written by: UM Development (PL)
 Date Written: 09/2014
 Revised: (JH) 07/2015, (SF) 07/2016, 07/2017, 07/2018 (no clinical changes), 07/2019 (no clinical changes), (SF) 03/2020 (added CVD/ CV risk factor indication)
 Reviewed: Medical Affairs: (SES) 09/2014, (DNC) 07/2015; (MES) 07/2016, 07/2017, (CHART) 08/01/2019, 03/12/2020
 External Review: 10/2014, 10/2015, 10/2016, 10/2017, 10/2018, 10/2019, (FYI) 04/2020

CRITERIA FOR APPROVAL

- | | | | |
|---|--|-----|----|
| 1 | Has the patient been receiving GLP-1 Agonist therapy for at least 3 months?
[Note: Examples of GLP-1 Agonists are Adlyxin, Bydureon, Byetta, Ozempic, Tanzeum, Trulicity, Victoza]
[If no, then skip to question 3.] | Yes | No |
| 2 | Has the patient demonstrated a reduction in A1c (hemoglobin A1c) since starting GLP-1 Agonist therapy?
[If yes, then skip to question 7.]
[If no, then skip to question 6.] | Yes | No |
| 3 | Does the patient have a diagnosis of type 2 diabetes mellitus? | Yes | No |
| 4 | Has the patient experienced an inadequate treatment response, intolerance or contraindication to metformin?
[If yes, then skip to question 7.] | Yes | No |
| 5 | Does the patient require combination therapy AND have an A1c (hemoglobin A1c) of 7.5 percent or greater?
[If yes, then skip to question 7.] | Yes | No |
| 6 | Does the patient have established cardiovascular disease or multiple cardiovascular risk factors? | Yes | No |
| 7 | Does the patient require more than 4 pens per 28 days (or 12 pens per 84 days)?
[RPh Note: If yes, then deny and enter a partial approval for 4 pens (2 mL) /21 days (12 pens (6 mL)/63 days).] | Yes | No |

Mapping Instructions

DENIAL REASONS – DO NOT USE FOR MEDICARE PART D

	Yes	No	
1.	Go to 2	Go to 3	
2.	Go to 7	Go to 6	
3.	Go to 4	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have type 2 diabetes mellitus. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
4.	Go to 7	Go to 5	
5.	Go to 7	Go to 6	

6.	Go to 7	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you meet any of these conditions:</p> <ul style="list-style-type: none"> -You have been taking the requested drug for at least 3 months and you had a reduction in A1c (hemoglobin A1c) since starting this therapy - You have tried metformin and it did not work for you, or you cannot use it - You require combination therapy and you have an A1c (hemoglobin A1c) of 7.5 percent or greater - You have established cardiovascular (heart) disease or multiple cardiovascular risk factors <p>Your request has been denied based on the information we have. [Short description: No inadequate treatment response, intolerance or contraindication to metformin, No requirement for combination therapy or No established cardiovascular disease or multiple cardiovascular risk factors]</p>
7.	Deny	<p>Approve, 36 Months, 4 pens (2 mL) /21 days* (12 pens (6 mL) /63 days*)</p>	<p>You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 4 pens per month (or 12 pens per 3 months) of the requested drug and strength. You have been approved for the maximum quantity that your plan covers for a duration of 36 months. Your request for additional quantities of the requested drug and strength has been denied. [Short description: Over max quantity]</p>

**The duration of 21 days is used for a 28-day fill period and 63 days is used for an 84-day fill period to allow time for refill processing.*

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	GLUCAGON-LIKE PEPTIDE 1 (GLP-1) RECEPTOR AGONIST
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BRAND NAME* (generic)	TRULICITY (dulaglutide)
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Status: CVS Caremark Criteria

Type: Initial Prior Authorization

Ref # 1194-A

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Trulicity is indicated:

- as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
- to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus who have established cardiovascular disease or multiple cardiovascular risk factors.

Limitations of Use

- Trulicity has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.
- Trulicity should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis. Trulicity is not a substitute for insulin.
- Trulicity has not been studied in patients with severe gastrointestinal disease, including severe gastroparesis. The use of Trulicity is not recommended in patients with pre-existing severe gastrointestinal disease.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has been receiving GLP-1 Agonist therapy for at least 3 months
AND
 - The patient has demonstrated a reduction in A1c (hemoglobin A1c) since starting GLP-1 Agonist therapy [Note: Examples of GLP-1 Agonists are Adlyxin, Bydureon, Byetta, Ozempic, Tanzeum, Trulicity, Victoza]
OR
 - The patient has established cardiovascular disease or multiple cardiovascular risk factors

OR

- The patient has a diagnosis of type 2 diabetes mellitus
AND
 - The patient has experienced an inadequate treatment response, intolerance or contraindication to metformin
OR
 - The patient requires combination therapy **AND** has an A1c (hemoglobin A1c) of 7.5 percent or greater
OR
 - The patient has established cardiovascular disease or multiple cardiovascular risk factors

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Trulicity is indicated as an adjunct to diet and

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exercise to improve glycemic control in adults with type 2 diabetes mellitus. Trulicity is also indicated to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus who have established cardiovascular disease or multiple cardiovascular risk factors.

Clinical guidelines from the American Diabetes Association and the American Association of Clinical Endocrinologists and American College of Endocrinology for the management of hyperglycemia in type 2 diabetes indicate that metformin monotherapy should be started at diagnosis of type 2 diabetes unless there are contraindications. Metformin is effective and safe, is inexpensive, and may reduce risk of cardiovascular events and death. In patients with contraindications or intolerance of metformin, initial therapy should be based on patient factors; consider a drug from another class.⁴⁻⁵

The clinical guidelines also state that the A1c test is the major tool for assessing glycemic control and has strong predictive value for diabetes complications. Thus, A1c testing should be performed routinely in all patients with diabetes at initial assessment and as part of continuing care. The guidelines set goals for therapeutic effectiveness which must be evaluated frequently (e.g., every 3 months) until stable, using multiple criteria, including A1c. Less frequent monitoring is acceptable once targets are achieved.⁴⁻⁵ Therefore, continued use of any GLP-1 Agonist (e.g., Adlyxin, Byetta, Bydureon, Ozempic, Tanzeum, Trulicity, and Victoza) will be approved for patients who have demonstrated a reduction in A1c since starting GLP-1 Agonist therapy for at least three months.

If the A1c target is not achieved after approximately 3 months and patient does not have atherosclerotic cardiovascular disease (ASCVD) or chronic kidney disease (CKD), consider a combination of metformin and one of the preferred six treatment options: sulfonylurea, thiazolidinedione, dipeptidyl peptidase 4 (DPP-4) inhibitors, sodium-glucose cotransporter 2 (SGLT2) inhibitors, glucagon-like peptide 1 (GLP-1) receptor agonists, or basal insulin; the choice of which agent to add is based on drug-specific effects and patient factors. For patients in whom ASCVD, Heart Failure, or CKD predominates, the best choice for a second agent is a GLP-1 receptor agonist or SGLT2 inhibitor with demonstrated cardiovascular risk reduction, after consideration of drug-specific and patient factors.⁴⁻⁵

The REWIND trial compared the risk of Major Adverse Cardiovascular Events (MACE) outcome (which included CV death, non-fatal myocardial infarction (MI), and non-fatal stroke) between Trulicity 1.5 mg and placebo, both added to standard of care. During the trial, investigators were to modify antidiabetic and cardiovascular medications to achieve local standard of care treatment targets with respect to blood glucose, lipids, and blood pressure, and manage patients recovering from an acute coronary syndrome or stroke event per local treatment guidelines.¹ Therefore, Trulicity (dulaglutide) will be approved for initial therapy and continuation of therapy for patients have established cardiovascular disease or multiple cardiovascular risk factors.

In patients with an initial A1c of 7.5% or greater, or in patients who are unable to achieve their glycemic goals with monotherapy, combination therapy is recommended.⁴⁻⁵

REFERENCES

1. Trulicity [package insert]. Indianapolis, IN: Eli Lilly and Company; February 2020.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed July 2019.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed July 2019.
4. American Diabetes Association (ADA) Standards of Medical Care in Diabetes-2019—*Diabetes Care*. 2019; 42(Supplement 1).
5. Garber AJ, et al. AACE/ACE Consensus Statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the Comprehensive Type 2 Diabetes Management Algorithm 2019, *Endocr Pract*. 2019; 25 (No 1); 69-100.

Written by: UM Development (PL)
Date Written: 09/2014

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Revised: (CT) 04/2015 (CMS mandated change), (JH) 07/2015, (SF) 07/2016, 07/2017, 07/2018 (no clinical changes), 07/2019 (no clinical changes, removed MDC designation), (SF) 03/2020 (added CVD / CV risk factor indication)
Reviewed: Medical Affairs: (SES) 09/2014; (DHR) 04/2015; (DNC) 07/2015; (MES) 07/2016, 07/2017, (CHART) 08/01/2019, 03/12/2020
External Review: 10/2014, 10/2015, 10/2016, 10/2017, 10/2018, 10/2019, (FYI) 04/2020

CRITERIA FOR APPROVAL

1	Has the patient been receiving GLP-1 Agonist therapy for at least 3 months? [Note: Examples of GLP-1 Agonists are Adlyxin, Bydureon, Byetta, Ozempic, Tanzeum, Trulicity, Victoza] [If no, then skip to question 3.]	Yes	No
2	Has the patient demonstrated a reduction in A1c (hemoglobin A1c) since starting GLP-1 Agonist therapy? [If yes, then no further questions.] [If no, then skip to question 6.]	Yes	No
3	Does the patient have a diagnosis of type 2 diabetes mellitus?	Yes	No
4	Has the patient experienced an inadequate treatment response, contraindication or intolerance to metformin? [If yes, then no further questions.]	Yes	No
5	Does the patient require combination therapy AND have an A1c (hemoglobin A1c) of 7.5 percent or greater? [If yes, then no further questions.]	Yes	No
6	Does the patient have established cardiovascular disease or multiple cardiovascular risk factors?	Yes	No

Guidelines for Approval

Duration of Approval 12 Months

Set 1		Set 2	
Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)
1	None	1	2
2		6	
Set 3		Set 4	
Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)
3	1	3	1
4		5	4
Set 5			
Yes to question(s)	No to question(s)		
3	1		
6	4		
	5		

Mapping Instructions			
	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Go to 3	
2.	Approve, 12 Months	Go to 6	
3.	Go to 4	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have type 2 diabetes mellitus. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
4.	Approve, 12 Months	Go to 5	
5.	Approve, 12 months	Go to 6	
6.	Approve, 12 Months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet any of these conditions: - You have been receiving this drug or another drug in the same class for at least 3 months and you had a reduction in A1c (hemoglobin A1c) since starting therapy - You have tried metformin it did not work for you, or you cannot use it - You require combination therapy and you have an A1c (hemoglobin A1c) of 7.5 percent or greater - You have established cardiovascular (heart) disease or multiple cardiovascular risk factors Your request has been denied based on the information we have. [Short description: No inadequate treatment response, intolerance or contraindication to metformin, no requirement for combination therapy or No established cardiovascular disease or multiple cardiovascular risk factors]

SPECIALTY GUIDELINE MANAGEMENT

TURALIO (pexidartinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication^[1]

Turalio is indicated for the treatment of adult patients with symptomatic tenosynovial giant cell tumor (TGCT) associated with severe morbidity or functional limitations and not amenable to improvement with surgery.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Symptomatic Tenosynovial Giant Cell Tumor^[1]

Authorization of 12 months may be granted for the treatment of symptomatic tenosynovial giant cell tumor (TGCT) associated with severe morbidity or functional limitations and that is not amenable to improvement with surgery.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced an unacceptable toxicity or disease progression.

IV. REFERENCES

1. Turalio [package insert]. Rasking Ridge, NJ: Daiichi Sankyo, Inc.; August 2019.

SPECIALTY GUIDELINE MANAGEMENT

TYKERB (lapatinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Tykerb is indicated in combination with:

1. Capecitabine for the treatment of patients with advanced or metastatic breast cancer whose tumors overexpress human epidermal growth factor receptor 2 (HER2) and who have received prior therapy including an anthracycline, a taxane, and trastuzumab
2. Letrozole for the treatment of postmenopausal women with hormone receptor (HR)-positive metastatic breast cancer that overexpresses the HER2 receptor for whom hormonal therapy is indicated

B. Compendial Uses

1. Recurrent or metastatic HER2-positive breast cancer in combination with trastuzumab
2. Recurrent or stage IV hormone receptor-positive, HER2-positive breast cancer in combination with aromatase inhibition in postmenopausal women
3. Central Nervous System (CNS) metastases from breast cancer
4. Recurrent epidermal growth factor receptor (EGFR)-positive chordoma

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Hormone receptor status, HER2 status, EGFR mutation testing results (where applicable).

III. CRITERIA FOR INITIAL APPROVAL

A. **Breast cancer**

Authorization of 12 months may be granted for the treatment of recurrent, advanced, or metastatic HER2-positive breast cancer when any of the following criteria are met:

1. Tykerb is used in combination with an aromatase inhibitor (e.g., letrozole, anastrozole, or exemestane) either with or without trastuzumab for the treatment of hormone receptor-positive disease; or
2. Tykerb will be used in combination with capecitabine or trastuzumab.

B. **Central nervous system metastases (CNS) from breast cancer**

Authorization of 12 months may be granted for the treatment of recurrent brain metastases from HER2-positive breast cancer in combination with capecitabine.

C. **Chordoma**

Reference number(s)
1902-A

Authorization of 12 months may be granted for the treatment of EGFR-positive recurrent chordoma, as a single agent.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication in Section III who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES

1. Tykerb [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; December 2018.
2. The NCCN Drugs & Biologics Compendium 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed August 14, 2019.
3. National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology: breast cancer. Version 3.2018. http://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed January 16, 2019.
4. National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology: central nervous system cancer. Version 2.2018. http://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed January 16, 2019.
5. National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology: bone cancer. Version 1.2019. http://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed January 16, 2019.

SPECIALTY GUIDELINE MANAGEMENT

TYMLOS (abaloparatide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Tymlos is indicated for the treatment postmenopausal women with osteoporosis at high risk for fracture defined as history of osteoporotic fracture, multiple risk factors for fracture, or patients who have failed or are intolerant to other available osteoporosis therapy.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Supporting chart notes or medical record indicating a history of fractures, T-score, and FRAX fracture probability as applicable to section III.

III. CRITERIA FOR APPROVAL

Postmenopausal osteoporosis

Authorization of a lifetime total of 24 months for parathyroid hormone analogs (e.g., abaloparatide or teriparatide) may be granted to postmenopausal members with osteoporosis when ANY of the following criteria are met:

- A. Member has a history of fragility fractures
- B. Member has a pre-treatment T-score less than or equal to -2.5 OR member has osteopenia (i.e., pre-treatment T-score greater than -2.5 and less than -1) with a high pre-treatment FRAX fracture probability (See Appendix B) and meets ANY of the following criteria:
 1. Member has indicators of higher fracture risk (e.g., advanced age, frailty, glucocorticoid use, very low T-scores [less than or equal to -3.5], or increased fall risk)
 2. Member has failed prior treatment with or is intolerant to previous injectable osteoporosis therapy (e.g., zoledronic acid [Reclast], denosumab [Prolia])
 3. Member has had an oral bisphosphonate trial of at least 1-year duration or there is a clinical reason to avoid treatment with an oral bisphosphonate (See Appendix A)

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet ALL

initial authorization criteria AND have received less than 24 months of total lifetime therapy with parathyroid hormone analogs (e.g., abaloparatide or teriparatide).

V. APPENDIX

Appendix A. Clinical reasons to avoid oral bisphosphonate therapy

- Esophageal abnormality that delays emptying such as stricture of achalasia
- Active upper gastrointestinal problem (e.g., dysphagia, gastritis, duodenitis, erosive esophagitis, ulcers)
- Inability to stand or sit upright for at least 30 to 60 minutes
- Inability to take at least 30 to 60 minutes before first food, drink, or medication of the day
- Renal insufficiency (creatinine clearance < 35 mL/min)
- History of intolerance to an oral bisphosphonate

Appendix B. WHO Fracture Risk Assessment Tool

- High FRAX fracture probability: 10 year major osteoporotic fracture risk \geq 20% or hip fracture risk \geq 3%.
- 10-year probability; calculation tool available at: <https://www.sheffield.ac.uk/FRAX/>
- The estimated risk score generated with FRAX should be multiplied by 1.15 for major osteoporotic fracture and 1.2 for hip fracture if glucocorticoid treatment is greater than 7.5 mg per day.

VI. REFERENCES

1. Tymlos [package insert]. Waltham, MA: Radius Health, Inc. October 2018.
2. Bisphosphonates. *Drug Facts and Comparisons*. Facts & Comparisons [database online]. St. Louis, MO: Wolters Kluwer Health Inc; March 21, 2019. Accessed April 10, 2019.
3. Miller PD, Hattersley G, Riis BJ, et al. Effect of Abaloparatide Vs Placebo on New Vertebral Fractures in Postmenopausal Women with Osteoporosis: A Randomized Clinical Trial. *JAMA*. 2016; 316 (7): 722:733.
4. Watts NB, Bilezikian JP, Camacho PM, et al. American Association of Clinical Endocrinologists medical guidelines for clinical practice for the diagnosis and treatment of postmenopausal osteoporosis. *Endocr Pract*. 2016;22 (Suppl 4):1-42.
5. FRAX® WHO fracture risk assessment tool. © World Health Organization Collaborating Centre for Metabolic Bone Diseases: University of Sheffield, UK. Available at: <https://www.sheffield.ac.uk/FRAX/>. Accessed April 10, 2019.
6. Ensrud KE, Crandall CJ. Osteoporosis. *Ann Intern Med* 2017;167(03):ITC17–ITC32.

SPECIALTY GUIDELINE MANAGEMENT

TYSABRI (natalizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

1. Tysabri is indicated for inducing and maintaining clinical response and remission in adult patients with moderately to severely active Crohn's disease with evidence of inflammation who have had an inadequate response to, or are unable to tolerate, conventional CD therapies and inhibitors of TNF- α .
2. Tysabri is indicated as monotherapy for the treatment of relapsing forms of multiple sclerosis, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Moderately to severely active Crohn's disease (CD)

Authorization of 12 months may be granted to members who have received any other biologic indicated for the treatment of moderately to severely active Crohn's disease.

B. Relapsing forms of multiple sclerosis (MS)

Authorization of 12 months may be granted to members who have been diagnosed with a relapsing forms of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse) and those who have been tested for anti-JCV antibodies.

C. Clinically isolated syndrome (CIS)

Authorization of 12 months may be granted to members for the treatment of clinically isolated syndrome and those who have been tested for anti-JCV antibodies.

III. CONTINUATION OF THERAPY

A. Crohn's disease (CD)

Authorization of 12 months may be granted for all members (including new members) who achieve or maintain a positive clinical response with Tysabri as evidenced by low disease activity or improvement in signs and symptoms of the condition.

B. Relapsing forms of multiple sclerosis (MS) or clinically isolated syndrome (CIS)

Authorization of 12 months may be granted for all members (including new members) who achieve or maintain a positive clinical response with Tysabri as evidenced by experiencing disease stability or improvement.

IV. OTHER

For all indications: Members cannot use Tysabri concomitantly with any other disease modifying MS agents (Note: Ampyra and Nuedexta are not disease modifying), immunosuppressants, or TNF inhibitors (e.g., adalimumab, infliximab).

V. REFERENCES

1. Tysabri [package insert]. Cambridge, MA: Biogen Idec, Inc; August 2019.
2. Talley NJ, Abreu MT, Achkar J, et al. An evidence-based systematic review on medical therapies for inflammatory bowel disease. *Am J Gastroenterol*. 2011;106(Suppl 1):S2-S25.
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SPECIALTY GUIDELINE MANAGEMENT

Tyvaso (treprostinil inhalation solution)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Tyvaso is indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to improve exercise ability.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of PAH when ALL of the following criteria are met:

- A. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
- B. PAH was confirmed by either criterion (1) or criterion (2) below:
 1. Pretreatment right heart catheterization with all of the following results:
 - i. mPAP \geq 25 mmHg
 - ii. PCWP \leq 15 mmHg
 - iii. PVR $>$ 3 Wood units
 2. For infants less than one year of age with any of the following conditions, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed:
 - i. Post cardiac surgery
 - ii. Chronic heart disease
 - iii. Chronic lung disease associated with prematurity
 - iv. Congenital diaphragmatic hernia

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with an indication listed in Section II who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

IV. APPENDIX

WHO Classification of Pulmonary Hypertension

1 PAH

- 1.1 Idiopathic (PAH)
- 1.2 Heritable PAH
- 1.3 Drug- and toxin-induced PAH

- 1.4. PAH associated with:
 - 1.4.1 Connective tissue diseases
 - 1.4.2 HIV infection
 - 1.4.3 Portal hypertension
 - 1.4.4 Congenital heart diseases
 - 1.4.5 Schistosomiasis
- 1.5 PAH long-term responders to calcium channel blockers
- 1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement
- 1.7 Persistent PH of the newborn syndrome

2 PH due to left heart disease

- 2.1 PH due to heart failure with preserved LVEF
- 2.2 PH due to heart failure with reduced LVEF
- 2.3 Valvular heart disease
- 2.4 Congenital/acquired cardiovascular conditions leading to post-capillary PH

3 PH due to lung diseases and/or hypoxia

- 3.1 Obstructive lung disease
- 3.2 Restrictive lung disease
- 3.3 Other lung disease with mixed restrictive/obstructive pattern
- 3.4 Hypoxia without lung disease
- 3.5 Developmental lung disorders

4 PH due to pulmonary artery obstruction

- 4.1 Chronic thromboembolic PH
- 4.2 Other pulmonary artery obstructions
 - 4.2.1 Sarcoma (high or intermediate grade) or angiosarcoma
 - 4.2.2 Other malignant tumors
 - Renal carcinoma
 - Uterine carcinoma
 - Germ cell tumours of the testis
 - Other tumours
 - 4.2.3 Non-malignant tumours
 - Uterine leiomyoma
 - 4.2.4 Arteritis without connective tissue disease
 - 4.2.5 Congenital pulmonary artery stenosis
 - 4.2.6 Parasites
 - Hydatidosis

5 PH with unclear and/or multifactorial mechanisms

- 5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders
- 5.2 Systemic and metabolic disorders: Pulmonary Langerhans cell histiocytosis, Gaucher disease, glycogen storage disease, neurofibromatosis, sarcoidosis
- 5.3 Others: chronic renal failure with or without hemodialysis, fibrosing mediastinitis
- 5.4 Complex congenital heart disease

V. REFERENCES

1. Tyvaso [package insert]. Research Triangle Park, NC: United Therapeutics Corp.; October 2017.
2. Chin KM, Rubin LJ. Pulmonary arterial hypertension. *J Am Coll Cardiol.* 2008;51(16):1527-1538.
3. McLaughlin VV, Archer SL, Badesch DB, et al. ACCF/AHA 2009 expert consensus document on pulmonary hypertension a report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents and the American Heart Association developed in collaboration with the American College of Chest Physicians; American Thoracic Society, Inc.; and the Pulmonary Hypertension Association. *J Am Coll Cardiol.* 2009;53(17):1573-1619.

4. Badesch DB, Champion HC, Gomez-Sanchez MA, et al. Diagnosis and assessment of pulmonary arterial hypertension. *J Am Coll Cardiol*. 2009;54:S55-S66.
5. Simonneau G, Robbins IM, Beghetti M, et al. Updated clinical classification of pulmonary hypertension. *J Am Coll Cardiol*. 2013;62:D34-S41.
6. Rubin LJ; American College of Chest Physicians. Diagnosis and management of pulmonary arterial hypertension: ACCP evidence-based clinical practice guidelines. *Chest*. 2004;126(1 Suppl):7S-10S.
7. Barst RJ, Gibbs SR, Ghofrani HA, et al. Updated evidence-based treatment algorithm in pulmonary arterial hypertension. *J Am Coll Cardiol*. 2009;54:S78-S84.
8. Taichman DB, Ornelas J, Chung L, et al. Pharmacologic therapy for pulmonary arterial hypertension in adults. CHEST guideline and expert panel report. *Chest*. 2014;46(2):449-475.
9. Abman, SH, Hansmann G, Archer SL, et al. Pediatric pulmonary hypertension: guidelines from the American Heart Association and American Thoracic Society. *Circulation*. 2015;132(21):2037-99.
10. Klinger, JR., Elliott, CG, Levine, DJ, et al. Therapy for Pulmonary Arterial Hypertension in Adults: Update of the CHEST Guidelines and Expert Panel Report. *Chest*. 2019;155(3): 565-586.
11. Galie, N., McLaughlin, VV, Rubin, LJ, Simonneau, G. An overview of the 6th World Symposium on Pulmonary Hypertension. *Eur Respir J* 2019; 53: 1802148; DOI: 10.1183/13993003.02148-2018. Published 24 January 2019.

SPECIALTY GUIDELINE MANAGEMENT

ULTOMIRIS (ravulizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

1. Ultomiris is indicated for the treatment of adult patients with paroxysmal nocturnal hemoglobinuria.
2. Ultomiris is indicated for the treatment of patients with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy (TMA).

Limitations of Use: Ultomiris is not indicated for the treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS).

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review for new requests for treatment of:

- A. Paroxysmal nocturnal hemoglobinuria: flow cytometry used to show results of GPI-APs deficiency
- B. Atypical hemolytic uremic syndrome: ADAMTS 13 level

III. CRITERIA FOR INITIAL APPROVAL

A. Paroxysmal nocturnal hemoglobinuria

Authorization of 6 months may be granted for treatment of paroxysmal nocturnal hemoglobinuria (PNH) when all of the following criteria are met:

1. The diagnosis of PNH was confirmed by detecting a deficiency of glycosylphosphatidylinositol-anchored proteins (GPI-APs) as demonstrated by either of the following:
 1. At least 5% PNH cells
 2. At least 51% of GPI deficient poly-morphonuclear cells
2. Flow cytometry is used to demonstrate GPI-APs deficiency

B. Atypical hemolytic uremic syndrome (aHUS)

Authorization of 6 months may be granted for treatment of atypical hemolytic uremic syndrome (aHUS) not caused by Shiga toxin when all of the following criteria are met:

1. Absence of Shiga toxin
2. ADAMTS 13 activity level above 5%

IV. CONTINUATION OF THERAPY

A. Paroxysmal nocturnal hemoglobinuria

Authorization of 12 months may be granted to all members requesting continuation of therapy provided they meet all initial authorization criteria and demonstrate a positive response to therapy (e.g., improvement in hemoglobin levels normalization of lactate dehydrogenase [LDH] levels).

B. Atypical hemolytic uremic syndrome (aHUS)

Authorization of 12 months may be granted to all members requesting continuation of therapy provided they meet all initial authorization criteria and demonstrate a positive response to therapy (e.g., normalization of lactate dehydrogenase (LDH) levels, platelet counts).

V. REFERENCES

1. Ultomiris [package insert]. Boston, MA: Alexion Pharmaceuticals, Inc.; December 2018.
2. Parker CJ. Management of paroxysmal nocturnal hemoglobinuria in the era of complement inhibitory therapy. *Hematology*. 2011; 21-29.
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4. Borowitz MJ, Craig F, DiGiuseppe JA, et al. Guidelines for the Diagnosis and Monitoring of Paroxysmal Nocturnal Hemoglobinuria and Related Disorders by Flow Cytometry. *Cytometry B Clin Cytom*. 2010; 78: 211-230.
5. Preis M, Lowrey CH. Laboratory tests for paroxysmal nocturnal hemoglobinuria (PNH). *Am J Hematol*. 2014;89(3):339-341.
6. Loirat C, Fakhouri F, Ariceta G, et al. An international consensus approach to the management of atypical hemolytic uremic syndrome in children. *Pediatr Nephrol*. Published online: April 11, 2015.

SPECIALTY GUIDELINE MANAGEMENT

Uptravi (selexipag)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Uptravi is indicated for the treatment of pulmonary arterial hypertension (PAH, WHO Group I) to delay disease progression and reduce the risk of hospitalization for PAH.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of PAH when ALL of the following criteria are met:

- A. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix)
- B. PAH was confirmed by either criterion (1) or criterion (2) below:
 1. Pretreatment right heart catheterization with all of the following results:
 - i. mPAP \geq 25 mmHg
 - ii. PCWP \leq 15 mmHg
 - iii. PVR $>$ 3 Wood units
 2. For infants less than one year of age with any of the following conditions, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed:
 - i. Post cardiac surgery
 - ii. Chronic heart disease
 - iii. Chronic lung disease associated with prematurity
 - iv. Congenital diaphragmatic hernia

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with an indication listed in Section II who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

IV. APPENDIX

WHO Classification of Pulmonary Hypertension

1 PAH

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- 1.2 Heritable PAH
- 1.3 Drug- and toxin-induced PAH
- 1.4. PAH associated with:

- 1.4.1 Connective tissue diseases
- 1.4.2 HIV infection
- 1.4.3 Portal hypertension
- 1.4.4 Congenital heart diseases
- 1.4.5 Schistosomiasis
- 1.5 PAH long-term responders to calcium channel blockers
- 1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement
- 1.7 Persistent PH of the newborn syndrome

2 PH due to left heart disease

- 2.1 PH due to heart failure with preserved LVEF
- 2.2 PH due to heart failure with reduced LVEF
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- 2.4 Congenital/acquired cardiovascular conditions leading to post-capillary PH

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- 3.1 Obstructive lung disease
- 3.2 Restrictive lung disease
- 3.3 Other lung disease with mixed restrictive/obstructive pattern
- 3.4 Hypoxia without lung disease
- 3.5 Developmental lung disorders

4 PH due to pulmonary artery obstruction

- 4.1 Chronic thromboembolic PH
- 4.2 Other pulmonary artery obstructions
 - 4.2.1 Sarcoma (high or intermediate grade) or angiosarcoma
 - 4.2.2 Other malignant tumors
 - Renal carcinoma
 - Uterine carcinoma
 - Germ cell tumours of the testis
 - Other tumours
 - 4.2.3 Non-malignant tumours
 - Uterine leiomyoma
 - 4.2.4 Arteritis without connective tissue disease
 - 4.2.5 Congenital pulmonary artery stenosis
 - 4.2.6 Parasites
 - Hydatidosis

5 PH with unclear and/or multifactorial mechanisms

- 5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders
- 5.2 Systemic and metabolic disorders: Pulmonary Langerhans cell histiocytosis, Gaucher disease, glycogen storage disease, neurofibromatosis, sarcoidosis
- 5.3 Others: chronic renal failure with or without hemodialysis, fibrosing mediastinitis
- 5.4 Complex congenital heart disease

V. REFERENCES

1. Uptravi [package insert]. South San Francisco, CA: Actelion Pharmaceuticals US, Inc.; December 2017.
2. Sitbon O, Channick R, Chin K, et al. Selexipag for the treatment of pulmonary arterial hypertension. *N Engl J Med*. 2015;373:2522-33.
3. Clinical Consult: CVS Caremark Clinical Programs Review. Focus on Uptravi Clinical Programs. January 8, 2016.
4. Simonneau G, Robbins IM, Beghetti M, et al. Updated clinical classification of pulmonary hypertension. *J Am Coll Cardiol*. 2013;62:D34-S41.

Reference number(s)
1645-A

5. Rubin LJ; American College of Chest Physicians. Diagnosis and management of pulmonary arterial hypertension: ACCP evidence-based clinical practice guidelines. *Chest*. 2004;126(1 Suppl):7S-10S.
6. McLaughlin V, et al. ACCF/AHA 2009 Expert Consensus Document on Pulmonary Hypertension. *J Am Coll Cardiol*. 2009;53:1573-1619.
7. Klinger, JR., Elliott, CG, Levine, DJ, et al. Therapy for Pulmonary Arterial Hypertension in Adults: Update of the CHEST Guidelines and Expert Panel Report. *Chest*. 2019;155(3): 565-586.
8. Galie, N., McLaughlin, VV, Rubin, LJ, Simonneau, G. An overview of the 6th World Symposium on Pulmonary Hypertension. *Eur Respir J* 2019; 53: 1802148; DOI: 10.1183/13993003.02148-2018. Published 24 January 2019.

SPECIALTY GUIDELINE MANAGEMENT

VALCHLOR (mechlorethamine gel)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Valchlor is indicated for the topical treatment of Stage IA and IB mycosis fungoides-type cutaneous T-cell lymphoma in patients who have received prior skin-directed therapy.

B. Compendial Uses

1. Chronic or smoldering adult T-cell leukemia/lymphoma
2. Mycosis fungoides/Sezary syndrome
3. Primary cutaneous B-cell lymphoma:
 - a. Primary cutaneous marginal zone lymphoma
 - b. Primary cutaneous follicle center lymphoma
4. Lymphomatoid papulosis

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Mycosis Fungoides/Sezary Syndrome**

Authorization of 12 months may be granted for the treatment of mycosis fungoides or Sezary syndrome.

B. **Adult T-cell leukemia/lymphoma**

Authorization of 12 months may be granted for the treatment of chronic or smoldering adult T-cell leukemia/lymphoma.

C. **Primary cutaneous B-cell lymphoma**

Authorization of 12 months may be granted for the treatment of primary cutaneous marginal zone or follicle center lymphoma.

D. **Lymphomatoid Papulosis**

Authorization of 12 months may be granted for the treatment of lymphomatoid papulosis.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced disease progression or an unacceptable toxicity.

Reference number
1862-A

IV. REFERENCES

1. Valchlor [package insert]. South San Francisco, CA: Actelion Pharmaceuticals US, Inc.; December 2016.
2. The NCCN Drugs & Biologics Compendium™ © 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed January 24, 2019.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

VALTOCO
(diazepam nasal spray)

Status: CVS Caremark Criteria

Type: Initial Prior Authorization

Ref # 3517-C

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Valtoco is indicated for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from a patient's usual seizure pattern in patients with epilepsy 6 years of age and older.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from the patient's usual seizure pattern in a patient with epilepsy

AND

- The patient is 6 years of age or older

Quantity Limits apply.

RATIONALE

Valtoco is indicated for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from a patient's usual seizure pattern in patients with epilepsy 6 years of age and older. Prior to treatment, healthcare professionals should instruct the individual administering Valtoco on how to identify seizure clusters and use the product appropriately

The recommended dose of Valtoco nasal spray is 0.2 mg/kg or 0.3 mg/kg, depending on the patient's age and weight. The following table provides the acceptable weight ranges for each dose and age category, such that patients will receive between 90% and 180% of the calculated recommended dose.

Recommended Valtoco Dosage for Adults and Pediatric Patients 6 Years of Age and Older

Dose Based on Age and Weight		Administration		
6 to 11 Years of Age (0.3 mg/kg)	12 Years of Age and Older (0.2 mg/kg)	Dose (mg)	Number of Nasal Spray Devices	Number of Sprays
Weight (kg)	Weight (kg)			
10 to 18	14 to 27	5	One 5 mg device	One spray in one nostril
19 to 37	28 to 50	10	One 10 mg device	One spray in one nostril
38 to 55	51 to 75	15	Two 7.5 mg devices	One spray in each nostril
56 to 74	76 and up	20	Two 10 mg devices	One spray in each nostril

A second dose of Valtoco, when required, may be administered after at least 4 hours after the initial dose. If the second dose is to be administered, use a new blister pack of Valtoco. Do not use more than 2 doses of Valtoco to treat a single episode. It is recommended that Valtoco be used to treat no more than one episode every five days and no more than five episodes per month.

Valtoco is available in 5 mg, 7.5 mg, and 10 mg strengths. Valtoco is supplied and packed in doses of 5 mg, 10 mg, 15 mg, or 20 mg cartons.

Available Packaging Configurations

Description	Contents
5 mg carton	2 individual blister packs, each containing one 5 mg nasal spray device
10 mg carton	2 individual blister packs, each containing one 10 mg nasal spray device
15 mg carton	2 individual blister packs, each containing two 7.5 mg nasal spray devices
20 mg carton	2 individual blister packs, each containing two 10mg nasal spray devices

Each blister pack contains enough Valtoco to administer one dose of the prescribed quantity. Each carton contains two blister packs, which is enough to treat one to two episodes. Because it is not recommended to treat more than 5 episodes per month and each episode could require up to 2 doses, the limit will be set at 5 cartons (10 blister packs).

REFERENCES

1. Valtoco [package insert]. San Diego, CA: Neurelis, Inc.; January, 2020.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed January 2020.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed January 2020.

Written by: UM Development (DS)
 Date Written: 01/2020
 Revised:
 Reviewed: Medical Affairs (CHART) 02/06/2020
 External Review: 04/2020

CRITERIA FOR APPROVAL

- | | | | |
|---|--|-----|----|
| 1 | Is the requested drug being prescribed for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from the patient's usual seizure pattern in a patient with epilepsy? | Yes | No |
| 2 | Is the patient 6 years of age or older? | Yes | No |
| 3 | Does the patient require more than the plan allowance per month of 10 blister packs (5 cartons) of the requested drug?
[Note: Coverage is provided up to an amount sufficient for treating up to five episodes per month at the maximum dose of the requested drug.]

[RPh Note: If yes, then deny and enter a partial approval for 10 blister packs (5 cartons) per month of Valtoco.] | Yes | No |

Mapping Instructions

	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Deny	<p>You do not meet the requirements of your plan.</p> <p>Your plan covers this drug when you meet all of the following:</p> <ul style="list-style-type: none"> - You have epilepsy - The requested drug is being used for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from your usual seizure pattern <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No approvable diagnosis]</p>
2.	Go to 3	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you are 6 years of age or older.</p> <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No approvable diagnosis]</p>
3.	Deny	Approve, 12 months, See Quantity Limit Chart	<p>You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 5 cartons per month of the requested drug and strength. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied.</p> <p>[Short Description: Over max quantity]</p>

QUANTITY LIMIT

Limits should accumulate across all drugs and strengths up to highest quantity listed depending on the order the claims are processed. Accumulation does not apply if limit is coded for daily dose.

Drug	1 Month Limit*	3 Month Limit*
Valtoco 5 mg carton	10 blister packs (5 cartons) / 25 days	30 blister packs (15 cartons) / 75 days
Valtoco 10 mg carton	10 blister packs (5 cartons) / 25 days	30 blister packs (15 cartons) / 75 days
Valtoco 15 mg carton	10 blister packs (5 cartons) / 25 days	30 blister packs (15 cartons) / 75 days
Valtoco 20 mg carton	10 blister packs (5 cartons) / 25 days	30 blister packs (15 cartons) / 75 days

*The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.

QUANTITY LIMIT CRITERIA

BRAND NAME*
(generic)

VALTOCO
(diazepam nasal spray)

Status: CVS Caremark Criteria

Type: Quantity Limit

Ref # 3518-H

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Valtoco is indicated for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from a patient's usual seizure pattern in patients with epilepsy 6 years of age and older.

RATIONALE

Valtoco is indicated for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from a patient's usual seizure pattern in patients with epilepsy 6 years of age and older. Prior to treatment, healthcare professionals should instruct the individual administering Valtoco on how to identify seizure clusters and use the product appropriately.

The recommended dose of Valtoco nasal spray is 0.2 mg/kg or 0.3 mg/kg, depending on the patient's age and weight. The following table provides the acceptable weight ranges for each dose and age category, such that patients will receive between 90% and 180% of the calculated recommended dose.

Recommended Valtoco Dosage for Adults and Pediatric Patients 6 Years of Age and Older

Dose Based on Age and Weight		Administration		
6 to 11 Years of Age (0.3 mg/kg)	12 Years of Age and Older (0.2 mg/kg)	Dose (mg)	Number of Nasal Spray Devices	Number of Sprays
Weight (kg)	Weight (kg)			
10 to 18	14 to 27	5	One 5 mg device	One spray in one nostril
19 to 37	28 to 50	10	One 10 mg device	One spray in one nostril
38 to 55	51 to 75	15	Two 7.5 mg devices	One spray in each nostril
56 to 74	76 and up	20	Two 10 mg devices	One spray in each nostril

A second dose of Valtoco, when required, may be administered after at least 4 hours after the initial dose. If the second dose is to be administered, use a new blister pack of Valtoco. Do not use more than 2 doses of Valtoco to treat a single episode. It is recommended that Valtoco be used to treat no more than one episode every five days and no more than five episodes per month.

Valtoco is available in 5 mg, 7.5 mg, and 10 mg strengths. Valtoco is supplied and packed in doses of 5 mg, 10 mg, 15 mg, or 20 mg cartons.

Available Packaging Configurations

Description	Contents
5 mg carton	2 individual blister packs, each containing one 5 mg nasal spray device
10 mg carton	2 individual blister packs, each containing one 10 mg nasal spray device
15 mg carton	2 individual blister packs, each containing two 7.5 mg nasal spray devices
20 mg carton	2 individual blister packs, each containing two 10mg nasal spray devices

Each blister pack contains enough Valtoco to administer one dose of the prescribed quantity. Each carton contains two blister packs, which is enough to treat one to two episodes. Because it is not recommended to treat more than 5 episodes per month and each episode could require up to 2 doses, the limit will be set at 5 cartons (10 blister packs).

REFERENCES

1. Valtoco [package insert]. San Diego, CA: Neurelis, Inc.; January, 2020.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed January 2020.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed January 2020.

Written by: UM Development (DS)
 Date Written: 01/2020
 Revised:
 Reviewed: Medical Affairs (CHART) 02/06/2020
 External Review: 04/2020

LIMIT CRITERIA

Limits should accumulate across all drugs and strengths up to highest quantity listed depending on the order the claims are processed. Accumulation does not apply if limit is coded for daily dose.

Drug	1 Month Limit*	3 Month Limit*
Valtoco 5 mg carton	10 blister packs (5 cartons) / 25 days	30 blister packs (15 cartons) / 75 days
Valtoco 10 mg carton	10 blister packs (5 cartons) / 25 days	30 blister packs (15 cartons) / 75 days
Valtoco 15 mg carton	10 blister packs (5 cartons) / 25 days	30 blister packs (15 cartons) / 75 days
Valtoco 20 mg carton	10 blister packs (5 cartons) / 25 days	30 blister packs (15 cartons) / 75 days

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

SPECIALTY GUIDELINE MANAGEMENT

VANTAS (histrelin acetate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Palliative treatment of advanced prostate cancer

B. Compendial Uses

1. Prostate cancer
2. Gender dysphoria (also known as gender non-conforming or transgender persons)

NOTE: Some plans may opt-out of coverage for gender dysphoria.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Prostate cancer

Authorization of 12 months may be granted for treatment of prostate cancer.

B. Gender dysphoria

1. Authorization of 12 months may be granted for pubertal suppression in preparation for gender reassignment in an adolescent member when all of the following criteria are met:
 - a. The member has a diagnosis of gender dysphoria.
 - b. The member has reached Tanner stage 2 of puberty.
2. Authorization of 12 months may be granted for gender reassignment in an adult member when all of the following criteria are met:
 - a. The member has a diagnosis of gender dysphoria.
 - b. The member will receive Vantas concomitantly with cross sex hormones.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Vantas [package insert]. Malvern, PA: Endo Pharmaceuticals; February 2019.
2. The NCCN Drugs & Biologics Compendium® © 2018 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed October 11, 2018.

Reference number(s)
1969-A, 2086-A

3. National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology: prostate cancer. Version 4.2018. http://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed October 11, 2018.
4. Hembree WC, Cohen-Kettenis PT, Gooren L, et al. Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*. 2017;102(11):3869–3903.
5. Gender Identity Research and Education Society. Guidance for GPs and other clinicians on the treatment of gender variant people. UK Department of Health. Published March 10, 2008.
6. Standards of care for the health of transsexual, transgender, and gender-nonconforming people, 7th version. ©2012 World Professional Association for Transgender Health. Available at <http://www.wpath.org>.

SPECIALTY GUIDELINE MANAGEMENT

VECTIBIX (panitumumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Vectibix is indicated for the treatment of patients with wild-type *RAS* (defined as wild-type in both *KRAS* and *NRAS* as determined by an FDA-approved test for this use) metastatic colorectal cancer (mCRC):

1. As first-line therapy in combination with FOLFOX (fluorouracil, leucovorin, and oxaliplatin).
2. As monotherapy following disease progression after prior treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy.

Limitation of Use: Vectibix is not indicated for the treatment of patients with *RAS*-mutant mCRC or for whom *RAS* mutation status is unknown.

B. Compendial Use

Colorectal cancer

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: documentation of *Ras* wild-type status, where applicable.

III. CRITERIA FOR INITIAL APPROVAL

Colorectal Cancer (CRC)

Authorization of 6 months may be granted for the treatment of colorectal cancer, including small bowel adenocarcinoma, appendiceal carcinoma, and anal adenocarcinoma, for unresectable/inoperable, advanced, or metastatic disease when all of the following criteria are met:

- A. The *RAS* (*KRAS* and *NRAS*) mutation status is negative (wild-type).
- B. Member has not previously experienced clinical failure on cetuximab.

IV. CONTINUATION OF THERAPY

Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced disease progression or an unacceptable toxicity.

Reference number(s)
2035-A

V. REFERENCES

1. Vectibix [package insert]. Thousand Oaks, CA: Amgen Inc.; June 2017.
2. The NCCN Drugs & Biologics Compendium™ © 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed July 11, 2019.

SPECIALTY GUIDELINE MANAGEMENT

VENCLEXTA (venetoclax)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Venclexta is indicated for the treatment of patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL).
2. Venclexta is indicated in combination with azacitidine, or decitabine, or low-dose cytarabine for the treatment of newly-diagnosed acute myeloid leukemia (AML) in adults who are age 75 years or older, or who have comorbidities that preclude use of intensive induction chemotherapy.

B. Compendial Uses

1. Mantle cell lymphoma
2. In combination with rituximab for relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) in patients who have indications for treatment

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL)**

Authorization of 12 months may be granted for treatment of chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) when Venclexta will be used as monotherapy, in combination with rituximab (Rituxan), or in combination with obinutuzumab (Gazyva).

B. **Newly-diagnosed Acute Myeloid Leukemia (AML)**

Authorization of 12 months may be granted for treatment of newly-diagnosed acute myeloid leukemia (AML) when all of the following criteria is met:

1. Venclexta will be used in combination with decitabine, azacitidine, or low-dose cytarabine
2. Member meets any of the following:
 - a. The member is 75 years of age or older.
 - b. The member has comorbidities that preclude treatment with intensive induction chemotherapy.
 - c. The member is 60 years of age or older and is a candidate for intensive remission induction therapy with unfavorable-risk cytogenetics
 - d. The member is 60 years of age or older and has AML without actionable mutations and is not a candidate for intensive remission induction therapy or declines intensive therapy
 - e. The member is 60 years of age or older and will use Venclexta as post-induction therapy following response to previous lower intensity therapy with the same regimen

C. **Relapsed or Refractory Acute Myeloid Leukemia (AML)**

Authorization of 12 months may be granted for treatment of relapsed or refractory acute myeloid leukemia when Venclexta will be used as component of repeating the initial successful induction treatment if the patient experiences late relapse (12 months or longer).

Reference number(s)
2374-A

D. Mantle Cell Lymphoma

Authorization of 12 months may be granted for treatment of mantle cell lymphoma when Venclexta will not be used as induction therapy.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced unacceptable toxicity or disease progression while on the current regimen. For members with CLL/SLL who will use Venclexta with Rituxan, Venclexta will not be used longer than 24 months from cycle 1 day 1 of Rituxan initiation. For members with CLL/SLL who will use Venclexta with Gazyva, Venclexta will not be used longer than 12 cycles.

IV. REFERENCES

1. Venclexta® [package insert]. North Chicago, IL: AbbVie Inc.; May 2019.
2. The NCCN Drugs & Biologics Compendium® © 2018 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed May 16, 2019.
3. The NCCN Clinical Practice Guidelines in Oncology® Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (Version 1.2019) © 2018 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed March 26, 2019.
4. The NCCN Clinical Practice Guidelines in Oncology® B-Cell Lymphomas (Version 4.2018) © 2018 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed March 26, 2019.
5. The NCCN Clinical Practice Guidelines in Oncology® Acute Myeloid Leukemia (Version 2.2019) © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed March 28, 2019.

SPECIALTY GUIDELINE MANAGEMENT

Ventavis (iloprost inhalation solution)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Ventavis is indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to improve a composite endpoint consisting of exercise tolerance, symptoms (NYHA Class), and lack of deterioration.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of PAH when ALL of the following criteria are met:

- A. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
- B. PAH was confirmed by either criterion (1) or criterion (2) below:
 1. Pretreatment right heart catheterization with all of the following results:
 - i. mPAP \geq 25 mmHg
 - ii. PCWP \leq 15 mmHg
 - iii. PVR $>$ 3 Wood units
 2. For infants less than one year of age with any of the following conditions, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed:
 - i. Post cardiac surgery
 - ii. Chronic heart disease
 - iii. Chronic lung disease associated with prematurity
 - iv. Congenital diaphragmatic hernia

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with an indication listed in Section II who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

IV. APPENDIX

WHO Classification of Pulmonary Hypertension

1 PAH

- 1.1 Idiopathic (PAH)
- 1.2 Heritable PAH
- 1.3 Drug- and toxin-induced PAH

- 1.4. PAH associated with:
 - 1.4.1 Connective tissue diseases
 - 1.4.2 HIV infection
 - 1.4.3 Portal hypertension
 - 1.4.4 Congenital heart diseases
 - 1.4.5 Schistosomiasis
- 1.5 PAH long-term responders to calcium channel blockers
- 1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement
- 1.7 Persistent PH of the newborn syndrome

2 PH due to left heart disease

- 2.1 PH due to heart failure with preserved LVEF
- 2.2 PH due to heart failure with reduced LVEF
- 2.3 Valvular heart disease
- 2.4 Congenital/acquired cardiovascular conditions leading to post-capillary PH

3 PH due to lung diseases and/or hypoxia

- 3.1 Obstructive lung disease
- 3.2 Restrictive lung disease
- 3.3 Other lung disease with mixed restrictive/obstructive pattern
- 3.4 Hypoxia without lung disease
- 3.5 Developmental lung disorders

4 PH due to pulmonary artery obstruction

- 4.1 Chronic thromboembolic PH
- 4.2 Other pulmonary artery obstructions
 - 4.2.1 Sarcoma (high or intermediate grade) or angiosarcoma
 - 4.2.2 Other malignant tumors
 - Renal carcinoma
 - Uterine carcinoma
 - Germ cell tumours of the testis
 - Other tumours
 - 4.2.3 Non-malignant tumours
 - Uterine leiomyoma
 - 4.2.4 Arteritis without connective tissue disease
 - 4.2.5 Congenital pulmonary artery stenosis
 - 4.2.6 Parasites
 - Hydatidosis

5 PH with unclear and/or multifactorial mechanisms

- 5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders
- 5.2 Systemic and metabolic disorders: Pulmonary Langerhans cell histiocytosis, Gaucher disease, glycogen storage disease, neurofibromatosis, sarcoidosis
- 5.3 Others: chronic renal failure with or without hemodialysis, fibrosing mediastinitis
- 5.4 Complex congenital heart disease

V. REFERENCES

1. Ventavis [package insert]. South San Francisco, CA: Actelion Pharmaceuticals US, Inc.; October 2017.
2. Chin KM, Rubin LJ. Pulmonary arterial hypertension. *J Am Coll Cardiol.* 2008;51(16):1527-1538.
3. McLaughlin VV, Archer SL, Badesch DB, et al. ACCF/AHA 2009 expert consensus document on pulmonary hypertension a report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents and the American Heart Association developed in collaboration with the American College of Chest Physicians; American Thoracic Society, Inc.; and the Pulmonary Hypertension Association. *J Am Coll Cardiol.* 2009;53(17):1573-1619.

4. Badesch DB, Champion HC, Gomez-Sanchez MA, et al. Diagnosis and assessment of pulmonary arterial hypertension. *J Am Coll Cardiol*. 2009;54:S55-S66.
5. Simonneau G, Robbins IM, Beghetti M, et al. Updated clinical classification of pulmonary hypertension. *J Am Coll Cardiol*. 2013;62:D34-S41.
6. Rubin LJ; American College of Chest Physicians. Diagnosis and management of pulmonary arterial hypertension: ACCP evidence-based clinical practice guidelines. *Chest*. 2004;126(1 Suppl):7S-10S.
7. Barst RJ, Gibbs SR, Ghofrani HA, et al. Updated evidence-based treatment algorithm in pulmonary arterial hypertension. *J Am Coll Cardiol*. 2009;54:S78-S84.
8. Taichman DB, Ornelas J, Chung L, et al. Pharmacologic therapy for pulmonary arterial hypertension in adults. CHEST guideline and expert panel report. *Chest*. 2014;46(2):449-475.
9. Abman, SH, Hansmann G, Archer SL, et al. Pediatric pulmonary hypertension: guidelines from the American Heart Association and American Thoracic Society. *Circulation*. 2015;132(21):2037-99.
10. Klinger, JR., Elliott, CG, Levine, DJ, et al. Therapy for Pulmonary Arterial Hypertension in Adults: Update of the CHEST Guidelines and Expert Panel Report. *Chest*. 2019;155(3): 565-586.
11. Galie, N., McLaughlin, VV, Rubin, LJ, Simonneau, G. An overview of the 6th World Symposium on Pulmonary Hypertension. *Eur Respir J* 2019; 53: 1802148; DOI: 10.1183/13993003.02148-2018. Published 24 January 2019.

SPECIALTY GUIDELINE MANAGEMENT

VERZENIO (abemaciclib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Verzenio is indicated:

- A. In combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer.
- B. In combination with fulvestrant for the treatment of women with HR-positive, HER2-negative advanced or metastatic breast cancer with disease progression following endocrine therapy.
- C. As monotherapy for the treatment of adult patients with HR-positive, HER2-negative advanced or metastatic breast cancer with disease progression following endocrine therapy and prior chemotherapy in the metastatic setting.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Hormone receptor status, HER2 status testing results.

III. CRITERIA FOR INITIAL APPROVAL

Breast Cancer

Authorization of 12 months may be granted for the treatment of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative recurrent, advanced, or metastatic breast cancer when the following criteria are met:

- A. Verzenio will be used as monotherapy for a member who has experienced disease progression following endocrine therapy and prior chemotherapy in the metastatic setting; or
- B. Verzenio will be used in combination with fulvestrant; or
- C. Verzenio will be used in combination with an aromatase inhibitor (e.g., letrozole, anastrozole, exemestane).

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for breast cancer who have not experienced disease progression or an unacceptable toxicity.

Reference number(s)
2342-A

V. REFERENCES

1. Verzenio [package insert]. Indianapolis, IN: Eli Lilly and Company; August 2018.
2. The NCCN Drugs & Biologics Compendium 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed August 12, 2019.
3. Dickler MN, Tolaney SM, Rugo HS, et al. MONARCH 1, a phase II study of abemaciclib, a CDK4 and CDK6 inhibitor, as a single agent, in patients with refractory HR+/HER2- metastatic breast cancer. *Clin Cancer Res*. 2017;23(17):5218-5224.
4. Sledge, GW Jr, Toi M, Neven P, et al. MONARCH 2: abemaciclib in combination with fulvestrant in women with HR+/HER2- advanced breast cancer who had progressed while receiving endocrine therapy. *J Clin Oncol*. 2017;35(25):2875-2884.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

VIBERZI
(eluxadoline)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

Ref# 1287-A
Ref# MDC-2 1271-A

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated

FDA-APPROVED INDICATIONS

Viberzi is indicated in adults for the treatment of irritable bowel syndrome with diarrhea (IBS-D).

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has the diagnosis of irritable bowel syndrome with diarrhea (IBS-D)

AND

- The patient does not have any of the following: A) A history of cholecystectomy, B) A history of chronic or severe constipation or sequelae from constipation, or known or suspected mechanical gastrointestinal obstruction, C) Known or suspected biliary duct obstruction; or sphincter of Oddi disease or dysfunction, D) A history of pancreatitis; or structural diseases of the pancreas, including known or suspected pancreatic duct obstruction, E) Severe hepatic impairment (Child-Pugh Class C), F) Alcoholism, alcohol abuse or alcohol addiction, or a patient who drinks more than 3 alcoholic beverages per day

RATIONALE

These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Viberzi is indicated in adults for the treatment of irritable bowel syndrome with diarrhea (IBS-D).

Viberzi is contraindicated in patients with a history of cholecystectomy, known or suspected biliary duct obstruction or sphincter of Oddi disease or dysfunction, alcoholism, alcohol abuse, or alcohol addiction, or in patients who drink more than 3 alcoholic beverages per day, a history of pancreatitis or structural diseases of the pancreas, including known or suspected pancreatic duct obstruction, severe hepatic impairment (Child-Pugh class C) and a history of chronic or severe constipation or sequelae from constipation, or known or suspected mechanical gastrointestinal obstruction.¹⁻³

REFERENCES

1. Viberzi [package insert]. Madison, New Jersey: Allergan; June 2018.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed September 2018.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed September 2018.

Written by: UM Development (CT)
Date Written: 06/2015
Revised: 08/2015, (SE) 06/2016 (created separate Med D): (KM) 08/2016 (no clinical changes); (DS) 08/2017, 09/2018 (no clinical changes) (combined comm and MDC-2)
Reviewed: Medical Affairs (LCB) 06/2015, 08/2015; (JG) 08/2017
External Review: 06/2015, 12/2015, 12/2017, 12/2018

CRITERIA FOR APPROVAL

- | | | | |
|---|---|-----|----|
| 1 | Does the patient have the diagnosis of irritable bowel syndrome with diarrhea (IBS-D)? | Yes | No |
| 2 | Does the patient have any of the following: A) A history of cholecystectomy, B) A history of chronic or severe constipation or sequelae from constipation, or known or suspected mechanical gastrointestinal obstruction, C) Known or suspected biliary duct obstruction; or sphincter of Oddi disease or dysfunction, D) A history of pancreatitis; or structural diseases of the pancreas, including known or suspected pancreatic duct obstruction, E) Severe hepatic impairment (Child-Pugh Class C), F) Alcoholism, alcohol abuse or alcohol addiction, or a patient who drinks more than 3 alcoholic beverages per day? | Yes | No |

Mapping Instructions (1287-A)			
	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you have irritable bowel syndrome with diarrhea.</p> <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No approvable diagnosis]</p>
2.	Deny	Approve, 36 months	<p>You do not meet the requirements of your plan. Your plan covers this drug when you do not have any of these conditions:</p> <ul style="list-style-type: none"> - A history of cholecystectomy (gallbladder removal surgery) - A history of chronic or severe constipation or sequelae from constipation, or known or suspected mechanical gastrointestinal obstruction - Known or suspected biliary duct obstruction; or sphincter of Oddi disease or dysfunction - A history of pancreatitis; or structural diseases of the pancreas, including known or suspected pancreatic duct obstruction - Severe hepatic impairment (Child-Pugh Class C) - Alcoholism, alcohol abuse or alcohol addiction, or you drink more than 3 alcoholic beverages per day <p>Your request has been denied based on the information we have.</p> <p>[Short Description: Contraindication to therapy]</p>

Guidelines for Approval (MDC-2 1271-A)	
Duration of Approval	12 Months
Set 1	
Yes to question(s)	No to question(s)
1	2

Mapping Instructions (MDC-2 1271-A)			
	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you have irritable bowel syndrome with diarrhea.</p> <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No approvable diagnosis]</p>
2.	Deny	Approve, 12 months	<p>You do not meet the requirements of your plan. Your plan covers this drug when you do not have any of these conditions:</p> <ul style="list-style-type: none"> - A history of cholecystectomy (gallbladder removal surgery) - A history of chronic or severe constipation or sequelae from constipation, or known or suspected mechanical gastrointestinal obstruction - Known or suspected biliary duct obstruction; or sphincter of Oddi disease or dysfunction - A history of pancreatitis; or structural diseases of the pancreas, including known or suspected pancreatic duct obstruction - Severe hepatic impairment (Child-Pugh Class C) - Alcoholism, alcohol abuse or alcohol addiction, or you drink more than 3 alcoholic beverages per day <p>Your request has been denied based on the information we have.</p> <p>[Short Description: Contraindication to therapy]</p>

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS **GLUCAGON-LIKE PEPTIDE 1 (GLP-1) RECEPTOR AGONIST**

BRAND NAME*
(generic)

VICTOZA
(liraglutide)

Status: CVS Caremark Criteria

Type: Initial Prior Authorization with Quantity Limit

Ref # 479-C

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Victoza is indicated:

- as an adjunct to diet and exercise to improve glycemic control in patients 10 years and older with type 2 diabetes mellitus.
- to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease.

Limitations of Use

- Victoza should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis, as it would not be effective in these settings.
- The concurrent use of Victoza and prandial insulin has not been studied.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has been receiving GLP-1 Agonist therapy for at least 3 months. [Note: Examples of GLP-1 Agonists are Adlyxin, Bydureon, Byetta, Ozempic, Tanzeum, Trulicity, Victoza].

AND

- The patient has demonstrated a reduction in A1c (hemoglobin A1c) since starting GLP-1 Agonist therapy
- OR**
- The patient has established cardiovascular disease

OR

- The patient has a diagnosis of type 2 diabetes mellitus

AND

- The patient has experienced an inadequate treatment response, intolerance or contraindication to metformin

OR

- The patient requires combination therapy AND has an A1c (hemoglobin A1c) of 7.5 percent or greater

OR

- The patient has established cardiovascular disease

Quantity Limits apply.

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Victoza is indicated as an adjunct to diet and

exercise to improve glycemic control in adults with type 2 diabetes mellitus. Victoza is also indicated to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease. Victoza can be administered once daily at any time of day, independently of meals, and can be injected subcutaneously in the abdomen, thigh or upper arm. The injection site and timing can be changed without dose adjustment.¹⁻³

Clinical guidelines from the American Diabetes Association and the American Association of Clinical Endocrinologists and American College of Endocrinology for the management of hyperglycemia in type 2 diabetes indicate that metformin monotherapy should be started at diagnosis of type 2 diabetes unless there are contraindications. Metformin is effective and safe, is inexpensive, and may reduce risk of cardiovascular events and death. In patients with contraindications or intolerance of metformin, initial therapy should be based on patient factors; consider a drug from another class.

The clinical guidelines also state that the A1c test is the major tool for assessing glycemic control and has strong predictive value for diabetes complications. Thus, A1c testing should be performed routinely in all patients with diabetes at initial assessment and as part of continuing care. The guidelines set goals for therapeutic effectiveness which must be evaluated frequently (e.g., every 3 months) until stable, using multiple criteria, including A1c. Less frequent monitoring is acceptable once targets are achieved.⁴⁻⁵ Therefore, continued use of any GLP-1 Agonist (e.g., Adlyxin, Byetta, Bydureon, Ozempic, Tanzeum, Trulicity, and Victoza) will be approved for patients who have demonstrated a reduction in A1c since starting GLP-1 Agonist therapy for at least three months.

If the A1c target is not achieved after approximately 3 months and patient does not have atherosclerotic cardiovascular disease (ASCVD) or chronic kidney disease (CKD), consider a combination of metformin and one of the preferred six treatment options: sulfonylurea, thiazolidinedione, dipeptidyl peptidase 4 (DPP-4) inhibitors, sodium-glucose cotransporter 2 (SGLT2) inhibitors, glucagon-like peptide 1 (GLP-1) receptor agonists, or basal insulin; the choice of which agent to add is based on drug-specific effects and patient factors. For patients in whom ASCVD, Heart Failure, or CKD predominates, the best choice for a second agent is a GLP-1 receptor agonist or SGLT2 inhibitor with demonstrated cardiovascular risk reduction, after consideration of drug-specific and patient factors.⁴⁻⁵

In patients with an initial A1c of 7.5% or greater, or in patients who are unable to achieve their glycemic goals with monotherapy, combination therapy is recommended⁴⁻⁵

The LEADER trial was a multi-national, multi-center, placebo-controlled, double-blind trial. Patients with inadequately controlled type 2 diabetes and atherosclerotic cardiovascular disease were randomized to Victoza 1.8 mg or placebo. During the trial, investigators could modify anti-diabetic and cardiovascular medications to achieve local standard of care treatment targets with respect to blood glucose, lipid, and blood pressure.¹ Treatment with subcutaneous liraglutide daily in addition to standard care significantly reduced the rate of composite cardiovascular events (cardiovascular death, nonfatal stroke, and nonfatal myocardial infarction) compared with placebo.¹ Therefore, Victoza (liraglutide) will be approved for initial therapy and continuation of therapy for patients have established cardiovascular disease.

Victoza slows gastric emptying, which reduces the rate at which postprandial glucose appears in the circulation, reduces food intake, and is associated with weight loss.¹⁻³ A quantity limit is in place to aid proper utilization of Victoza. At maximum approved dosing for Victoza, three (3) prefilled pens will be allowed for a 30 day supply (9 prefilled pens per 90 day supply).

REFERENCES

1. Victoza [package insert]. Princeton, NJ: Novo Nordisk; June 2019.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed July 2019.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed July 2019.
4. American Diabetes Association (ADA) Standards of Medical Care in Diabetes-2019—*Diabetes Care*. 2019; 42(Supplement 1).

5. Garber AJ, et al. AACE/ACE Consensus Statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the Comprehensive Type 2 Diabetes Management Algorithm 2019, *Endocr Pract.* 2019; 25 (No 1). 69-100

Written by: UM Development (NB)

Date Written: 02/2010

Revised: (SE) 08/2010, 04/2011 (revised renewal question) 08/2010 (2)), (SE/SB) 08/2011, 08/2012, (PL) 10/2012 (extended duration), (SE) 11/2012, (SE) 07/2013 (created commercial version); (PL) 07/2013, (PL) 07/2014; (CF) 07/2015, (SF) 07/2016, 07/2017, 08/2017 (added CV indication), 07/2018 (updated renewal question), 07/2019 (no clinical changes)

Reviewed: Medical Affairs (WF, MD) 02/2010, (KP) 08/2010, 04/2011, 08/2011, (DHR) 08/2012, 10/2012, (KP) 11/2012; (DNC) 07/2013, 07/2014, 07/2015; (MES) 07/2016, 07/2017, (MC) 09/2017, (ME) 07/2018. (CHART) 08/01/2019
External Review: 03/2010, 12/2010, 12/2011, 10/2012, 10/2013, 10/2014, 10/2015, 10/2016, 10/2017, 10/2018, 10/2019

CRITERIA FOR APPROVAL

1	Has the patient been receiving GLP-1 Agonist therapy for at least 3 months? [Note: Examples of GLP-1 Agonists are Adlyxin, Bydureon, Byetta, Ozempic, Tanzeum, Trulicity, Victoza] [If no, then skip to question 3.]	Yes	No
2	Has the patient demonstrated a reduction in A1c (hemoglobin A1c) since starting GLP-1 Agonist therapy? [If no, then skip to question 6.] [If yes, then skip to question 7.]	Yes	No
3	Does the patient have a diagnosis of type 2 diabetes mellitus?	Yes	No
4	Has the patient experienced an inadequate treatment response, intolerance or contraindication to metformin? [If yes, then skip to question 7.]	Yes	No
5	Does the patient require combination therapy AND have an A1c (hemoglobin A1c) of 7.5 percent or greater?	Yes	No
6	Does the patient have established cardiovascular disease?	Yes	No
7	Does the patient require more than 3 prefilled pens per month (or 9 prefilled pens per 3 months)? [RPh Note: If yes, then deny and enter a partial approval for 3 prefilled pens per 25 days (9 per 75 days)]	Yes	No

Mapping Instructions

	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Go to 3	
2.	Go to 7	Go to 6	
3.	Go to 4	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have type 2 diabetes mellitus. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
4.	Go to 7	Go to 5	
5.	Go to 7	Go to 6	

6.	Go to 7	Deny	<p>You do not meet the requirements of your plan. Your plan covers this drug when you meet one of these conditions:</p> <ul style="list-style-type: none"> - You have tried metformin it did not work for you, or you cannot use it - You require combination therapy and you have an A1c (hemoglobin A1c) of 7.5 percent or greater - You have established cardiovascular (heart) disease <p>Your request has been denied based on the information we have. [Short description: No inadequate treatment response, intolerance or contraindication to metformin, No requirement for combination therapy or No established cardiovascular disease]</p>
7.	Deny	Approve, 36 months, 3 prefilled pens per 25 days* (9 per 75 days*)	<p>You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 3 prefilled pens per month (or 9 prefilled pens per 3 months) of the requested drug and strength. You have been approved for the maximum quantity that your plan covers for a duration of 36 months. Your request for additional quantities of the requested drug and strength has been denied. [Short description: Over max quantity]</p>

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS **GLP-1 AGONIST**

BRAND NAME*
(generic)

VICTOZA
(liraglutide)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

Ref # 1006-A

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Victoza is indicated:

- as an adjunct to diet and exercise to improve glycemic control in patients 10 years and older with type 2 diabetes mellitus.
- to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease.

Limitations of Use

- Victoza should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis, as it would not be effective in these settings.
- The concurrent use of Victoza and prandial insulin has not been studied.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has been receiving GLP-1 Agonist therapy for at least 3 months
[Note: Examples of GLP-1 Agonists are Adlyxin, Bydureon, Byetta, Ozempic, Tanzeum, Trulicity, Victoza].
AND
 - The patient has demonstrated a reduction in A1c (hemoglobin A1c) since starting GLP-1 Agonist therapy
OR
 - The patient has established cardiovascular disease**OR**
- The patient has a diagnosis of type 2 diabetes mellitus
AND
 - The patient has experienced an inadequate treatment response, intolerance or contraindication to metformin
OR
 - The patient requires combination therapy **AND** has an A1c (hemoglobin A1c) of 7.5 percent or greater
OR
 - The patient has established cardiovascular disease

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Victoza is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Victoza is also indicated to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease. Victoza can be administered once daily at any time

of day, independently of meals, and can be injected subcutaneously in the abdomen, thigh or upper arm. The injection site and timing can be changed without dose adjustment.¹⁻³

Clinical guidelines from the American Diabetes Association and the American Association of Clinical Endocrinologists and American College of Endocrinology for the management of hyperglycemia in type 2 diabetes indicate that metformin monotherapy should be started at diagnosis of type 2 diabetes unless there are contraindications. Metformin is effective and safe, is inexpensive, and may reduce risk of cardiovascular events and death. In patients with contraindications or intolerance of metformin, initial therapy should be based on patient factors; consider a drug from another class.

The clinical guidelines also state that the A1c test is the major tool for assessing glycemic control and has strong predictive value for diabetes complications. Thus, A1c testing should be performed routinely in all patients with diabetes at initial assessment and as part of continuing care. The guidelines set goals for therapeutic effectiveness which must be evaluated frequently (e.g., every 3 months) until stable, using multiple criteria, including A1c. Less frequent monitoring is acceptable once targets are achieved.⁴⁻⁵ Therefore; continued use of any GLP-1 Agonist (e.g., Adlyxin, Byetta, Bydureon, Ozempic, Tanzeum, Trulicity, and Victoza) will be approved for patients who have demonstrated a reduction in A1c since starting GLP-1 Agonist therapy for at least three months.

If the A1c target is not achieved after approximately 3 months and patient does not have atherosclerotic cardiovascular disease (ASCVD) or chronic kidney disease (CKD), consider a combination of metformin and one of the preferred six treatment options: sulfonylurea, thiazolidinedione, dipeptidyl peptidase 4 (DPP-4) inhibitors, sodium-glucose cotransporter 2 (SGLT2) inhibitors, glucagon-like peptide 1 (GLP-1) receptor agonists, or basal insulin; the choice of which agent to add is based on drug-specific effects and patient factors. For patients in whom ASCVD, Heart Failure, or CKD predominates, the best choice for a second agent is a GLP-1 receptor agonist or SGLT2 inhibitor with demonstrated cardiovascular risk reduction, after consideration of drug-specific and patient factors.⁴⁻⁵

In patients with an initial A1c of 7.5% or greater, or in patients who are unable to achieve their glycemic goals with monotherapy, combination therapy is recommended⁴⁻⁵

The American Diabetes Association reports that because A1c is thought to reflect average glycemia over several months and has strong predictive value for diabetes complications, A1c testing should be performed routinely in all patients with diabetes, at initial assessment and as part of continuing care. Measurement approximately every 3 months determines whether the patient's glycemic targets have been reached and maintained.⁴ Therefore; continued use of any GLP-1 Agonist (e.g., Adlyxin, Byetta, Bydureon, Ozempic, Tanzeum, Trulicity, and Victoza) will be approved for patients who have demonstrated a reduction in A1c since starting GLP-1 Agonist therapy for at least three months.

The LEADER trial was a multi-national, multi-center, placebo-controlled, double-blind trial. Patients with inadequately controlled type 2 diabetes and atherosclerotic cardiovascular disease were randomized to Victoza 1.8 mg or placebo. During the trial, investigators could modify anti-diabetic and cardiovascular medications to achieve local standard of care treatment targets with respect to blood glucose, lipid, and blood pressure.¹ Treatment with subcutaneous liraglutide daily in addition to standard care significantly reduced the rate of composite cardiovascular events (cardiovascular death, nonfatal stroke, and nonfatal myocardial infarction) compared with placebo.¹ Therefore, Victoza (liraglutide) will be approved for initial therapy and continuation of therapy for patients have established cardiovascular disease.

REFERENCES

1. Victoza [package insert]. Princeton, NJ: Novo Nordisk; June 2019.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed July 2019.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed July 2019.
4. American Diabetes Association (ADA) Standards of Medical Care in Diabetes-2019—*Diabetes Care*. 2019; 42(Supplement 1).
5. Garber AJ, et al. AACE/ACE Consensus Statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the Comprehensive Type 2 Diabetes Management Algorithm 2019, *Endocr Pract*. 2019; 25 (No 1). 69-100.

Written by: UM Development (NB)

Date Written: 02/2010

Revised: (SE) 08/2010, 04/2011 (revised renewal question) 08/2010 (2)), (SE/SB) 08/2011, 08/2012, (PL) 10/2012 (extended duration), (SE) 11/2012, (SE) 07/2013 (created MDC-2 version/DOA 12 months/removed quantity limits); (PL) 07/2013, (PL) 12/2013 (clarified Q#2), (PL) 07/2014, (SE) 04/2015 (Removed examples of GLP-1 agonists within criteria question), 04/2015 (CMS Mandated Change); (CF) 07/2015, (SE) 06/2016 (created separate Med D), (SF) 07/2016, 07/2017, 08/2017 (added CV indication), 07/2018 (updated renewal question), 07/2019 (no clinical changes; removed MDC designation)

Reviewed: Medical Affairs (WF, MD) 02/2010, (KP) 08/2010, 04/2011, 08/2011, (DHR) 08/2012, 10/2012, (KP) 11/2012; (DNC) 07/2013, 07/2014; (DHR) 04/2015; (DNC) 07/2015; (MES) 07/2016, 07/2017, (MC) 09/2017, (ME) 07/2018, (CHART) 08/01/2019

External Review: 03/2010, 12/2010, 12/2011, 10/2012, 10/2013, 10/2014, 10/2015, 10/2016, 10/2017, 10/2018, 10/2019

CRITERIA FOR APPROVAL

1	Has the patient been receiving GLP-1 Agonist therapy for at least 3 months? [Note: Examples of GLP-1 Agonists are Adlyxin, Bydureon, Byetta, Ozempic, Tanzeum, Trulicity, Victoza] [If no, then skip to question 3.]	Yes	No
2	Has the patient demonstrated a reduction in A1c (hemoglobin A1c) since starting GLP-1 Agonist therapy? [If no, then skip to question 6.] [If yes, then no further questions.]	Yes	No
3	Does the patient have a diagnosis of type 2 diabetes mellitus?	Yes	No
4	Has the patient experienced an inadequate treatment response, intolerance, or contraindication to metformin? [If yes, then no further questions.]	Yes	No
5	Does the patient require combination therapy AND have an A1c (hemoglobin A1c) of 7.5 percent or greater? [If yes, then no further questions.]	Yes	No
6	Does the patient have established cardiovascular disease?	Yes	No

Guidelines for Approval

Duration of Approval 12 Months

Set 1		Set 2	
Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)
1	None	1	2
2		6	
Set 3		Set 4	
Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)
3	1	3	1
4		5	4
Set 5			
Yes to question(s)	No to question(s)		
3	1		

6	4		
	5		

Mapping Instructions			
	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Go to 3	
2.	Approve, 12 months	Go to 6	
3.	Go to 4	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have type 2 diabetes mellitus. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
4.	Approve, 12 months	Go to 5	
5.	Approve, 12 months	Go to 6	
6.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet one of these conditions: - You have tried metformin it did not work for you, or you cannot use it - You require combination therapy and you have an A1c (hemoglobin A1c) of 7.5 percent or greater - You have established cardiovascular (heart) disease Your request has been denied based on the information we have. [Short description: No inadequate treatment response, intolerance or contraindication to metformin, no requirement for combination therapy or no established cardiovascular disease]

SPECIALTY GUIDELINE MANAGEMENT

VIEKIRA PAK VIEKIRA XR (ombitasvir/paritaprevir/ritonavir/dasabuvir)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Viekira Pak/Viekira XR is indicated for the treatment of adult patients with chronic hepatitis C virus (HCV):

- A. genotype 1b infection without cirrhosis or with compensated cirrhosis
- B. genotype 1a infection without cirrhosis or with compensated cirrhosis for use in combination with ribavirin (RBV)

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

Coverage will not be provided for members with decompensated cirrhosis/moderate or severe hepatic impairment (Child Turcotte Pugh Class B or C).

Note: When the requested drug is being used in a combination therapy regimen, exclusions to the other antiviral drugs also apply.

III. CRITERIA FOR APPROVAL

A. Chronic hepatitis C virus infection, in combination with ribavirin

Note: Members with mixed genotype 1 infection or unknown genotype 1 subtype should follow the criteria for approval for genotype 1a infection.

1. Genotype 1a infection

- a. Authorization of up to 12 weeks total may be granted for members without cirrhosis who are either of the following:
 - i. Treatment-naïve
 - ii. Failed prior treatment with peginterferon alfa (PEG-IFN) and RBV
- b. Authorization of up to 24 weeks total may be granted for members with compensated cirrhosis who are either of the following:
 - i. Treatment-naïve
 - ii. Failed prior treatment with PEG-IFN and RBV

2. Recurrent HCV infection post liver transplantation

Authorization of up to 24 weeks total may be granted for members with recurrent HCV infection post liver transplantation who meet all of the following criteria:

- a. Genotype 1 infection (irrespective of subtype)
- b. Metavir fibrosis score of 2 or lower

B. Chronic hepatitis C virus infection, without ribavirin

Genotype 1b infection

Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who are either of the following:

- 1. Treatment-naïve
- 2. Failed prior treatment with PEG-IFN and RBV

C. HCV and HIV coinfection

Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in section A or B above are met.

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. REFERENCES

- 1. Viekira Pak [package insert]. North Chicago, IL: AbbVie Inc.; July 2018.
- 2. Viekira XR [package insert]. North Chicago, IL: AbbVie Inc.; July 2018.
- 3. AASLD/IDSA/IAS–USA. Recommendations for testing, managing, and treating hepatitis C. <http://www.hcvguidelines.org>. Last changes made May 24, 2018. Accessed August 03, 2018.

SPECIALTY GUIDELINE MANAGEMENT

SABRIL (vigabatrin) tablets and powder for oral solution VIGADRONE (vigabatrin) powder for oral solution vigabatrin powder for oral solution

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. **Infantile spasms:** Monotherapy for pediatric patients with infantile spasms one month to two years of age for whom the potential benefits outweigh the potential risk of vision loss.
2. **Complex Partial Seizures:** Adjunctive therapy for adults and pediatric patients ten years of age and older with refractory complex partial seizures who have inadequately responded to several alternative treatments and for whom the potential benefits outweigh the risk of vision loss. Vigabatrin products are not indicated as a first line agent for complex partial seizures.

- B. Compendial Use: Refractory complex partial seizures in children younger than ten years of age who have inadequately responded to at least two alternative treatments.⁴⁻⁶

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Infantile Spasms**

Authorization of 4 weeks may be granted for treatment of infantile spasms in patients less than 2 years of age.

B. **Complex Partial Seizures**

Authorization of 3 months may be granted for treatment of complex partial seizures when member has had an inadequate response to at least two alternative treatments for complex partial seizures.

III. CONTINUATION OF THERAPY

A. **Infantile Spasms**

Authorization of 6 months may be granted for members requesting vigabatrin for continuation of therapy when member has shown substantial clinical benefit from vigabatrin therapy.

B. **Complex Partial Seizures**

Authorization of 12 months may be granted for members requesting vigabatrin for continuation of therapy when member has shown substantial clinical benefit from vigabatrin therapy.

Reference number
1770-A

IV. REFERENCES

1. Sabril [package insert]. Deerfield, IL: Lundbeck Inc.; February 2019.
2. Vigabatrin for oral solution [package insert]. Chestnut Ridge, NY: Par Pharmaceutical; July 2017.
3. Vigadrone [package insert]. Maple grove, MN: Upsher-Smith Laboratories, LLC; May, 2018.
4. CVS Caremark Clinical Program Review. Focus on Seizure Disorders Programs; October 1, 2013.
5. Livingston JH, Beaumont D, Arzimanoglou A, et al: Vigabatrin in the treatment of epilepsy in children. *Br J Clin Pharmacol*. 1989; 27:109S-112S.
6. Luna D, Dulac O, Pajot N, et al: Vigabatrin in the treatment of childhood epilepsies: a single-blind placebo-controlled study. *Epilepsia*. 1989; 30:430-437.
7. Pellock JM, Hrachovy R, Shinnar S, et al. Infantile spasms: A U.S. consensus report. *Epilepsia*. 2010;51:2175-2189.
8. Go CY, Mackay MT, Weiss SK, et al. Evidence-based guideline update: Medical treatment of infantile spasms: Report of the Guideline Development Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. *Neurology*. 2012; 78:1974-1980.
9. Hancock EC, Osborne JP, Edwards SW. Treatment of infantile spasms. *Cochrane Database Syst Rev*. 2013;6:CD001770.
10. Riikonen R. Recent advances in the pharmacotherapy of infantile spasms. *CNS Drugs* 2014; 28:279-290.
11. Pavone P, Striano P, Falsaperla R, et al. Infantile spasms syndrome, West Syndrome and related phenotypes: what we know in 2013. *Brain & Development* 2014; 739-751.
12. Willmore LJ, Abelson MB, Ben-Menachem E, Pellock JM, Shields WD. Vigabatrin: 2008 Update. *Epilepsia*. 2009; 50(2):163-173.
13. Faught E. Vigabatrin therapy for refractory complex partial seizures: review of clinical trial experience in the United States. *Acta Neurol Scand* 2011; 124(Suppl.192):29-35.

SPECIALTY GUIDELINE MANAGEMENT

VIMIZIM (elosulfase alfa)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Vimizim is indicated for patients with Mucopolysaccharidosis type IVA (MPS IVA, Morquio A syndrome).

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: N-acetylgalactosamine 6-sulfatase enzyme assay or genetic testing results supporting diagnosis.

III. CRITERIA FOR INITIAL APPROVAL

Mucopolysaccharidosis IVA (MPS IVA)

Authorization of 12 months may be granted for treatment of MPS IVA when the diagnosis of MPS IVA was confirmed by enzyme assay demonstrating a deficiency of N-acetylgalactosamine 6-sulfatase enzyme activity or by genetic testing.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for Mucopolysaccharidosis type IVA (MPS IVA, Morquio A syndrome) who are responding to therapy (e.g., improvement, stabilization, or slowing of disease progression for 6-minute walk test [6-MWT]).

V. REFERENCES

1. Vimizim [package insert]. Novato, CA: BioMarin Pharmaceutical Inc.; February 2014.

SPECIALTY GUIDELINE MANAGEMENT

VISUDYNE (verteporfin injection)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Visudyne for injection is indicated for the treatment of patients with predominantly classic subfoveal choroidal neovascularization due to age-related macular degeneration, pathologic myopia or presumed ocular histoplasmosis.

B. Compendial Indications

1. Classic subfoveal choroidal neovascularization due to chronic central serous chorioretinopathy
2. Choroidal hemangioma

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Choroidal neovascularization**

Authorization of 6 months may be granted for treatment of predominantly classic subfoveal choroidal neovascularization (CNV) when both of the following criteria are met:

1. Member has predominantly classic subfoveal choroidal neovascularization due to ONE of the following:
 - a. Age-related macular degeneration, **OR**
 - b. Pathologic myopia, **OR**
 - c. Presumed ocular histoplasmosis, **OR**
 - d. Chronic central serous chorioretinopathy (also includes retinal pigment epithelium leakage without evident CNV), **AND**
2. The treatment spot size is less than or equal to 6.4 mm in diameter.

B. **Choroidal hemangioma**

Authorization of 6 months may be granted for treatment of choroidal hemangioma.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment of an indication listed in Section II for members who have demonstrated a positive clinical response to Visudyne therapy.

IV. REFERENCES

1. Visudyne [package insert]. Charleston, SC: Alcamis Carolinas Corporation.; February 2017.

Reference number(s)
3011-A

2. van Rijssen, T.J., van Dijk, E.H.C., Yzer, S., Ohno-Matsui, K., Keunen, J.E.E., Schlingemann, R.O., Sivaprasad, S., Querques, G., Downes, S.M., Fauser, S., Hoyng, C.B., Piccolino, F.C., Chhablani, J.K., Lai, T.Y.Y., Lotery, A.J., Larsen, M., Holz, F.G., Freund, K.B., Yannuzzi, L.A., Boon, C.J.F., Central serous chorioretinopathy: Towards an evidence-based treatment guideline, *Progress in Retinal and Eye Research* (2019), doi: <https://doi.org/10.1016/j.preteyeres.2019.07.003>.
3. Tsipursky MS, Golchet PR, Jampol LM. Photodynamic therapy of choroidal hemangioma in sturge-weber syndrome, with a review of treatments for diffuse and circumscribed choroidal hemangiomas. *Surv Ophthalmol.* 2011; 56 (1): 68-85.

SPECIALTY GUIDELINE MANAGEMENT

VITRAKVI (larotrectinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Vitrakvi is indicated for the treatment of adult and pediatric patients with solid tumors that:

1. have a neurotrophic receptor tyrosine kinase (NTRK) gene fusion without a known acquired resistance mutation,
2. are metastatic or where surgical resection is likely to result in severe morbidity, and
3. have no satisfactory alternative treatments or that have progressed following treatment.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Chart documentation indicating a NTRK gene fusion status.

III. CRITERIA FOR INITIAL APPROVAL

Solid tumors with a NTRK gene fusion

Authorization of 12 months may be granted for treatment of solid tumors when all of the following criteria are met:

- A. The tumors have a NTRK gene fusion without a known acquired resistance mutation, as demonstrated by laboratory testing (e.g., next-generation sequencing [NGS] or fluorescence in situ hybridization [FISH]).
- B. The disease is metastatic or surgical resection is likely to result in severe morbidity.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES

1. Vitrakvi [package insert]. Stamford, CT: Loxo Oncology, Inc.; July 2019.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed September 12, 2019.

SPECIALTY GUIDELINE MANAGEMENT

VIVITROL (naltrexone for extended-release injectable suspension)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

- A. Vivitrol is indicated for the treatment of alcohol dependence in patients who are able to abstain from alcohol in an outpatient setting prior to initiation of treatment with Vivitrol. Patients should not be actively drinking at the time of initial Vivitrol administration.
- B. Vivitrol is indicated for the prevention of relapse to opioid dependence, following opioid detoxification.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Alcohol Dependence

Authorization of 24 months may be granted for treatment of alcohol dependence.

B. Opioid Dependence

Authorization of 24 months may be granted for prevention of relapse to opioid dependence.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Vivitrol [package insert]. Waltham, MA: Alkermes, Inc.; December 2015.

SPECIALTY GUIDELINE MANAGEMENT

VIZIMPRO (dacomitinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Vizimpro is indicated for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletion or exon 21 L858R substitution mutations as detected by an FDA-approved test.

All other indications are considered experimental/investigational and not medically necessary.

Compendial Uses

NSCLC, recurrent, advanced or metastatic sensitizing EGFR mutation-positive

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: For NSCLC, EGFR mutation testing results.

III. CRITERIA FOR INITIAL APPROVAL

Non-small cell lung cancer (NSCLC)

Authorization of 12 months may be granted for treatment of recurrent, advanced or metastatic NSCLC when the member has sensitizing EGFR mutation-positive disease.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced an unacceptable toxicity.

V. REFERENCES

1. Vizimpro [package insert]. New York, NY: Pfizer, Inc.; September 2018.
2. The NCCN Drugs & Biologics Compendium 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 15, 2019.
3. The NCCN Clinical Practice Guidelines in Oncology Non-Small Cell Lung Cancer (Version 3.2019). 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 14, 2019.

Reference number(s)
2770-A

4. Wu YL, Cheng Y, Zhou X, et al. Dacomitinib versus gefitinib as first-line treatment for patients with *EGFR*-mutation-positive non-small-cell lung cancer (ARCHER 1050): a randomised, open-label, phase 3 trial. *Lancet Oncology*. 2017; 18:1454-66.

SPECIALTY GUIDELINE MANAGEMENT

VONVENDI [von Willebrand factor (recombinant)]

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Vonvendi is indicated for use in adults (age 18 and older) diagnosed with von Willebrand disease (VWD) for:

1. On-demand treatment and control of bleeding episodes
2. Perioperative management of bleeding

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Von Willebrand Disease

Indefinite authorization may be granted for treatment of vWD when any of the following criteria is met:

- A. Member has type 1, 2A, 2M, or 2N vWD and has had an insufficient response to desmopressin or a documented clinical reason for not using desmopressin (see Appendix).
- B. Member has type 2B or type 3 vWD.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. APPENDIX

Clinical Reasons For Not Utilizing Desmopressin in Patients with Type 1, 2A, 2N and 2M vWD

- A. Age < 2 years
- B. Pregnancy
- C. Fluid/electrolyte imbalance
- D. High risk for cardiovascular or cerebrovascular disease (especially the elderly)
- E. Predisposition to thrombus formation
- F. Trauma requiring surgery
- G. Life-threatening bleed
- H. Contraindication or intolerance to desmopressin
- I. Severe type 1 von Willebrand disease

Reference number(s)
1951-A

V. REFERENCES

1. Vonvendi [package insert]. Westlake Village, CA: Baxalta US Inc.; July 2018.
2. National Hemophilia Foundation. MASAC recommendations concerning products licensed for the treatment of hemophilia and other bleeding disorders. Revised April 2018. MASAC Document # 253. Accessed December 19, 2018.
3. National Hemophilia Foundation. MASAC recommendations regarding the treatment of von Willebrand disease. Revised November 2016. MASAC Document #244. Accessed December 19, 2018.
4. National Institutes of Health. The diagnosis, evaluation, and management of von Willebrand disease. Bethesda, MD: US Dept of Health and Human Services, National Institutes of Health; 2007. NIH publication No. 08-5832.
5. Stimate [package insert]. King of Prussia, PA: CSL Behring LLC; June 2013.
6. Leissinger C, Carcao M, Gill JC, et al. Desmopressin (DDAVP) in the management of patients with congenital bleeding disorders. *Haemophilia*. 2014;20:158-167.

SPECIALTY GUIDELINE MANAGEMENT

VOSEVI (sofosbuvir/velpatasvir/voxilaprevir)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Vosevi is indicated for the treatment of adult patients with chronic hepatitis C virus (HCV) infection without cirrhosis or with compensated cirrhosis (Child-Pugh A) who have:

- Genotype 1, 2, 3, 4, 5, or 6 infection and have previously been treated with an HCV regimen containing an NS5A inhibitor
- Genotype 1a or 3 infection and have previously been treated with an HCV regimen containing sofosbuvir without an NS5A inhibitor

Additional benefit of Vosevi over sofosbuvir/velpatasvir was not shown in adults with genotype 1b, 2, 4, 5, or 6 infection previously treated with sofosbuvir without an NS5A inhibitor.

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

Coverage will not be provided for members with decompensated cirrhosis/moderate or severe hepatic impairment (Child Turcotte Pugh Class B or C)

Note: When the requested drug is being used in a combination therapy regimen, exclusions to the other antiviral drugs also apply.

III. CRITERIA FOR INITIAL APPROVAL

A. Chronic hepatitis C virus infection, without ribavirin

1. Genotype 1a infection

- a. Authorization of up to 12 weeks total may be granted for members who failed prior treatment with a sofosbuvir-containing regimen without an HCV NS5A inhibitor.
- b. Authorization of up to 12 weeks total may be granted for members who failed prior treatment with an HCV NS5A inhibitor-containing regimen.

2. Genotype 1b infection

Authorization of up to 12 weeks total may be granted for members who failed prior treatment with an HCV NS5A inhibitor-containing regimen.

3. Genotype 2 infection

Authorization of up to 12 weeks total may be granted for members who failed prior treatment with an HCV NS5A inhibitor-containing regimen.

4. Genotype 3 infection

- a. Authorization of up to 12 weeks total may be granted for members who failed prior treatment with any direct-acting antiviral regimen (eg, NS5A- or sofosbuvir-containing regimen).
- b. Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis who are treatment naïve and have the Y93H substitution associated with velpatasvir resistance.
- c. Authorization of up to 12 weeks total may be granted for members who failed prior treatment with PEG-IFN and RBV and meet one of the following:
 - i. Member does not have cirrhosis and has the Y93H substitution associated with velpatasvir resistance.
 - ii. Member has compensated cirrhosis.

5. Genotype 4, 5, or 6 infection

Authorization of up to 12 weeks total may be granted for members who failed prior treatment with any direct-acting antiviral regimen (eg, NS5A- or sofosbuvir-containing regimen).

B. Chronic hepatitis C virus infection, in combination with ribavirin

Genotype 3 infection

Authorization of up to 12 weeks total may be granted for members with cirrhosis who failed prior treatment with an HCV NS5A inhibitor-containing regimen.

C. HCV and HIV Coinfection

Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in Section A or B above are met.

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. REFERENCES

1. Vosevi [package insert]. Foster City, CA: Gilead Sciences, Inc.; November 2017.
2. AASLD/IDSA/IAS–USA. Recommendations for testing, managing, and treating hepatitis C. <http://www.hcvguidelines.org>. Last changes made May 24, 2018. Accessed August 03, 2018.

SPECIALTY GUIDELINE MANAGEMENT

VOTRIENT (pazopanib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Advanced renal cell carcinoma (RCC)
2. Advanced soft tissue sarcoma (STS) in patients who have received prior chemotherapy

Limitations of Use: The efficacy of Votrient for the treatment of patients with adipocytic STS or gastrointestinal stromal tumors has not been demonstrated.

B. Compendial Uses

1. Relapsed or surgically unresectable stage IV RCC
2. Uterine sarcoma
3. Soft tissue sarcoma that is not an adipocytic sarcoma
4. Thyroid carcinoma (medullary, papillary, Hürthle cell, or follicular)
5. Bone cancer of one of the following subtypes:
 - a. Chordoma
 - b. Chondrosarcoma
 - c. Osteosarcoma

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Renal Cell Carcinoma**

Authorization of 12 months may be granted for treatment of relapsed, metastatic, or unresectable renal cell carcinoma.

B. **Soft Tissue Sarcoma (STS)**

Authorization of 12 months may be granted for treatment of soft tissue sarcoma (STS) that is not an adipocytic sarcoma.

C. **Uterine Sarcoma**

Authorization of 12 months may be granted for treatment of recurrent or metastatic uterine sarcoma.

D. **Thyroid Carcinoma**

Authorization of 12 months may be granted for treatment of radioiodine refractory papillary, Hürthle cell, or follicular thyroid carcinoma.

Reference number
2009-A

E. Medullary Thyroid Carcinoma

Authorization of 12 months may be granted for the treatment of medullary thyroid carcinoma when either of the following criteria are met:

1. Member has an intolerance or contraindication to cabozantinib and vandetanib.
2. Member has disease progression on cabozantinib or vandetanib.

F. Bone cancer

Authorization of 12 months may be granted for treatment of one of the following subtypes of bone cancer:

1. Chordoma
2. Chondrosarcoma
3. Osteosarcoma

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy for an indication outlined in Section II when there is no evidence of unacceptable toxicity or disease progression on the current regimen.

IV. REFERENCES

1. Votrient [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; May 2017.
2. The NCCN Drugs & Biologics Compendium®© 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed May 28, 2019.
3. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Kidney Cancer. Version 4.2019. Accessed May 28, 2019. https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf.
4. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Soft Tissue Sarcoma. Version 2.2019. Accessed May 28, 2019. https://www.nccn.org/professionals/physician_gls/pdf/sarcoma.pdf.
5. Ganjoo KN, Villalobos VM, Kamaya A, et al. A multicenter phase II study of pazopanib in patients with advanced gastrointestinal stromal tumors (GIST) following failure of at least imatinib and sunitinib. *Ann Oncol* 2014;25(1):236-40.
6. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Uterine Neoplasms. Version 3.2019. Accessed May 28, 2019. https://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf.
7. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Thyroid Carcinoma. Version 1.2019. Accessed May 28, 2019. https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf.
8. Winette TA van der Graaf, Jean-Yves Blay, et al. Pazopanib for metastatic soft-tissue sarcoma (PALETTE): a randomized, double blind, placebo-controlled phase 3 trial. *The Lancet*. 2012; 379 (9829): 1879-1886.
9. Kenji Nakano, Noriko Motoi, et al. Differences in the responses to pazopanib and the prognoses of soft tissue sarcomas by their histological eligibility for the PALETTE study. *Japanese Journal of Clinical Oncology*. 2015. 45 (5): 449-455.
10. Astrid Lippelaar, Sander Dijkstra, et al. Efficacy of pazopanib and sunitinib in advanced axial chordoma: a single reference centre case series. *Clin Sarcoma Res*. 2016. 6: 19..Robin L. Jones, Daniela Katz, et al. Clinical benefit of antiangiogenic therapy in advanced and metastatic chondrosarcoma. *Med Oncol*. 2017. 34: 167
11. Akmal Safwat, Anders Boysen, Arne Lücke & Philip Rossen. Pazopanib in metastatic osteosarcoma: Significant clinical response in three consecutive patients, *Acta Oncologica*. 53:10, 1451-1454.

SPECIALTY GUIDELINE MANAGEMENT

VPRIV (velaglucerase alfa)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

VPRIV is indicated for long-term enzyme replacement therapy (ERT) for patients with type 1 Gaucher disease.

B. Compendial Uses

Type 3 Gaucher disease

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: beta-glucocerebrosidase enzyme assay or genetic testing results supporting diagnosis

III. CRITERIA FOR INITIAL APPROVAL

Gaucher disease type 1

Authorization of 12 months may be granted for treatment of Gaucher disease type 1 when the diagnosis of Gaucher disease was confirmed by enzyme assay demonstrating a deficiency of beta-glucocerebrosidase (glucosidase) enzyme activity or by genetic testing.

Gaucher disease type 3

Authorization of 12 months may be granted for treatment of Gaucher disease type 3 when the diagnosis of Gaucher disease was confirmed by enzyme assay demonstrating a deficiency of beta-glucocerebrosidase (glucosidase) enzyme activity or by genetic testing.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for Gaucher disease type 1 or type 3 who are not experiencing an inadequate response or any intolerable adverse events from therapy.

V. REFERENCES

1. VPRIV [package insert]. Lexington, MA: Shire Human Genetic Therapies, Inc.; April 2015.

Reference number
2058-A

2. Pastores GM, Hughes DA. Gaucher Disease. [Updated June 21, 2018]. In: Pagon RA, Adam MP, Ardinger HH, et al, editors. GeneReviews® [Internet]. Seattle, WA: University of Washington, Seattle; 1993-2018.
3. Kaplan P, Baris H, De Meirleir L, et al. Revised recommendations for the management of Gaucher disease in children. *Eur J Pediatr*. 2013;172:447-458.
4. Vellodi A, Tylki-Szymanska A, Davies EH, et al. Management of neuronopathic Gaucher disease: revised recommendations. European Working Group on Gaucher Disease. *J Inherit Metab Dis*. 2009;32(5):660.

SPECIALTY GUIDELINE MANAGEMENT

VUMERITY (diroximel fumarate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Vumerity is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Relapsing forms of multiple sclerosis (MS)

Authorization of 12 months may be granted to members who have been diagnosed with a relapsing form of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse).

B. Clinically isolated syndrome

Authorization of 12 months may be granted to members for the treatment of clinically isolated syndrome.

III. CONTINUATION OF THERAPY

For all indications: Authorization of 12 months may be granted to members who are experiencing disease stability or improvement while receiving Vumerity.

IV. OTHER CRITERIA

Members will not use Vumerity concomitantly with other medications used for the treatment of multiple sclerosis, excluding Ampyra.

V. REFERENCES

1. Vumerity [package insert]. Cambridge, MA: Biogen; October 2019.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME (generic)	VUMERITY (diroximel fumarate)
Status: CVS Caremark Criteria Type: Initial Prior Authorization	MDC Ref # 3397-A

FDA-APPROVED INDICATIONS¹

Vumerity is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

CRITERIA FOR APPROVAL			
1	Does the patient have a relapsing form of multiple sclerosis (MS) (e.g., relapsing-remitting MS, active secondary progressive MS)? [If yes, no further questions.]	Yes	No
2	Is the requested drug prescribed for clinically isolated syndrome?	Yes	No

Guidelines for Approval			
Duration of Approval		12 Months	
Set 1: Relapsing form of MS		Set 2: Clinically isolated syndrome	
Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)
1	None	2	1

Mapping Instructions			
	Yes		No
1.	Approve, 12 months		Go to 2
2.	Approve, 12 months		Deny

RATIONALE

These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to ensure that patients follow selection elements noted in labeling and/or practice guidelines in order to decrease the potential for inappropriate utilization.

REFERENCES

1. Vumerity [package insert]. Cambridge, MA: Biogen; October 2019.

DOCUMENT HISTORY

Created: Specialty Clinical Development (SP) 11/2019
 Revised:
 Reviewed: CDPR/ MMF 11/2019
 External Review: 11/2019

SPECIALTY GUIDELINE MANAGEMENT

VYND AQEL (tafamidis meglumine) VYNDAMAX (tafamidis)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Vyndaqel and Vyndamax are transthyretin stabilizers indicated for the treatment of the cardiomyopathy of wild type or hereditary transthyretin-mediated amyloidosis (ATTR-CM) in adults to reduce cardiovascular mortality and cardiovascular-related hospitalization.

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

- A. Biopsy results or technetium-labeled bone scintigraphy tracing results confirming presence of amyloid deposits
- B. Echocardiography or cardiac magnetic resonance imaging results confirming cardiac involvement
- C. For members with hereditary ATTR-CM: results confirming a mutation of the transthyretin (TTR) gene
- D. For members with wild type ATTR-CM: immunohistochemical analysis, scintigraphy, or mass spectrometry results confirming transthyretin precursor proteins
- E. For continuation of therapy: Medical record documentation confirming the member demonstrates a beneficial response to treatment (e.g., improvement in rate of disease progression as demonstrated by distance walked on the 6-minute walk test, the Kansas City Cardiomyopathy Questionnaire—Overall Summary (KCCQ-OS) score, cardiovascular-related hospitalizations, NYHA classification of heart failure, left ventricular stroke volume, NT-proBNP level)

III. CRITERIA FOR INITIAL APPROVAL

Cardiomyopathy of Wild Type or Hereditary Transthyretin-mediated Amyloidosis¹⁻²

Authorization of 12 months may be granted for treatment of cardiomyopathy of wild type or hereditary transthyretin-mediated amyloidosis (ATTR-CM) when all of the following criteria are met:

- A. The diagnosis is confirmed by presence of amyloid deposits on analysis of biopsy from cardiac or noncardiac sites (e.g., fat aspirate, gastrointestinal sites, salivary glands, bone marrow) or by technetium-labeled bone scintigraphy tracing
- B. Cardiac involvement was confirmed by echocardiography or cardiac magnetic resonance imaging (e.g., end-diastolic interventricular septal wall thickness exceeding 12 mm)
- C. For members with hereditary ATTR-CM, presence of a mutation of the TTR gene was confirmed.

- D. For members with wild type ATTR-CM, presence of transthyretin precursor proteins was confirmed by immunohistochemical analysis, scintigraphy, or mass spectrometry.
- E. The member exhibits clinical symptoms of cardiomyopathy and heart failure (e.g., dyspnea, fatigue, orthostatic hypotension, syncope, peripheral edema).
- F. The member is not a liver transplant recipient.
- G. The requested medication will not be used in combination with inotersen (Tegsedi) or patisiran (Onpattro).

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for the continued treatment of ATTR-CM when all of the following criteria are met:

- A. The member must have met all initial authorization criteria.
- B. The member must have demonstrated a beneficial response to treatment with tafamidis therapy [e.g., improvement in rate of disease progression as demonstrated by distance walked on the 6-minute walk test, the Kansas City Cardiomyopathy Questionnaire–Overall Summary (KCCQ-OS) score, cardiovascular-related hospitalizations, NYHA classification of heart failure, left ventricular stroke volume, N-terminal B-type natriuretic peptide (NT-proBNP) level]. Documentation from the medical record must be provided.

REFERENCES

1. Vyndaqel and Vydamax [package insert]. New York, NY: Pfizer Labs.; May 2019.
2. Maurer MS, Schwartz JH, Gundapaneni B, et al. Tafamidis treatment for patients with transthyretin amyloid cardiomyopathy. N Engl J Med. 2018 Sep 13; 379(11):1007-1016.

SPECIALTY GUIDELINE MANAGEMENT

VYONDYS 53 (golodirsen)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Vyondys 53 is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping.

This indication is approved under accelerated approval based on an increase in dystrophin production in skeletal muscle observed in patients treated with Vyondys 53. Continued approval for this indication may be contingent upon verification of a clinical benefit in confirmatory trials.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
Laboratory confirmation of Duchenne muscular dystrophy (DMD) diagnosis with a *DMD* gene mutation that is amenable to exon 53 skipping (refer to examples in Appendix).

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a physician who specializes in the treatment of DMD.

IV. CRITERIA FOR INITIAL APPROVAL

A. Duchenne Muscular Dystrophy

Authorization of 6 months may be granted for treatment of DMD when all of the following criteria are met:

1. Genetic testing was conducted to confirm the diagnosis of DMD and to identify the specific type of *DMD* gene mutation.
2. The *DMD* gene mutation is amenable to exon 53 skipping (refer to examples in appendix).
3. Treatment with Vyondys 53 is initiated before the age of 16.
4. Member is able to achieve an average distance of at least 250 meters while walking independently over 6 minutes.

V. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members requesting continuation of therapy when the member has demonstrated a response to therapy as evidenced by remaining ambulatory (e.g. able to walk with or without assistance, not wheelchair dependent).

VI. APPENDIX

Examples of DMD gene mutations (exon deletions) amenable to exon 53 skipping

1. Deletion of exon 52
2. Deletion of exon 45-52
3. Deletion of exon 47-52
4. Deletion of exon 48-52
5. Deletion of exon 49-52
6. Deletion of exon 50-52

VII. REFERENCES

1. Vyondys 53 [package insert]. Cambridge, MA: Sareta Therapeutics; December 2019.
2. Watanabe N, Nagata T, Satou Y, et al. NS-065/NCNP-01: An Antisense Oligonucleotide for Potential Treatment of Exon 53 Skipping in Duchenne Muscular Dystrophy. *Mol Ther Nucleic Acids*. 2018;13:442–449. doi:10.1016/j.omtn.2018.09.017
3. Vyondys 53™ (golodirsen) eDossier. AMCP Formulary Decisions. AmerisourceBergen Corporation. Conshohocken, PA. Available at: www.formularydecisions.com. Accessed December 20, 2019.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME (generic)	VYONDYS 53 (golodirsen)
Status: CVS Caremark Criteria Type: Initial Prior Authorization	MDC Ref #3464-A

FDA-APPROVED INDICATIONS

Vyondys 53 is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping.

CRITERIA FOR APPROVAL

1	Does the patient have a diagnosis of Duchenne muscular dystrophy? [If no, no further questions.]	Yes	No
2	Does the patient have a confirmed mutation of the <i>DMD</i> gene that is amenable to exon 53 skipping?	Yes	No

Guidelines for Approval	
Duration of Approval	12 months
Set 1: Duchenne muscular dystrophy	
Yes to question(s)	No to question(s)
1	None
2	

Mapping Instructions	
	Yes
1. Go to 2	Deny
2. Approve, 12 months	Deny

RATIONALE

These criteria meet the Medicare Part D definition of a medically accepted indication. This definition includes uses which are approved by the FDA or supported by a citation included, or approved for inclusion, in one of the Medicare approved compendia.

The intent of the criteria is to ensure that patients follow selection elements noted in labeling and/or practice guidelines in order to decrease the potential for inappropriate utilization.

REFERENCES

1. Vyondys 53 [package insert]. Cambridge, MA: Sarepta Therapeutics; December 2019.
2. Watanabe N, Nagata T, Satou Y, et al. NS-065/NCNP-01: An Antisense Oligonucleotide for Potential Treatment of Exon 53 Skipping in Duchenne Muscular Dystrophy. *Mol Ther Nucleic Acids*. 2018;13:442–449. doi:10.1016/j.omtn.2018.09.017
3. Vyondys 53™ (golodirsen) eDossier. AMCP Formulary Decisions. AmerisourceBergen Corporation. Conshohocken, PA. Available at: www.formularydecisions.com. Accessed December 20, 2019.

DOCUMENT HISTORY

Created: Specialty Clinical Development (ST) 12/2019

Vyondys 53 3464-A MDC 2020.docx

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Revised:
Reviewed: CDPR / MMF 01/2020
External Review: 01/2020

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS **NARCOLEPSY AGENTS**

BRAND NAME*
(generic)

WAKIX
(pitolisant)

Status: CVS Caremark Criteria

Type: Initial Prior Authorization with Quantity Limit

Ref # 3176-C

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Wakix is indicated for the treatment of excessive daytime sleepiness (EDS) in adult patients with narcolepsy.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has narcolepsy confirmed by sleep lab evaluation

AND

- The patient has experienced an inadequate treatment response to a central nervous system (CNS) stimulant (e.g., amphetamine, dextroamphetamine, methylphenidate)

OR

- The patient has experienced an intolerance to a central nervous system (CNS) stimulant (e.g., amphetamine, dextroamphetamine, methylphenidate)

OR

- The patient has a contraindication that would prohibit a trial of central nervous system (CNS) stimulants (e.g., amphetamine, dextroamphetamine, methylphenidate)

AND

- The patient has experienced an inadequate treatment response to armodafinil OR modafinil

OR

- The patient has experienced an intolerance to armodafinil OR modafinil

OR

- The patient has a contraindication that would prohibit a trial of ALL of the following: A) armodafinil, B) modafinil

Quantity Limits Apply.

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Wakix is indicated for the treatment of excessive daytime sleepiness (EDS) in adult patients with narcolepsy.

According to the American Academy of Sleep Medicine (AASM), successful treatment of hypersomnia of central origin requires an accurate diagnosis, individual tailoring of therapy to produce the fullest possible return of normal function, and regular follow-up to monitor response to treatment. The evaluation should include a thorough evaluation of other possible contributing causes of excessive daytime sleepiness. The International Classification of Sleep Disorders, Third Edition (ICSD-3) specifies necessary diagnostic tests and criteria for each disorder of central origin. For narcolepsy, a sleep lab evaluation consisting of an overnight polysomnography (PSG) and mean sleep latency tests (MSLT) is recommended to

confirm the diagnosis. Many other conditions produce such sleepiness and can mimic or coexist with a hypersomnia of central origin.⁴

According to AASM guidelines, modafinil is effective for the treatment of daytime sleepiness due to narcolepsy. One additional study of 196 subjects involved assessment of armodafinil (the longer half-life enantiomer of modafinil) for treatment of excessive sleepiness in patients with narcolepsy.⁴ Subjects receiving armodafinil experienced significant improvement in sleepiness as measured by the Mean Wakefulness Test (MWT) mean sleep latency, and in the Clinical Global Impression of Change.⁴ The guidelines also state that amphetamine, dextroamphetamine, and methylphenidate are effective for treatment of daytime sleepiness due to narcolepsy.⁴ Therefore, patients who have an inadequate treatment response, intolerance, or contraindication to a CNS stimulant and either modafinil or armodafinil will be considered for approval.

The recommended dosage range of Wakix in patients with narcolepsy is 17.8 mg to 35.6 mg once daily. Dosage should be titrated, starting with 8.9 mg once daily and increasing to 17.8 mg after one week of therapy. After one week of therapy at 17.8 mg once daily, dosage may be increased to the maximum recommended dosage of 35.6 mg once daily. Patients with moderate hepatic impairment and renal impairment should initiate Wakix at 8.9 mg once daily and increase to a maximum recommended dose of 17.8 mg once daily. Wakix is available as 4.45 mg tablets and 17.8 mg tablets. Approvals will have a limit of 60 tablets per month to allow for the initial starting dose and then up to the maximum recommended daily dose of 35.6 mg.

REFERENCES

1. Wakix [package insert]. Plymouth Meeting, PA: Harmony Biosciences, LLC; August 2019.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed August 2019.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed August 2019.
4. Morgenthaler TI, Vishesh KK, Brown T, et al. Practice Parameters for the Treatment of Narcolepsy and other Hypersomnias of Central Origin. *Sleep* 2007;30(12):1705-11.
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Written by: UM Development (KC)
Date Written: 08/2019
Revised:
Reviewed: Medical Affairs (CHART) 09/05/2019
External Review: 10/2019

CRITERIA FOR APPROVAL

1	Does the patient have a diagnosis of narcolepsy confirmed by sleep lab evaluation?	Yes	No
2	Has the patient experienced an inadequate treatment response to a central nervous system (CNS) stimulant (e.g., amphetamine, dextroamphetamine, methylphenidate)? [If yes, then skip to question 5.]	Yes	No
3	Has the patient experienced an intolerance to a central nervous system (CNS) stimulant (e.g., amphetamine, dextroamphetamine, methylphenidate)? [If yes, then skip to question 5.]	Yes	No
4	Does the patient have a contraindication that would prohibit a trial of central nervous system (CNS) stimulants (e.g., amphetamine, dextroamphetamine, methylphenidate)?	Yes	No

5	Has the patient experienced an inadequate treatment response to armodafinil OR modafinil? [If yes, then skip to question 8.]	Yes	No
6	Has the patient experienced an intolerance to armodafinil OR modafinil? [If yes, then skip to question 8.]	Yes	No
7	Does the patient have a contraindication to that would prohibit a trial of ALL of the following: A) armodafinil, B) modafinil?	Yes	No
8	Does the patient require MORE than the plan allowance of 60 tablets per month? [RPh Note: If yes, then deny and enter a partial approval for 60 tablets/25 days or 180 tablets/75 days.]	Yes	No

Mapping Instructions			
	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have narcolepsy confirmed by sleep lab testing. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
2.	Go to 5	Go to 3	
3.	Go to 5	Go to 4	
4.	Go to 5	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have tried a central nervous system (CNS) stimulant drug (e.g., amphetamine, dextroamphetamine, or methylphenidate) and it either did not work for you, or you cannot use it. Your request has been denied based on the information we have. [Short Description: No inadequate response, intolerance, or contraindication to a CNS stimulant drug]
5.	Go to 8	Go to 6	
6.	Go to 8	Go to 7	
7.	Go to 8	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have tried armodafinil or modafinil and it did not work for you, or you cannot use it. Your request has been denied based on the information we have. [Short Description: No inadequate response, intolerance, or contraindication to armodafinil or modafinil]
8.	Deny	Approve, 12 months, 60 tablets/25 days* or 180 tablets/75 days*	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 60 tablets/month of the requested drug and strength. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity]

*The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.

SPECIALTY GUIDELINE MANAGEMENT

WILATE (von Willebrand factor/coagulation factor VIII complex [human])

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

1. Wilate is indicated in children and adults with von Willebrand Disease (vWD) for:
 - a. On-demand treatment and control of bleeding episodes
 - b. Perioperative management of bleeding
2. Wilate is indicated in adolescents and adults with hemophilia A for:
 - a. Routine prophylaxis to reduce the frequency of bleeding episodes
 - b. On-demand treatment and control of bleeding episodes

B. Compendial Use

Acquired von Willebrand Syndrome

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Von Willebrand Disease**

Indefinite authorization may be granted for treatment of vWD when either of the following criteria is met:

1. Member has type 1, 2A, 2M, or 2N vWD and has had an insufficient response to desmopressin or a documented clinical reason for not using desmopressin (see Appendix B).
2. Member has type 2B or type 3 vWD.

B. **Acquired von Willebrand Syndrome**

Indefinite authorization may be granted for treatment of acquired von Willebrand syndrome.

C. **Hemophilia A**

Indefinite authorization may be granted for the treatment of hemophilia A when the requested medication will be used for either of the following:

1. Member has mild disease (see Appendix A) and has had an insufficient response to desmopressin or a documented clinical reason for not using desmopressin (see Appendix B).
2. Member has moderate or severe disease (see Appendix A).

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. APPENDICES

Appendix A: Classification of Hemophilia by Clotting Factor Level (% Activity) and Bleeding Episodes

Severity	Clotting Factor Level % activity*	Bleeding Episodes
Severe	<1%	Spontaneous bleeding episodes, predominantly into joints and muscles Severe bleeding with trauma, injury or surgery
Moderate	1% to 5%	Occasional spontaneous bleeding episodes Severe bleeding with trauma, injury or surgery
Mild	6% to 40%	Severe bleeding with serious injury, trauma or surgery

*Factor assay levels are required to determine the diagnosis and are of value in monitoring treatment response.

Appendix B: Clinical Reasons For Not Utilizing Desmopressin in Patients with Hemophilia A and Type 1, 2A, 2N and 2M vWD

- Age < 2 years
- Pregnancy
- Fluid/electrolyte imbalance
- High risk for cardiovascular or cerebrovascular disease (especially the elderly)
- Predisposition to thrombus formation
- Trauma requiring surgery
- Life-threatening bleed
- Contraindication or intolerance to desmopressin
- Severe type 1 von Willebrand disease

IV. REFERENCES

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- National Institutes of Health. The diagnosis, evaluation, and management of von Willebrand disease. Bethesda, MD: US Dept of Health and Human Services, National Institutes of Health; 2007. NIH publication No. 08-5832.
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- Leissinger C, Carcao M, Gill JC, et al. Desmopressin (DDAVP) in the management of patients with congenital bleeding disorders. *Haemophilia*. 2014;20:158-167.

Reference number(s)
1952-A

SPECIALTY GUIDELINE MANAGEMENT

WILATE (von Willebrand factor/coagulation factor VIII complex [human])

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

1. Wilate is indicated in children and adults with von Willebrand Disease (VWD) for:
 - a. On-demand treatment and control of bleeding episodes
 - b. Perioperative management of bleeding
2. Wilate is indicated in adolescents and adults with hemophilia A for:
 - a. Routine prophylaxis to reduce the frequency of bleeding episodes
 - b. On-demand treatment and control of bleeding episodes

B. Compendial Use

Acquired von Willebrand Syndrome

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Von Willebrand Disease**

Indefinite authorization may be granted for treatment of VWD when either of the following criteria is met:

1. Member has type 1, 2A, 2M, or 2N VWD and has had an insufficient response to desmopressin or a documented clinical reason for not using desmopressin (see Appendix B).
2. Member has type 2B or type 3 VWD.

B. **Acquired von Willebrand Syndrome**

Indefinite authorization may be granted for treatment of acquired von Willebrand syndrome.

C. **Hemophilia A**

Indefinite authorization may be granted for the treatment of hemophilia A when the requested medication will be used for either of the following:

1. Member has mild disease (see Appendix A) and has had an insufficient response to desmopressin or a documented clinical reason for not using desmopressin (see Appendix B).
2. Member has moderate or severe disease (see Appendix A).

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. APPENDICES

Appendix A: Classification of Hemophilia by Clotting Factor Level (% Activity) and Bleeding Episodes

Severity	Clotting Factor Level % activity*	Bleeding Episodes
Severe	<1%	Spontaneous bleeding episodes, predominantly into joints and muscles Severe bleeding with trauma, injury or surgery
Moderate	1% to 5%	Occasional spontaneous bleeding episodes Severe bleeding with trauma, injury or surgery
Mild	6% to 40%	Severe bleeding with serious injury, trauma or surgery

*Factor assay levels are required to determine the diagnosis and are of value in monitoring treatment response.

Appendix B: Clinical Reasons For Not Utilizing Desmopressin in Patients with Hemophilia A and Type 1, 2A, 2M and 2N VWD

- Age < 2 years
- Pregnancy
- Fluid/electrolyte imbalance
- High risk for cardiovascular or cerebrovascular disease (especially the elderly)
- Predisposition to thrombus formation
- Trauma requiring surgery
- Life-threatening bleed
- Contraindication or intolerance to desmopressin
- Severe type 1 von Willebrand disease

IV. REFERENCES

- Wilate [package insert]. Hoboken, NJ: Octapharma USA Inc.; September 2019.
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Reference number(s)
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SPECIALTY GUIDELINE MANAGEMENT

XALKORI (crizotinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Xalkori is indicated for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK) or ROS1-positive as detected by an FDA-approved test.

B. Compendial Uses

1. NSCLC, recurrent, advanced or metastatic ALK rearrangement-positive or ROS1 rearrangement-positive tumors
2. NSCLC with high-level MET amplification or MET exon 14 skipping mutation
3. Inflammatory myofibroblastic tumor (IMT) with ALK translocation
4. Anaplastic large cell lymphoma, relapsed or refractory ALK-positive
5. Recurrent brain metastases from ALK rearrangement-positive NSCLC or ROS1 rearrangement-positive NSCLC

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: ALK mutation or translocation status, ROS-1 mutation status, MET exon 14 skipping mutation status, or high-level MET amplification status (where applicable).

III. CRITERIA FOR INITIAL APPROVAL

A. **Non-small cell lung cancer (NSCLC)**

Authorization of 12 months may be granted for treatment of NSCLC when the member meets any of the following criteria:

1. Member has recurrent, advanced or metastatic ALK-positive NSCLC (including brain metastases from NSCLC).
2. Member has recurrent, advanced or metastatic ROS1-positive NSCLC (including brain metastases from NSCLC).
3. Member has NSCLC with high-level MET amplification or MET exon 14 skipping mutation.

B. **Inflammatory myofibroblastic tumor (IMT)**

Authorization of 12 months may be granted for treatment of ALK-positive IMT.

Reference number(s)
1666-A

C. Anaplastic large cell lymphoma (ALCL)

Authorization of 12 months may be granted for treatment of relapsed or refractory ALK-positive ALCL.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication in Section III who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES

1. Xalkori [package insert]. New York, NY: Pfizer Inc.; January 2019.
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SPECIALTY GUIDELINE MANAGEMENT

XELJANZ (tofacitinib) XELJANZ XR (tofacitinib extended release tablets)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

- A. Adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response or intolerance to methotrexate.
- B. Adult patients with active psoriatic arthritis who have had an inadequate response or intolerance to methotrexate or other DMARDs.
- C. Adult patients with moderately to severely active ulcerative colitis who have had an inadequate response or intolerance to TNF blockers.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Moderately to severely active rheumatoid arthritis (RA)

1. Authorization of 12 months may be granted to members who have previously received a biologic or targeted synthetic DMARD (e.g., Rinvoq, Olumiant) indicated for the treatment of moderately to severely active rheumatoid arthritis.
2. Authorization of 12 months may be granted for treatment of moderately to severely active RA when any of the following criteria is met:
 - a. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to 20 mg/week).
 - b. Member has an intolerance or contraindication to methotrexate (see Appendix).

B. Active psoriatic arthritis (PsA)

Authorization of 12 months may be granted for treatment of active psoriatic arthritis (PsA) when used in combination with a nonbiologic DMARD.

C. Moderately to severely active ulcerative colitis (UC)

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for moderately to severely active ulcerative colitis.
2. Authorization of 12 months may be granted for the treatment of moderately to severely active UC for members who had an inadequate response, intolerance or contraindication to at least one tumor necrosis factor inhibitor (TNF-i).

3. Authorization of 12 months may be granted for members who have been hospitalized for fulminant UC (e.g., continuous bleeding, severe toxic symptoms including, fever and anorexia).

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who are using tofacitinib for an indication outlined in section II and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

For all indications: Member has had a documented negative TB test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic DMARDs and repeated yearly for members with risk factors** for TB that are continuing therapy with biologics.

* If the screening testing for TB is positive, there must be documentation of further testing to confirm there is no active disease. Do not administer tofacitinib to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of tofacitinib.

** Risk factors for TB include: Persons with close contact to people with infectious TB disease; persons who have recently immigrated from areas of the world with high rates of TB (e.g., Africa, Asia, Eastern Europe, Latin America, Russia); children less than 5 years of age who have a positive TB test; groups with high rates of TB transmission (e.g., homeless persons, injection drug users, persons with HIV infection); persons who work or reside with people who are at an increased risk for active TB (e.g., hospitals, long-term care facilities, correctional facilities, homeless shelters).

For all indications: Member cannot use Xeljanz, Xeljanz XR concomitantly with biologic DMARDs (e.g., adalimumab, infliximab), targeted synthetic DMARDS, or potent immunosuppressants (i.e., azathioprine, cyclosporine).

V. APPENDICES

Appendix A: Examples of Contraindications to Methotrexate

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
4. Elevated liver transaminases
5. History of intolerance or adverse event
6. Hypersensitivity
7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
8. Myelodysplasia
9. Pregnancy or planning pregnancy
10. Renal impairment
11. Significant drug interaction

VI. REFERENCES

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SPECIALTY GUIDELINE MANAGEMENT

XELODA (capecitabine)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Colorectal Cancer
 - a. Xeloda is indicated as a single agent for adjuvant treatment in patients with Dukes' C colon cancer who have undergone complete resection of the primary tumor when treatment with fluoropyrimidine therapy alone is preferred.
 - b. Xeloda is indicated as first-line treatment in patients with metastatic colorectal carcinoma when treatment with fluoropyrimidine therapy alone is preferred.
2. Breast Cancer
 - a. Xeloda in combination with docetaxel is indicated for the treatment of patients with metastatic breast cancer after failure of prior anthracycline-containing chemotherapy.
 - b. Xeloda monotherapy is also indicated for the treatment of patients with metastatic breast cancer resistant to both paclitaxel and an anthracycline-containing chemotherapy regimen or resistant to paclitaxel and for whom further anthracycline therapy is not indicated, for example, patients who have received cumulative doses of 400 mg/m² of doxorubicin or doxorubicin equivalents.

B. Compendial Uses

1. Anal cancer
2. Breast cancer
3. Central nervous system (CNS) metastases from breast cancer
4. Colorectal Cancer
5. Esophageal and esophagogastric junction cancer
6. Gastric cancer
7. Head and neck cancers (including very advanced head and neck cancer)
8. Hepatobiliary cancers (including extrahepatic and intra-hepatic cholangiocarcinoma and gallbladder cancer)
9. Occult primary tumors (cancer of unknown primary)
10. Ovarian cancer (epithelial ovarian cancer, fallopian tube cancer, and primary peritoneal cancer, and mucinous cancer)
11. Pancreatic adenocarcinoma
12. Penile cancer
13. Neuroendocrine and adrenal tumors
14. Thymomas and Thymic Carcinomas
15. Gestational Trophoblastic Neoplasia

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Reference number(s)
1993-A

A. Colorectal Cancer (CRC)

Authorization of 12 months may be granted for the treatment of colorectal cancer.

B. Breast Cancer

Authorization of 12 months may be granted for the treatment of breast cancer in members when any of the following criteria are met:

1. Member has human epidermal growth factor receptor 2 (HER2) negative recurrent or metastatic disease, as a single agent or in combination with docetaxel; or
2. Member has human epidermal growth factor receptor 2 (HER2) positive recurrent or metastatic disease, in combination with trastuzumab or lapatinib; or
3. Xeloda will be used in combination with ixabepilone for treatment of metastatic or locally advanced disease; or
4. Xeloda will be used as adjuvant therapy.

C. Neuroendocrine and Adrenal Tumors

Authorization of 12 months may be granted for the treatment of ANY of the following:

1. Member has neuroendocrine and adrenal tumors of the gastrointestinal tract, lung, or thymus (carcinoid tumors), in combination with temozolomide; or
2. Member has neuroendocrine and adrenal tumors of the pancreas, as a single agent or in combination with temozolomide; or
3. Member has poorly differentiated (high grade)/large or small cell disease, in combination with temozolomide.

D. Pancreatic Adenocarcinoma

Authorization of 12 months may be granted for the treatment of pancreatic adenocarcinoma.

E. Esophageal and Esophagogastric Junction Cancers

Authorization of 12 months may be granted for the treatment of esophageal and esophagogastric junction cancers.

F. Gastric Cancer

Authorization of 12 months may be granted for the treatment of gastric cancer.

G. Hepatobiliary Cancers

Authorization of 12 months may be granted for the treatment of hepatobiliary cancers (including extrahepatic and intrahepatic cholangiocarcinoma and gallbladder cancer).

H. Ovarian Cancer

Authorization of 12 months may be granted for the treatment of ANY of the following:

1. Member has persistent or recurrent epithelial ovarian cancer, fallopian tube cancer, or primary peritoneal cancer, as a single agent; or
2. Member has mucinous carcinoma and when either of the following criteria are met:
 - a. Xeloda will be used in combination with oxaliplatin as adjuvant treatment; or
 - b. Xeloda will be used in combination with oxaliplatin for treatment of persistent or recurrent disease

I. Head and Neck Cancers

Authorization of 12 months may be granted for the treatment of head and neck cancers (including very advanced head and neck cancer), as a single agent.

Reference number(s)
1993-A

J. Central Nervous System (CNS) Metastases from Breast Cancer

Authorization of 12 months may be granted for the treatment of recurrent brain metastases from breast cancer, as a single agent or in combination with lapatinib.

K. Occult Primary Tumors (cancer of unknown primary)

Authorization of 12 months may be granted for the treatment of occult primary tumors, in combination with oxaliplatin.

L. Penile Cancer

Authorization of 12 months may be granted for the treatment of penile cancer, as a single agent.

M. Anal Cancer

Authorization of 12 months may be granted for the treatment of anal cancer with concurrent chemoradiation in combination with mitomycin.

N. Thymomas and Thymic Carcinomas

Authorization of 12 months may be granted for the treatment of thymomas and thymic carcinomas, as second-line therapy in combination with gemcitabine.

O. Gestational Trophoblastic Neoplasia

Authorization of 12 months may be granted for the treatment of gestational trophoblastic neoplasia in members when either of the following criteria are met:

1. Member has recurrent or progressive intermediate trophoblastic tumors; or
2. Member has methotrexate-resistant high-risk disease

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who are experiencing clinical benefit to therapy or who have not experienced an unacceptable toxicity.

IV. REFERENCES

1. Xeloda [package insert]. South San Francisco, CA: Genentech, Inc.; February 2019.
2. The NCCN Drugs & Biologics Compendium 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed July 12, 2019.
3. Clinical Pharmacology powered by ClinicalKey [database online]. Tampa, FL. Elsevier; <https://www.clinicalkey.com/pharmacology/> [available with subscription]. Accessed (July 2019).
4. Ixempra [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; January 2016.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

XENLETA
(lefamulin)

Status: CVS Caremark Criteria

Type: Initial Prior Authorization

Ref # 3181-A

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Xenleta is indicated for the treatment of adults with community-acquired bacterial pneumonia (CABP) caused by the following susceptible microorganisms: *Streptococcus pneumoniae*, *Staphylococcus aureus* (methicillin-susceptible isolates), *Haemophilus influenzae*, *Legionella pneumophila*, *Mycoplasma pneumoniae*, and *Chlamydia pneumoniae*.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient is being converted from intravenous (IV) lefamulin (Xenleta) as prescribed or directed by an Infectious Disease specialist
OR
- The requested drug is being prescribed for community-acquired bacterial pneumonia (CABP) caused by any of the following susceptible microorganisms: A) *Streptococcus pneumoniae*, B) *Staphylococcus aureus* (methicillin-susceptible isolates), C) *Haemophilus influenzae*, D) *Legionella pneumophila*, E) *Mycoplasma pneumoniae*, F) *Chlamydia pneumoniae*.
AND
 - The infection is proven or strongly suspected to be caused by susceptible bacteria
AND
 - The patient has experienced an inadequate treatment response, intolerance, or contraindication to alternative therapies **OR** the bacteria are NOT susceptible to any other antibiotics

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Xenleta is indicated for the treatment of adults with community-acquired bacterial pneumonia (CABP) caused by the following susceptible microorganisms: *Streptococcus pneumoniae*, *Staphylococcus aureus* (methicillin-susceptible isolates), *Haemophilus influenzae*, *Legionella pneumophila*, *Mycoplasma pneumoniae*, and *Chlamydia pneumoniae*.

Xenleta (lefamulin) will be approved if being requested for a patient converted from intravenous (IV) Xenleta as prescribed or directed by an Infectious Disease specialist.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Xenleta and other antibacterial drugs, Xenleta should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.¹ To limit potential for widespread resistance, clinicians should consider reserving lefamulin for use in more severe infections in consultation with an infectious disease specialist. Choices should be modified on the basis of susceptibility test results and advice from specialists.^{4,5}

For treatment of adults with CABP, the recommended dosage of Xenleta is 150 mg every 12 hours by intravenous infusion over 60 minutes for 5 to 7 days and 600 mg orally every 12 hours for 5 days. Therefore, to allow for max recommended duration of therapy, the approval will be for 7 days.

REFERENCES

1. Xenleta [package insert]. King of Prussia, PA: Nabriva Therapeutics US, Inc.; August 2019.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed August 2019.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed August 2019.
4. Mandell L, Wunderink R, Anzueto A, et al. Infectious Diseases Society of America/American Thoracic Society Consensus Guidelines on the Management of Community-Acquired Pneumonia in Adults. *Clinical Infectious Diseases* 2007;44:S27–72.
5. Gorwitz RJ, Jernigan DB, Powers JH, Jernigan JA, and Participants in the CDC Convened Experts' Meeting on Management of MRSA in the Community. Strategies for clinical management of MRSA in the community: Summary of an experts' meeting convened by the Centers for Disease Control and Prevention. 2006. Available at <http://www.cdc.gov/mrsa/community/clinicians/index.html>. Accessed August 2019.

Written by: ME
 Date Written: 08/2019
 Revised:
 Reviewed: (CHART) 9/05/19
 External Review: 10/2019

CRITERIA FOR APPROVAL

1	Is the patient being converted from intravenous (IV) lefamulin (Xenleta) as prescribed or directed by an Infectious Disease specialist? [If yes, then no further questions.]	Yes	No
2	Is the requested drug being prescribed for community-acquired bacterial pneumonia (CABP) caused by any of the following susceptible microorganisms: A) Streptococcus pneumoniae, B) Staphylococcus aureus (methicillin-susceptible isolates), C) Haemophilus influenzae, D) Legionella pneumophila, E) Mycoplasma pneumoniae, F) Chlamydia pneumoniae?	Yes	No
3	Is the infection proven or strongly suspected to be caused by susceptible bacteria?	Yes	No
4	Has the patient experienced an inadequate treatment response, intolerance, or contraindication to alternative therapies OR are the bacteria NOT susceptible to any other antibiotics?	Yes	No

Mapping Instructions			
	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Approve, 7 days	Go to 2	
2.	Go to 3	Deny	You do not meet the requirements of your plan. Your plan covers this drug when all of these conditions apply: - You have pneumonia that is caused by a specific bacteria - The specific bacteria are susceptible to the drug Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
3.	Go to 4	Deny	You do not meet the requirements of your plan. Your plan covers this drug when all of these conditions apply: - Tests show or strongly suggest you have an infection - The pneumonia is caused by a specific bacteria - The specific bacteria are susceptible to the drug Your request has been denied based on the information we have.

			[Short Description: No approvable diagnosis]
4.	Approve, 7 days	Deny	<p>You do not meet the requirements of your plan.</p> <p>Your plan covers this drug when you meet one of these conditions:</p> <ul style="list-style-type: none"> - You have tried other drugs and they either did not work for you or you cannot use them - The specific bacteria are not susceptible to any other drugs <p>Your request has been denied based on the information we have.</p> <p>[Short Description: No approvable diagnosis]</p>

SPECIALTY GUIDELINE MANAGEMENT

XEOMIN (incobotulinumtoxinA)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

- A. Treatment of cervical dystonia in adult patients
- B. Treatment of blepharospasm in adult patients
- C. Treatment of upper limb spasticity in adult patients
- D. Treatment of chronic sialorrhea in adult patients

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

Coverage will not be provided for cosmetic use.

III. CRITERIA FOR INITIAL APPROVAL

A. Cervical dystonia

Authorization of 12 months may be granted for treatment of cervical dystonia (e.g., torticollis) when there is sustained head torsion and/or tilt with limited range of motion.

B. Blepharospasm

Authorization of 12 months may be granted for treatment of blepharospasm.

C. Upper limb spasticity

Authorization of 12 months may be granted for treatment of upper limb spasticity.

D. Excessive salivation

Authorization of 12 months may be granted for treatment of excessive salivation (chronic sialorrhea) when the member has been refractory to pharmacotherapy (e.g. anticholinergics).

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. REFERENCES

1. Xeomin [package insert]. Dessau-Rosslau, Germany: Merz Pharmaceuticals, LLC; May 2019.
2. Restivo D, Panebianco M, Casabona A et al. Botulinum Toxin A for Sialorrhea Associated with Neurological Disorders: Evaluation of the Relationship between Effect of Treatment and the Number of Glands Treated. *Toxins* 2018;55:1-10.
3. Lakraj AA, Moghimi N, Jabbari B. Sialorrhea: Anatomy, Pathophysiology and Treatment with Emphasis on the Role of Botulinum Toxins. *Toxins* 2013, 5, 1010-1031
4. Glader L, Delsing C, Hughes A et al. Sialorrhea in cerebral palsy. American Academy for Cerebral Palsy and Developmental Medicine Care Pathways. <https://www.aacpdm.org/publications/care-pathways/sialorrhea>. Accessed August 23, 2019.
5. Garuti G, Rao F, Ribuffo V et al. Sialorrhea in patients with ALS: current treatment options. *Degener Neurol Neuromuscul Dis*. 2019; 9: 19–26.

SPECIALTY GUIDELINE MANAGEMENT

XERMELO (telotristat ethyl)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Xermelo is indicated for the treatment of carcinoid syndrome diarrhea in combination with somatostatin analog (SSA) therapy in adults inadequately controlled by SSA therapy.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Carcinoid syndrome diarrhea

Authorization of 3 months may be granted for the treatment of carcinoid syndrome diarrhea when all of the following criteria are met:

- A. Member has had an inadequate response to somatostatin analog (SSA) therapy alone
- B. Xermelo will be used in combination with SSA therapy

III. CONTINUATION OF THERAPY

Authorization of 6 months may be granted for members who achieve or maintain positive clinical response with Xermelo therapy for carcinoid syndrome diarrhea, as evidenced by reduction in the number of daily bowel movements and are concurrently receiving treatment with SSA therapy.

IV. REFERENCES

1. Xermelo [package insert]. The Woodlands, TX: Lexicon Pharmaceuticals, Inc.; February 2017.

Reference number(s)
2152-A

SPECIALTY GUIDELINE MANAGEMENT

XGEVA (denosumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Prevention of skeletal-related events in patients with multiple myeloma and in patients with bone metastases from solid tumors
2. Treatment of adults and skeletally mature adolescents with giant cell tumor of bone that is unresectable or where surgical resection is likely to result in severe morbidity
3. Treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy

B. Compendial Uses

Second line therapy for osteopenia or osteoporosis in patients with systemic mastocytosis

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Multiple myeloma**

Authorization of 12 months may be granted for the prevention of skeletal-related events in members with multiple myeloma.

B. **Bone Metastases from a Solid Tumor**

Authorization of 12 months may be granted for the treatment of bone metastases from a solid tumor.

C. **Giant cell tumor of bone**

Authorization of 12 months may be granted for the treatment of giant cell tumor of bone.

D. **Hypercalcemia of malignancy**

Initial authorization of 2 months may be granted for the treatment of hypercalcemia of malignancy that is refractory to intravenous (IV) bisphosphonate therapy OR there is a clinical reason to avoid IV bisphosphonate therapy (See Appendix).

E. **Systemic mastocytosis**

Authorization of 12 months may be granted for second-line therapy for osteopenia or osteoporosis in members with systemic mastocytosis that have not responded to therapy with bisphosphonates or for patients who are not candidates for bisphosphonates because of renal insufficiency.

Reference number(s)
2152-A

III. CONTINUATION OF THERAPY

A. Hypercalcemia of malignancy

Authorization of 2 months will be granted for continued treatment in members requesting reauthorization for hypercalcemia of malignancy who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

B. All Diagnosis (excluding hypercalcemia of malignancy)

Authorization of 12 months will be granted for continued treatment in members requesting reauthorization for an indication listed in Section II (excluding hypercalcemia of malignancy) who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

IV. APPENDIX

Clinical reasons to avoid IV bisphosphonate therapy

- Renal insufficiency (creatinine clearance <35 mL/min)
- Acute renal impairment
- History of intolerance to an IV bisphosphonate
- Hypocalcemia

V. REFERENCES

1. Xgeva [package insert]. Thousand Oaks, CA: Amgen Inc.; May 2019.
2. The NCCN Drugs & Biologics Compendium™ © 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed May 30, 2019.
3. NCCN Clinical Practice Guidelines in Oncology: Bone Cancer. Version 2.2019. Accessed May 30, 2019.
4. Hu M, Glezerman IG, Leboulleux S, et al. Denosumab for treatment of hypercalcemia of malignancy. *J Clin Endocrinol Metab*. 2014; 99(9):3144-3152.
5. Bisphosphonates. *Drug Facts and Comparisons. Facts & Comparisons® eAnswers* [online]. 2019. Available from Wolters Kluwer Health, Inc. Accessed May 30, 2019.

SPECIALTY GUIDELINE MANAGEMENT

XIAFLEX (collagenase clostridium histolyticum)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

1. Xiaflex is indicated for the treatment of adult patients with Dupuytren's contracture with a palpable cord.
2. Xiaflex is indicated for the treatment of adult men with Peyronie's disease with a palpable plaque and curvature deformity of at least 30 degrees at the start of therapy.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

- A. Dupuytren's contracture: Chart notes or medical record indicating the affected joint, contracture, and a positive table top test (for new starts and continuation) and the number of injections the member has received (for continuation only).
- B. Peyronie's disease: Chart notes or medical record indicating palpable plaque, curvature, intact erectile function (for new starts and continuation) and the number of injections the member has received (for continuation only).

III. CRITERIA FOR INITIAL APPROVAL

A. Dupuytren's contracture¹

Authorization of 6 months may be granted for the treatment of Dupuytren's contracture when all of the following criteria are met:

1. The member has a finger flexion contracture with a palpable cord in a metacarpophalangeal joint or a proximal interphalangeal joint prior to initiating Xiaflex therapy.
2. The contracture is at least 20 degrees prior to initiating Xiaflex therapy.
3. The member had a positive table top test, defined as the inability to simultaneously place the affected finger(s) and palm flat against a table prior to initiating Xiaflex therapy.
4. The member will receive a maximum of 3 injections per cord (4 weeks apart) as part of the current treatment.

B. Peyronie's disease

Authorization of 12 months may be granted for the treatment of Peyronie's disease when the following criteria are met:

1. The member has stable Peyronie's disease without clinical changes (e.g., worsening curvature) for at least three months.

2. The member has a palpable plaque and curvature deformity of at least 30 degrees and less than 90 degrees prior to initiating Xiaflex therapy.
3. The member has intact erectile function (with or without medication).
4. The member is 18 years of age or older.
5. The member will receive a maximum of one treatment course with a maximum of 8 injections total, including any injections the patient has received for any previous treatment.

IV. CONTINUATION OF THERAPY

A. Dupuytren's contracture

Authorization of 6 months may be granted for the continuation of treatment for Dupuytren's contracture when all of the following criteria are met:

1. The patient meets all initial authorization criteria.
2. The member is continuing with a treatment course for the same cord. For treatment of a new cord or a previously-treated cord following recurrence, member must meet all initial authorization criteria.
3. The member has received less than 3 injections total per cord (4 weeks apart).

B. Peyronie's disease

Authorization of 12 months may be granted for the continuation of treatment for Peyronie's disease when all of the following criteria are met:

1. The member meets all initial authorization criteria.
2. The member has curvature deformity of at least 15 degrees at the time of the continuation request.
3. The member has received less than 8 injections total, including any injections the patient has received for any previous treatment.

V. REFERENCES

1. Xiaflex [package insert]. Endo Pharmaceuticals Inc.; June 2018.
2. Hurst LC, Badalamente MA, Hentz VR, et al. Injectable collagenase clostridium histolyticum for Dupuytren's contracture. *N Engl J Med*. 2009;361(10):968-979.
3. Nehra A, Alterowitz R, Culkin DJ, et al. Peyronie's Disease: AUA Guideline. *J Urol*. 2015;194(3):745-753.

SPECIALTY GUIDELINE MANAGEMENT

XOLAIR (omalizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

A. Allergic asthma

Xolair is indicated for patients 6 years of age and older with moderate to severe persistent asthma who have a positive skin test or in vitro reactivity to a perennial aeroallergen and whose symptoms are inadequately controlled with inhaled corticosteroids.

Limitations of use: Xolair is not indicated for the relief of acute bronchospasm or status asthmaticus, or for treatment of other allergic conditions.

B. Chronic idiopathic urticaria (CIU)

Xolair is indicated for the treatment of adults and adolescents 12 years of age and older with chronic idiopathic urticaria (CIU) who remain symptomatic despite H1 antihistamine treatment.

Limitations of use: Xolair is not indicated for treatment of other forms of urticaria.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

- A. Asthma: Member's chart or medical record showing pre-treatment IgE level (initial request only)
- B. CIU: Member's chart or medical record showing an inadequate treatment response to a second-generation H1 antihistamine (initial request only)

III. CRITERIA FOR INITIAL APPROVAL

A. Asthma

Authorization of 6 months may be granted for treatment of asthma when all of the following criteria are met:

1. Member is 6 years of age or older.
2. Member has a positive skin test or in vitro reactivity to at least one perennial aeroallergen.
3. Member has a pre-treatment IgE level greater than or equal to 30 IU/mL.
4. Member has inadequate asthma control (e.g., hospitalization or emergency medical care visit within the past year) despite current treatment with both of the following medications at optimized doses:
 - a. Inhaled corticosteroid

- b. Additional controller (long acting beta₂-agonist, leukotriene modifier, or sustained-release theophylline)
- 5. Member will not use Xolair as monotherapy.
- 6. Member will not use Xolair concomitantly with other biologics (e.g., Cinqair, Dupixent, Fasenra, Nucala).

B. Chronic idiopathic urticaria

Authorization of 6 months may be granted for treatment of chronic idiopathic urticaria when all of the following criteria are met:

- 1. Member is 12 years of age or older.
- 2. Member remains symptomatic despite treatment with a second-generation H₁ antihistamine (e.g., cetirizine, fexofenadine, levocetirizine, loratadine) for at least 2 weeks.
- 3. Member has been evaluated for other causes of urticaria, including bradykinin-related angioedema and interleukin-1-associated urticarial syndromes (auto-inflammatory disorders, urticarial vasculitis).
- 4. Member has experienced a spontaneous onset of wheals, angioedema, or both, for at least 6 weeks.

IV. CONTINUATION OF THERAPY

A. Asthma

Authorization of 12 months may be granted for treatment of asthma when all of the following criteria are met:

- 1. Member is 6 years of age or older.
- 2. Asthma control has improved on Xolair treatment as demonstrated by at least one of the following:
 - a. A reduction in the frequency and/or severity of symptoms and exacerbations
 - b. A reduction in the daily maintenance oral corticosteroid dose
- 3. Member will not use Xolair as monotherapy.
- 4. Member will not use Xolair concomitantly with other biologics (e.g., Cinqair, Dupixent, Fasenra, Nucala).

B. Chronic idiopathic urticaria

Authorization of 12 months may be granted for continuation of treatment of chronic idiopathic urticaria when all of the following criteria are met:

- 1. Member is 12 years of age or older.
- 2. Member has experienced a response (e.g., improved symptoms, decrease in weekly urticaria activity score [UAS7]) since initiation of therapy.

V. OTHER

Note: If the member is a current smoker, they should be counseled on the harmful effects of smoking on pulmonary conditions and available smoking cessation options.

VI. REFERENCES

- 1. Xolair [package insert]. South San Francisco, CA: Genentech, Inc.; May 2019.
- 2. National Institutes of Health. *National Asthma Education and Prevention Program Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma - Full Report 2007*. Bethesda, MD: National Heart Lung and Blood Institute; August 2007. <http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf>. Accessed March 18, 2019.

3. Global Initiative for Asthma (GINA). Global Strategy for Asthma Management and Prevention. 2018 update. <http://ginasthma.org/2018-gina-report-global-strategy-for-asthma-management-and-prevention/>. Accessed March 18, 2019.
4. Strunk RC, Bloomberg GR. Omalizumab for asthma. *N Engl J Med*. 2006;354(25):2689-2695.
5. Kew KM, Karner C, Mindus SM. Combination formoterol and budesonide as maintenance and reliever therapy versus combination inhaler maintenance for chronic asthma in adults and children (review). *Cochrane Database Syst Rev*. 2013;12:CD009019.
6. Zuberbier T, Aberer W, Asero R, et al. The EAACI/GA²LEN/EDF/WAO guideline for the definition, classification, diagnosis, and management of urticaria. *Allergy*. 2018;73(7):1393-1414. doi: 10.1111/all.13397.
7. Bernstein DI, Blessing-Moore J, Cox L, et al. The diagnosis and management of acute and chronic urticaria: 2014 update. American Academy of Allergy, Asthma & Immunology Practice Parameter. <http://www.aaaai.org/practice-resources/statements-and-practice-parameters/practice-parameter-guidelines.aspx>. Accessed March 21, 2019.
8. Maurer M, Rosen K, Hsieh HJ, et al. Omalizumab for the treatment of chronic idiopathic or spontaneous urticaria. *N Engl J Med*. 2013;368(10):924-935.

SPECIALTY GUIDELINE MANAGEMENT

XOSPATA (gilteritinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Xospata is indicated for the treatment of adult patients who have relapsed or refractory acute myeloid leukemia (AML) with a FLT3 mutation as detected by an FDA-approved test.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review (new starts only): medical record documentation of FLT3 mutation as detected by an FDA-approved test

III. CRITERIA FOR INITIAL APPROVAL

Acute Myeloid Leukemia (AML)

Authorization of 12 months may be granted for the treatment of FLT3 mutation-positive relapsed or refractory AML when the requested medication is used as a single-agent.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES

1. Xospata [package insert]. Northbrook, IL: Astellas Pharma Inc.; May 2019.
2. The NCCN Drugs & Biologics Compendium 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed July 17, 2019.

Specialty Guideline Management

XPOVIO (selinexor)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Xpovio is indicated in combination with dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least four prior therapies and whose disease is refractory to at least two proteasome inhibitors, at least two immunomodulatory agents, and an anti-CD38 monoclonal antibody.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Multiple Myeloma

Authorization of 12 months may be granted for the treatment of relapsed or refractory multiple myeloma in members who meet all of the following:

- A. Xpovio will be used in combination with dexamethasone
- B. The member has received at least four prior therapy regimens
- C. The member is refractory to at least two proteasome inhibitors
- D. The member is refractory to at least two immunomodulatory agents
- E. The member is refractory to an anti-CD38 monoclonal antibody

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced an unacceptable toxicity or disease progression.

IV. REFERENCES

1. Xpovio [package insert]. Newton, MA: Karyopharm Therapeutics; July 2019.

SPECIALTY GUIDELINE MANAGEMENT

XTANDI (enzalutamide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Xtandi is indicated for the treatment of patients with:

- A. Castration-resistant prostate cancer (CRPC)
- B. Metastatic castration-sensitive prostate cancer (mCSPC)

All other indications are considered experimental/investigational and are not medically necessary.

II. EXCLUSIONS

Coverage will not be provided if the requested medication is used in combination with a second-generation oral anti-androgen (e.g., apalutamide [Erleada]) or an oral androgen metabolism inhibitor (e.g., abiraterone acetate [Zytiga]).

III. CRITERIA FOR INITIAL APPROVAL

A. Castration-resistant prostate cancer (CRPC)

Authorization of 12 months may be granted to members for the treatment of castration-resistant prostate cancer when the member has had a bilateral orchiectomy or will be using the requested medication in combination with a GnRH analog.

B. Metastatic castration-sensitive prostate cancer (mCSPC)

Authorization of 12 months may be granted to members for the treatment of metastatic castration-sensitive prostate cancer when the member has had a bilateral orchiectomy or will be using the requested medication in combination with a GnRH analog.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES

1. Xtandi [package insert]. Northbrook, IL: Astellas Pharma US, Inc.; December 2019.
2. The NCCN Drugs & Biologics Compendium™ © 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed July 9, 2019.

Reference number(s)
1933-A

3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology™ Prostate Cancer (Version 2.2019). <https://www.nccn.org>. Accessed July 9, 2019.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

XYREM
(sodium oxybate)

Status: CVS Caremark Criteria

Type: Initial Prior Authorization with Quantity Limit

Ref # 254-C

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated*

FDA-APPROVED INDICATIONS

Xyrem oral solution is indicated for the treatment of cataplexy in narcolepsy.

Xyrem oral solution is indicated for the treatment of excessive daytime sleepiness (EDS) in narcolepsy.

Limitations of Use

Xyrem may only be dispensed to patients enrolled in the Xyrem REMS Program.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The request is for continuation of Xyrem (sodium oxybate) AND the patient experienced a decrease in daytime sleepiness with narcolepsy or a decrease in cataplexy episodes with narcolepsy

OR

- The diagnosis is confirmed by sleep lab evaluation

AND

- The requested drug is being prescribed for the treatment of cataplexy in narcolepsy

OR

- The requested drug is being prescribed for excessive daytime sleepiness in a patient with narcolepsy

AND

- The patient experienced an inadequate treatment response or intolerance to at least one central nervous system (CNS) stimulant drug (e.g., amphetamine, dextroamphetamine, or methylphenidate) AND one central nervous system (CNS) promoting wakefulness drug (e.g., modafinil, armodafinil)

OR

- The patient has a contraindication to at least one central nervous system (CNS) stimulant drug (e.g., amphetamine, dextroamphetamine, or methylphenidate) AND one central nervous system (CNS) wakefulness promoting drug (e.g., modafinil, armodafinil)

Quantity Limits apply.

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Xyrem oral solution is indicated for the treatment of cataplexy in narcolepsy and excessive daytime sleepiness (EDS) in narcolepsy.

Because of the risks of central nervous system depression and abuse/misuse, Xyrem is available only through a restricted distribution program called the Xyrem REMS Program. The Xyrem REMS Program required components are: medication is dispensed by a certified centralized pharmacy, prescribers must complete the enrollment forms and comply with the requirements, and patients must understand the risks and benefits of Xyrem.

According to the American Academy of Sleep Medicine (AASM), successful treatment of hypersomnia of central origin requires an accurate diagnosis, individual tailoring of therapy to produce the fullest possible return of normal function, and regular follow-up to monitor response to treatment. The evaluation should include a thorough evaluation of other possible contributing causes of excessive daytime sleepiness. The International Classification of Sleep Disorders, Third Edition (ICSD-3) specifies necessary diagnostic tests and criteria for each disorder of central origin. For narcolepsy, a sleep lab evaluation consisting of an overnight polysomnography (PSG) and mean sleep latency tests (MSLT) is recommended to confirm the diagnosis. Many other conditions produce such sleepiness and can mimic or coexist with a hypersomnia of central origin.^{4,5}

According to AASM guidelines, modafinil is effective for treatment of daytime sleepiness due to narcolepsy. One additional study of 196 subjects involved assessment of armodafinil (the longer half-life enantiomer of modafinil) for treatment of excessive sleepiness in patients with narcolepsy.⁴ Subjects receiving armodafinil experienced significant improvement in sleepiness as measured by the Mean Wakefulness Test (MWT) mean sleep latency, and in the Clinical Global Impression of Change.⁴ The guidelines also state that amphetamine, dextroamphetamine, and methylphenidate are effective for treatment of daytime sleepiness due to narcolepsy.⁴ Since Xyrem has risks associated with therapy and there are effective alternatives available, a trial of one central nervous system (CNS) promoting wakefulness drug (e.g., modafinil, armodafinil) and one central nervous system (CNS) stimulant drug (e.g., amphetamine, dextroamphetamine, or methylphenidate) will be required.

The guidelines state that the goal of therapy should be to produce the fullest possible return of normal function for patients.^{4,6} Therefore, if the request is for the continuation of Xyrem, it should be determined that the patient has experienced a decrease in daytime sleepiness with narcolepsy or a decrease in cataplexy episodes with narcolepsy.

The recommended starting dose of Xyrem is 4.5 grams (g) per night administered orally in two equal, divided doses: 2.25 g at bedtime and 2.25 g taken 2.5 to 4 hours later. The dose can be increased by 1.5 g per night at weekly intervals (additional 0.75 g at bedtime and 0.75 g taken 2.5 to 4 hours later) to the effective dose range of 6 g to 9 g per night orally. Doses higher than 9 g per night have not been studied and should not ordinarily be administered. Therefore, the approval will be limited to a maximum of three 180 milliliter (mL) bottles (540 mL) per month.

REFERENCES

1. Xyrem [package insert]. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; July 2017.
2. AHFS DI (Adult and Pediatric) [database online]. Hudson, OH: Lexi-Comp, Inc.; http://online.lexi.com/lco/action/index/dataset/complete_ashp [available with subscription]. Accessed November 2017.
3. Micromedex Healthcare Series [database online]. Greenwood Village, CO: Thomson Reuters (Healthcare) Inc. Updated periodically. <http://www.thomsonhc.com> [available with subscription]. Accessed November 2017.
4. Morgenthaler TI, Vishesh KK, Brown T, et al. Practice Parameters for the Treatment of Narcolepsy and Other Hypersomnias of Central Origin. *Sleep* 2007; 30(12):1705-11.
5. American Academy of Sleep Medicine. *International Classification of Sleep Disorders: Diagnostic and Coding Manual*. 3rd edition. Westchester, IL: American Academy of Sleep Medicine; 2014.
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Last Reviewed: CRC 09/2002; Medical Affairs (MM) 01/2005, 11/2005, 02/2006; (WF) 02/2007, 11/2007, 11/2008, 09/2009; (KP) 11/2010, 11/2011; (LMS) 11/2012; (DNC) 11/2013, (DC) 11/2014; (LMS) 11/2016, 05/2017; (TP) 11/2017
External P&T Review: 05/2005, 06/2006, 06/2007, 04/2008, 02/2009, 02/2010, 02/2011, 02/2012, 02/2013, 02/2014, 02/2015, 02/2016, 02/2017, 06/2017, 02/2018

CRITERIA FOR APPROVAL

- | | | | |
|----|---|-----|----|
| 1. | Is this request for the continuation of Xyrem (sodium oxybate)?
[If no, then skip to question 3.] | Yes | No |
| 2. | Has the patient experienced a decrease in daytime sleepiness with narcolepsy or a decrease in cataplexy episodes with narcolepsy?
[If yes, then skip to question 8.] | Yes | No |
| 3. | Is the requested drug being prescribed for the treatment of cataplexy in narcolepsy?
[If yes, then skip to question 7.] | Yes | No |
| 4. | Is the requested drug being prescribed for the treatment of excessive daytime sleepiness in a patient with narcolepsy? | Yes | No |
| 5. | Did the patient experience an inadequate treatment response or intolerance to at least one central nervous system (CNS) stimulant drug (e.g., amphetamine, dextroamphetamine, or methylphenidate) AND one central nervous system (CNS) promoting wakefulness drug (e.g., modafinil, armodafinil)?
[If yes, then skip to question 7.] | Yes | No |
| 6. | Does the patient have a contraindication to at least one central nervous system (CNS) stimulant drug (e.g., amphetamine, dextroamphetamine, or methylphenidate) AND one central nervous system (CNS) wakefulness promoting drug (e.g., modafinil, armodafinil)? | Yes | No |
| 7. | Has the diagnosis been confirmed by sleep lab evaluation? | Yes | No |
| 8. | Does the patient require the use of more than the plan allowance of 540 milliliters (mL) per month (270 grams per month)? | Yes | No |

[Rph Note: If yes, then deny and enter a partial approval for 540 mL per 25 days.]

Mapping Instructions			
	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Go to 3	
2.	Go to 8	Deny	Your plan covers this drug when you meet one of these conditions: - You have a decrease in daytime sleepiness with narcolepsy - You have a decrease in cataplexy episodes with narcolepsy Your use of this drug does not meet the requirement. This is based on the information we have.
3.	Go to 7	Go to 4	
4.	Go to 5	Deny	Your plan covers this drug when you have one of these conditions: - Cataplexy with narcolepsy - Excessive daytime sleepiness with narcolepsy Your use of this drug does not meet the requirement. This is based on the information we have.

5.	Go to 7	Go to 6	
6.	Go to 7	Deny	<p>Your plan covers this drug when you meet all of these conditions:</p> <ul style="list-style-type: none"> - You tried a central nervous system (CNS) stimulant drug (e.g., amphetamine, dextroamphetamine, or methylphenidate) and a central nervous system (CNS) wakefulness promoting drug (e.g., modafinil, armodafinil) - These drugs did not work for you or you cannot take them <p>Your use of this drug does not meet the requirements. This is based on the information we have.</p>
7.	Go to 8	Deny	<p>Your plan covers this drug when you have had a sleep lab test.</p> <p>Your use of this drug does not meet the requirement. This is based on the information we have.</p>
8.	Deny	Approve, 12 months, 540 milliliters /month*	<p>You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to:</p> <ul style="list-style-type: none"> - 540 milliliters/month of Xyrem. <p>You have been approved for the maximum quantity that your plan covers. Your request for additional quantities of the requested drug and strength has been denied.</p>

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

SPECIALTY GUIDELINE MANAGEMENT

YERVOY (ipilimumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. **Unresectable or Metastatic Melanoma**
Yervoy is indicated for the treatment of unresectable or metastatic melanoma in adults and pediatric patients (12 years and older).
2. **Adjuvant Treatment of Melanoma**
Yervoy is indicated for the adjuvant treatment of patients with cutaneous melanoma with pathologic involvement of regional lymph nodes of more than 1 mm who have undergone complete resection, including total lymphadenectomy.
3. **Advanced Renal Cell Carcinoma**
Yervoy, in combination with nivolumab, is indicated for the treatment of patients with intermediate or poor risk, previously untreated advanced renal cell carcinoma (RCC).
4. **Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Metastatic Colorectal Cancer**
Yervoy, in combination with nivolumab, is indicated for the treatment of adult and pediatric patients 12 years of age and older with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer (CRC) that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan.

B. Compendial Uses

1. Cutaneous melanoma
2. Uveal melanoma
3. Central nervous system (CNS) brain metastases
4. Small cell lung cancer
5. Non-small cell lung cancer
6. Kidney cancer
7. Colorectal cancer
8. Malignant pleural mesothelioma

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: documentation of laboratory report confirming MSI-H or mismatch repair deficient (dMMR) tumor status, where applicable.

III. CRITERIA FOR INITIAL APPROVAL

A. Cutaneous Melanoma

Authorization of 6 months may be granted for treatment of cutaneous melanoma when either of the following conditions is met:

1. Yervoy will be used as a single agent or in combination with nivolumab (for a maximum of 4 doses) for metastatic or unresectable disease.
2. Yervoy will be used as a high-dose single agent (up to 3 years) as adjuvant treatment following complete lymph node resection or complete resection of metastatic disease.

B. Uveal Melanoma

Authorization of 6 months may be granted as a single agent or in combination with nivolumab for treatment of uveal melanoma for distant metastatic disease.

C. CNS Brain Metastases

Authorization of 6 months may be granted as a single agent or in combination with nivolumab for treatment of CNS brain metastases in members with melanoma.

D. Small Cell Lung Cancer

Authorization of 6 months may be granted as subsequent therapy in combination with nivolumab for treatment of small cell lung cancer when either of the following conditions is met:

1. Member has relapse within 6 months following complete or partial response or stable disease with initial treatment.
2. Disease is primary progressive.

E. Non-small Cell Lung Cancer

Authorization of 6 months may be granted in combination with nivolumab for treatment of non-small cell lung cancer for disease with tumor mutational burden (TMB).

F. Kidney Cancer

Authorization of 6 months may be granted for treatment of kidney cancer, including renal cell carcinoma, in combination with nivolumab (for 4 cycles, followed by single agent nivolumab) for relapsed, advanced, or stage IV disease, in any of the following settings:

1. First-line therapy for poor or intermediate risk.
2. First-line therapy for clear cell histology and favorable risk.
3. Subsequent therapy for clear cell histology.

G. Colorectal Cancer

Authorization of 6 months may be granted for treatment of colorectal cancer, including small bowel adenocarcinoma, appendiceal carcinoma, and anal adenocarcinoma for microsatellite instability-high or mismatch repair deficient tumors when either of the following criteria is met:

1. Yervoy will be used in combination with nivolumab (for a maximum of 4 doses) as primary treatment for unresectable metachronous metastases and previous adjuvant FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin) within the past 12 months.
2. Yervoy will be used in combination with nivolumab (for a maximum of 4 doses and if no previous treatment with a checkpoint inhibitor) as subsequent therapy for unresectable advanced or metastatic disease following previous oxaliplatin- irinotecan- and/or fluoropyrimidine-based therapy.

H. Malignant Pleural Mesothelioma

Authorization of 6 months may be granted in combination with nivolumab for subsequent treatment of malignant pleural mesothelioma.

IV. CONTINUATION OF THERAPY

A. Adjuvant treatment of melanoma

Authorization of 6 months may be granted (up to 3 years) for continued treatment in members requesting reauthorization for adjuvant melanoma who have not experienced disease progression or an unacceptable toxicity.

B. Cutaneous Melanoma, Kidney Cancer, Colorectal Cancer

Authorization of 6 months may be granted (up to 4 doses maximum, if member has not already received 4 doses), for continued treatment in members requesting reauthorization for cutaneous melanoma, kidney cancer, and colorectal cancer who have not experienced disease progression or unacceptable toxicity.

C. All Other Indications

Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES

1. Yervoy [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; May 2019.
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3. Clinical Pharmacology powered by ClinicalKey [database online]. Tampa, FL: Elsevier/Gold Standard, Inc.; 2019. <http://www.clinicalpharmacology-ip.com/default.aspx>. Accessed July 17, 2019.
4. AHFS DI (Adult and Pediatric) [database online]. Hudson, OH: Lexi-Comp, Inc.; http://online.lexi.com/lco/action/index/dataset/complete_ashp [available with subscription]. Accessed July 17, 2019.
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SPECIALTY GUIDELINE MANAGEMENT

YESCARTA (axicabtagene ciloleucel)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Yescarta is a CD19-directed genetically modified autologous T-cell immunotherapy indicated for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified (NOS), primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma.

Limitations of use: Yescarta is not indicated for the treatment of patients with primary central nervous system lymphoma.

B. Compendial Uses

1. Acquired immunodeficiency syndrome (AIDS)-related diffuse large B-cell lymphoma
2. Diffuse large B-cell lymphoma
3. Human herpesvirus 8 (HHV8)-positive diffuse large B-cell lymphoma, NOS
4. Monomorphic post-transplant lymphoproliferative disorder (B-cell type)

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Testing or analysis confirming CD19 protein on the surface of the B-cell.

III. CRITERIA FOR INITIAL APPROVAL

Adult B-cell lymphomas

Authorization of 3 months may be granted for treatment of B-cell lymphomas in members 18 years of age or older when all of the following criteria are met:

A. Member has any of the following B-cell lymphoma subtypes:

1. Diffuse large B-cell lymphoma (DLBCL) arising from follicular lymphoma (also known as follicular lymphoma with histologic transformation to DLBCL)
2. Diffuse large B-cell lymphoma
3. Primary mediastinal large B-cell lymphoma
4. High-grade B-cell lymphoma (high-grade B-cell lymphoma with translocations of MYC and BCL2 and/or BCL6 [double/triple hit lymphoma], high-grade B-cell lymphoma, NOS)
5. Acquired immunodeficiency syndrome (AIDS)-related diffuse large B-cell lymphoma

6. Human herpesvirus 8 (HHV8)-positive diffuse large B-cell lymphoma, NOS
7. Monomorphic post-transplant lymphoproliferative disorder (B-cell type)
- B. The member does not have primary central nervous system lymphoma.
- C. The member has not received a previous treatment course of Yescarta or another CD19-directed chimeric antigen receptor (CAR) T-cell therapy.
- D. The B-cells must be CD19-positive as confirmed by testing or analysis
- E. For diffuse large B-cell lymphoma arising from follicular lymphoma: member received prior treatment with two or more chemoimmunotherapy regimens which included at least one anthracycline or anthracenedione-based regimen, unless contraindicated.
- F. For all other B-cell lymphoma subtypes: member has partial response following second-line therapy OR the disease is in second relapse or greater.

IV. REFERENCES

1. Yescarta [package insert]. Santa Monica, CA: Kite Pharma; October 2017.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed April 17, 2019.
3. The NCCN Clinical Practice Guidelines in Oncology® B-Cell Lymphomas (Version 2.2019).© 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed April 17, 2019.

SPECIALTY GUIDELINE MANAGEMENT

YONSA (abiraterone acetate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Yonsa is indicated in combination with methylprednisolone for the treatment of patients with metastatic castration-resistant prostate cancer (CRPC).

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

Coverage will not be provided if the requested medication is used in combination with a second-generation oral anti-androgen (e.g., apalutamide [Erleada]) or an oral androgen metabolism inhibitor (e.g., abiraterone acetate [Zytiga]).

III. CRITERIA FOR INITIAL APPROVAL

Metastatic castration-resistant prostate cancer

Authorization of 12 months may be granted for treatment of metastatic castration-resistant prostate cancer when the member has had a bilateral orchiectomy or will be using the requested medication in combination with a GnRH analog.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES

1. Yonsa [package insert]. Cranbury, NJ: Sun Pharmaceutical Industries, Inc.; May 2018.
2. The NCCN Drugs & Biologics Compendium™ © 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed July 9, 2019.
3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology™ Prostate Cancer (Version 2.2019). <https://www.nccn.org>. Accessed July 9, 2019.

SPECIALTY GUIDELINE MANAGEMENT

ZALTRAP (ziv-aflibercept)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Zaltrap is indicated for use in combination with 5-fluorouracil, leucovorin, and irinotecan (FOLFIRI) in patients with metastatic colorectal cancer (mCRC) that is resistant to or has progressed following an oxaliplatin-containing regimen.

B. Compendial Uses

1. Colorectal cancer with unresectable metachronous metastases and previous adjuvant FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin) within the past 12 months, as primary treatment in combination with irinotecan
2. Colorectal cancer, unresectable advanced or metastatic disease in combination with irinotecan or with FOLFIRI regimen not previously treated with irinotecan-based therapy, as subsequent therapy for disease progression

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Colorectal cancer (CRC)

Authorization of 12 months may be granted for treatment of metastatic CRC in combination with 5-fluorouracil, leucovorin, and irinotecan (FOLFIRI) or in combination with irinotecan.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication in Section II who have not experienced disease progression or an unacceptable toxicity.

IV. REFERENCES

1. Zaltrap [package insert]. Bridgewater, NJ: sanofi-aventis U.S. LLC; June 2016.
2. The NCCN Drugs & Biologics Compendium 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed March 15, 2019.
3. The NCCN Clinical Practice Guidelines in Oncology Colon Cancer (Version 1.2019). 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 15, 2019.
4. The NCCN Clinical Practice Guidelines in Oncology - Rectal Cancer (Version 1.2019). 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 15, 2019.

SPECIALTY GUIDELINE MANAGEMENT

ZEJULA (niraparib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy.
2. Treatment of adult patients with advanced ovarian, fallopian tube, or primary peritoneal cancer who have been treated with three or more prior chemotherapy regimens and whose cancer is associated with homologous recombination deficiency (HRD) positive status defined by either:
 - a. a deleterious or suspected deleterious BRCA mutation, or
 - b. genomic instability and who have progressed more than six months after response to the last platinum-based chemotherapy.

B. Compendial use

Ovarian, fallopian tube, or primary peritoneal cancer- single agent for maintenance treatment after completing two or more lines of platinum based therapy

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

Documentation of laboratory report confirming BRCA mutation status, where applicable.

Documentation of laboratory report confirming homologous recombination deficiency status, where applicable.

III. CRITERIA FOR INITIAL APPROVAL

Epithelial ovarian, fallopian tube, or primary peritoneal cancer

- A. Authorization of 12 months may be granted for maintenance treatment of recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer as a single agent when the member is in a complete or partial response to two or more lines of platinum-based chemotherapy.
- B. Authorization of 12 months may be granted for the treatment of advanced ovarian, fallopian tube, or primary peritoneal cancer as a single agent when the following criteria has been met:
 1. Member has been treated with three or more prior chemotherapy regimens
 2. Member's cancer is associated with homologous recombination deficiency (HRD) positive status defined by one of the following:
 - a. Member has a deleterious or suspected deleterious BRCA mutation
 - b. Member has genomic instability and has progressed more than six months after response to the last platinum-based chemotherapy

Reference number(s)
1687-A

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES

1. Zejula [package insert]. Waltham, MA: Tesaro, Inc.; October 2019.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed August 29, 2019.

SPECIALTY GUIDELINE MANAGEMENT

ZELBORAF (vemurafenib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Zelboraf is indicated for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E mutation as detected by an FDA-approved test.

Limitation of use: Zelboraf is not indicated for treatment of patients with wild-type BRAF melanoma.

2. Zelboraf is indicated for the treatment of patients with Erdheim-Chester Disease with BRAF V600 mutation.

B. Compendial Uses

1. Brain metastases with melanoma in combination with cobimetinib
2. Non-small cell lung cancer, BRAF V600E mutation-positive
3. Hairy cell leukemia
4. Thyroid carcinoma – papillary carcinoma, follicular carcinoma, Hurthle cell carcinoma, BRAF mutation-positive
5. Glioma, BRAF V600 activating mutation-positive
6. Meningioma, BRAF V600 activating mutation-positive
7. Astrocytoma, BRAF V600 activating mutation-positive
8. Rectal cancer, BRAF V600E mutation-positive
9. Colon cancer, BRAF V600E mutation-positive
10. Unresectable or metastatic cutaneous melanoma, BRAF V600 activating mutation-positive

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of BRAF mutation documentation is necessary to initiate the prior authorization review for applicable indications as outlined in Section III.

III. CRITERIA FOR INITIAL APPROVAL

A. **Melanoma**

1. Authorization of 12 months may be granted for treatment of unresectable or metastatic melanoma with a BRAF V600 activating mutation (e.g., BRAF V600E or V600K mutation).
2. Authorization of 12 months may be granted for the treatment of brain metastases with melanoma when all of the following criteria are met:

Reference number(s)
1685-A

- i. Zelboraf is used in combination with cobimetinib
- ii. Tumor is positive for BRAF V600 activating mutation (e.g., BRAF V600E or V600K mutation).

B. Erdheim-Chester Disease (ECD)

Authorization of 12 months may be granted for treatment of ECD with BRAF V600 mutation.

C. Non-small Cell Lung Cancer (NSCLC)

Authorization of 12 months may be granted for treatment of BRAF V600E mutation-positive NSCLC.

D. Hairy Cell Leukemia

Authorization of 12 months may be granted for treatment of hairy cell leukemia.

E. Thyroid Carcinoma (follicular, Hürthle cell, papillary)

Authorization of 12 months may be granted for treatment of BRAF mutation-positive radioiodine refractory papillary carcinoma, follicular carcinoma, or Hürthle cell carcinoma.

F. Central Nervous System Cancer

Authorization of 12 months may be granted for treatment of BRAF V600 mutation-positive gliomas, meningiomas, or astrocytomas.

G. Rectal Cancer

Authorization of 12 months may be granted for treatment of BRAF V600E mutation-positive rectal cancer.

H. Colon Cancer

Authorization of 12 months may be granted for treatment of BRAF V600E mutation-positive colon cancer.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy for an indication outlined in Section III when there is no evidence of unacceptable toxicity or disease progression on the current regimen.

V. REFERENCES

1. Zelboraf [package insert]. South San Francisco, CA: Genentech USA, Inc.; November 2017.
2. The NCCN Drugs & Biologics Compendium 2018 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed November 9, 2018.
3. Diamond EL, Dagna L, Hyman DM, et al. Consensus guidelines for the diagnosis and clinical management of Erdheim-Chester disease. *Blood*. 2014;124(4):483-492.
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Reference number(s)
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SPECIALTY GUIDELINE MANAGEMENT

ZEPATIER (elbasvir and grazoprevir)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Zepatier is indicated for the treatment of chronic hepatitis C virus genotype 1 or 4 infection in adults. Zepatier is indicated for use with ribavirin in certain patient populations.

B. Compendial Uses

Chronic hepatitis C genotype 3 infection

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

Coverage will not be provided for members with decompensated cirrhosis/moderate or severe hepatic impairment (Child Turcotte Pugh Class B or C)

Note: When the requested drug is being used in a combination therapy regimen, exclusions to the other antiviral drugs also apply.

III. CRITERIA FOR APPROVAL

A. **Chronic hepatitis C virus infection, in combination with ribavirin (RBV)**

1. **Genotype 1a infection**

- a. Authorization of up to 16 weeks total may be granted for members with baseline NS5A resistance-associated substitutions (RASs)/polymorphisms (see Section V) who are either of the following:
 - i. Treatment-naïve
 - ii. Failed prior treatment with peginterferon alfa (PEG-IFN) and RBV with or without an HCV protease inhibitor (boceprevir, simeprevir or telaprevir)
- b. Authorization of up to 12 weeks total may be granted for members without baseline NS5A resistance-associated substitutions (RASs)/polymorphisms (see Section V) who have failed prior treatment with PEG-IFN and RBV with an HCV protease inhibitor (boceprevir, simeprevir or telaprevir).

2. **Genotype 1b infection**

Authorization of up to 12 weeks total may be granted for members who failed prior treatment with PEG-IFN and RBV with an HCV protease inhibitor (boceprevir, simeprevir or telaprevir).

3. **Genotype 4 infection**

Reference number(s)
2145-A, 2684-A

Authorization of up to 16 weeks total may be granted for members who failed prior treatment with PEG-IFN and RBV.

B. Chronic hepatitis C virus infection, without RBV

1. Genotype 1a infection

- Authorization of up to 12 weeks total may be granted for members with end-stage renal disease (ESRD) or severe renal impairment (estimated glomerular filtration rate [eGFR] of less than 30 mL/min/1.73m²).
- Authorization of up to 12 weeks total may be granted for members without baseline NS5A resistance-associated substitutions (RASs)/polymorphisms who are either of the following:
 - Treatment-naïve
 - Failed prior treatment with PEG-IFN and RBV without an HCV protease inhibitor (boceprevir, simeprevir or telaprevir)

2. Genotype 1b infection

Authorization of up to 12 weeks total may be granted for members who are either of the following:

- Treatment-naïve
- Failed prior treatment with PEG-IFN and RBV without an HCV protease inhibitor (boceprevir, simeprevir or telaprevir)

3. Genotype 4 infection

Authorization of up to 12 weeks total may be granted for members who are either of the following:

- Treatment-naïve
- Failed prior treatment with PEG-IFN and RBV

C. Chronic hepatitis C virus infection, in combination with Sovaldi

Genotype 3 infection

Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV.

D. HCV and HIV coinfection

Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in Section A, B or C above are met.

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. APPENDIX: NS5A RESISTANCE-ASSOCIATED SUBSTITUTIONS (POLYMORPHISMS)

NS5A resistance-associated substitutions (polymorphisms) at amino acid positions M28, Q30, L31 or Y93. Examples include M28A/T, Q30H/R, L31M/V, and Y93C/H/N.

VI. REFERENCES

- Zepatier [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; June 2018.
- AASLD/IDSA/IAS–USA. Recommendations for testing, managing, and treating hepatitis C. <http://www.hcvguidelines.org>. Last changes made May 24, 2018. Accessed August 03, 2018.

SPECIALTY GUIDELINE MANAGEMENT

ZINBRYTA (daclizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication: Zinbryta is indicated for the treatment of adult patients with relapsing forms of multiple sclerosis (MS). Because of its safety profile, the use of Zinbryta should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Multiple Sclerosis

Authorization of 24 months may be granted to members with a diagnosis of a relapsing form of multiple sclerosis who have had an inadequate response to two or more drugs indicated for multiple sclerosis.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Zinbryta [package insert]. Cambridge, MA: Biogen Inc.; August 2017.

SPECIALTY GUIDELINE MANAGEMENT

ZOLADEX (goserelin acetate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Prostate cancer
 - a. For use in combination with flutamide for the management of locally confined stage T2b-T4 (Stage B2-C) carcinoma of the prostate. Treatment with Zoladex and flutamide should start 8 weeks prior to initiating radiation therapy and continue during radiation therapy.
 - b. In the palliative treatment of advanced carcinoma of the prostate
2. Endometriosis
For the management of endometriosis, including pain relief and reduction of endometriotic lesions for the duration of therapy. Experience with Zoladex for the management of endometriosis has been limited to women 18 years of age and older treated for 6 months (Zoladex 3.6 mg strength only)
3. Endometrial thinning
For use as an endometrial-thinning agent prior to endometrial ablation for dysfunctional uterine bleeding (Zoladex 3.6 mg strength only)
4. Advanced breast cancer
For use in the palliative treatment of advanced breast cancer in pre-and perimenopausal women

B. Compendial Uses

1. Breast cancer
2. Prostate cancer
3. Gender dysphoria (also known as gender non-conforming or transgender persons)
NOTE: Some plans may opt-out of coverage for gender dysphoria.
4. Preservation of ovarian function
5. Prevention of recurrent menstrual related attacks in acute porphyria
6. Uterine leiomyomata (fibroids)

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

Coverage will not be provided for members with any of the following exclusions: Use of the 10.8 mg strength for diagnoses other than prostate cancer, breast cancer, and gender dysphoria (if applicable).

III. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Hormone receptor status testing results (where applicable).

IV. CRITERIA FOR INITIAL APPROVAL

A. Breast Cancer

Authorization of 12 months may be granted for the treatment of hormone receptor-positive breast cancer.

B. Prostate Cancer

Authorization of 12 months may be granted for treatment of prostate cancer.

C. Endometriosis

Authorization of a total of 6 months may be granted to members for treatment of endometriosis.

D. Endometrial-thinning agent

Authorization of 2 doses may be granted for endometrial thinning prior to endometrial ablation for dysfunctional uterine bleeding.

E. Gender Dysphoria

1. Authorization of 12 months may be granted for pubertal suppression in preparation for gender reassignment in an adolescent member when all of the following criteria are met:
 - a. The member has a diagnosis of gender dysphoria.
 - b. The member has reached Tanner stage 2 of puberty.
2. Authorization of 12 months may be granted for gender reassignment in an adult member when all of the following criteria are met:
 - a. The member has a diagnosis of gender dysphoria.
 - b. The member will receive Zoladex concomitantly with cross sex hormones.

F. Preservation of ovarian function

Authorization of 3 months may be granted for preservation of ovarian function when the member is premenopausal and undergoing chemotherapy.

G. Prevention of recurrent menstrual related attacks in acute porphyria

Authorization of 12 months may be granted for prevention of recurrent menstrual related attacks in members with acute porphyria when the requested medication is prescribed by or in consultation with a physician experienced in the management of porphyrias.

H. Uterine leiomyomata (fibroids)

Authorization of a total of 3 months may be granted for treatment of uterine leiomyomata (fibroids) prior to surgery.

V. CONTINUATION OF THERAPY

- A. Authorization of 12 months may be granted for continued treatment in members requesting reauthorization who are experiencing clinical benefit to therapy or who have not experienced an unacceptable toxicity for the specified indications below:
 1. Breast cancer
 2. Prostate cancer
 3. Prevention of recurrent menstrual related attacks in acute porphyria
- B. Authorization of 12 months may be granted for continued treatment for gender dysphoria in all members (including new members) requesting reauthorization who meet all initial authorization criteria.

Reference number(s)
1918-A, 1919-A

- C. Authorization of 3 months may be granted for continued treatment for preservation of ovarian function in members requesting reauthorization who are premenopausal and are still undergoing chemotherapy.

VI. REFERENCES

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SPECIALTY GUIDELINE MANAGEMENT

RECLAST (zoledronic acid) zoledronic acid

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Treatment and prevention of osteoporosis in postmenopausal women
2. Treatment to increase bone mass in men with osteoporosis
3. Treatment and prevention of glucocorticoid-induced osteoporosis
4. Treatment of Paget's disease of bone in men and women

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Supporting chart notes or medical record indicating a history of fractures, T-score, and FRAX fracture probability as applicable to Sections III.A, III.B, and III.C.

III. CRITERIA FOR INITIAL APPROVAL

A. **Postmenopausal osteoporosis**

Authorization of 12 months may be granted to postmenopausal members with osteoporosis when ANY of the following criteria are met:

1. Member has a history of fragility fractures
2. Member has a pre-treatment T-score less than or equal to -2.5 OR member has osteopenia (i.e., pre-treatment T-score greater than -2.5 and less than -1) with a high pre-treatment FRAX fracture probability (See Appendix B) and meets ANY of the following criteria:
 - a. Member has indicators of higher fracture risk (e.g., advanced age, frailty, glucocorticoid use, very low T-scores [less than or equal to -3.5], or increased fall risk)
 - b. Member has failed prior treatment with or is intolerant to previous injectable osteoporosis therapy (e.g., denosumab [Prolia], teriparatide [Forteo])
 - c. Member has had an oral bisphosphonate trial of at least 1-year duration or there is a clinical reason to avoid treatment with an oral bisphosphonate (See Appendix A)

B. **Osteoporosis in men**

Authorization of 12 months may be granted to male members with osteoporosis when ANY of the following criteria are met:

1. Member has a history of an osteoporotic vertebral or hip fracture
2. Member meets criteria BOTH of the following criteria:
 - a. Member has a pre-treatment T-score less than or equal to -2.5 OR member has osteopenia (i.e., pre-treatment T-score greater than -2.5 and less than -1) with a high pre-treatment FRAX fracture probability (See Appendix B)
 - b. Member has had an oral bisphosphonate trial of at least 1-year duration OR there is a clinical reason to avoid treatment with an oral bisphosphonate (See Appendix A)

C. Glucocorticoid-induced osteoporosis

Authorization of 12 months may be granted for members with glucocorticoid-induced osteoporosis when ALL of the following criteria are met:

1. Member has had an oral bisphosphonate trial of at least 1-year duration OR there is a clinical reason to avoid treatment with an oral bisphosphonate (See Appendix A)
2. Member is currently receiving or will be initiating glucocorticoid therapy
3. Member meets ANY of the following criteria:
 - a. Member has a history of a fragility fracture
 - b. Member has a pre-treatment T-score of less than or equal to -2.5
 - c. Member has osteopenia (i.e., pre-treatment T-score greater than -2.5 and less than -1) with a high pre-treatment FRAX fracture probability (See Appendix B)

D. Paget's disease of bone

Authorization of one dose (5 mg) may be granted for the treatment of Paget's disease of bone.

IV. CONTINUATION OF THERAPY

A. Paget's disease of bone

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

B. All other indications

Authorization of 12 months may be granted for all members (including new members) who meet all initial authorization criteria and experiences clinical benefit after at least 24 months of therapy with zoledronic acid or Reclast as evidenced by improvement or stabilization in T-score.

V. APPENDIX

Appendix A. Clinical reasons to avoid oral bisphosphonate therapy

- Esophageal abnormality that delays emptying such as stricture of achalasia
- Active upper gastrointestinal problem (e.g., dysphagia, gastritis, duodenitis, erosive esophagitis, ulcers)
- Inability to stand or sit upright for at least 30 to 60 minutes
- Inability to take at least 30 to 60 minutes before first food, drink, or medication of the day
- Renal insufficiency (creatinine clearance <35 mL/min)
- History of intolerance to an oral bisphosphonate

Appendix B. WHO Fracture Risk Assessment Tool

- High FRAX fracture probability: 10 year major osteoporotic fracture risk $\geq 20\%$ or hip fracture risk $\geq 3\%$
- 10-year probability; calculation tool available at: <https://www.sheffield.ac.uk/FRAX/>
- The estimated risk score generated with FRAX should be multiplied by 1.15 for major osteoporotic fracture and 1.2 for hip fracture if glucocorticoid treatment is greater than 7.5 mg per day.

VI. REFERENCES

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SPECIALTY GUIDELINE MANAGEMENT

ZOMETA (zoledronic acid) zoledronic acid

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Zometa/zoledronic acid is indicated for the treatment of hypercalcemia of malignancy defined as an albumin-corrected calcium (cCa) of greater than or equal to 12mg/dL [3.0 mmol/L] using the formula: $cCa \text{ in mg/dL} = Ca \text{ in mg/dL} + 0.8 (4.0 \text{ g/dL} - \text{patient albumin [g/dL]})$.
2. Zometa/zoledronic acid is indicated for the treatment of patients with multiple myeloma and patients with documented bone metastases from solid tumors, in conjunction with standard antineoplastic therapy. Prostate cancer should have progressed after treatment with at least one hormonal therapy.

Limitation of Use: The safety and efficacy of Zometa/zoledronic acid in the treatment of hypercalcemia associated with hyperparathyroidism or with other non-tumor-related conditions have not been established.

B. Compendial Uses

1. Treatment or prevention of osteoporosis during androgen-deprivation therapy (ADT) in prostate cancer patients with high fracture risk
2. Treatment in postmenopausal patients with breast cancer who are receiving adjuvant therapy to maintain or improve bone mineral density and reduce risk of fractures
3. Treatment for osteopenia or osteoporosis in patients with systemic mastocytosis

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Hypercalcemia of Malignancy**

Authorization of 2 months may be granted for members who are prescribed zoledronic acid or Zometa for hypercalcemia of malignancy.

B. **Multiple Myeloma**

Authorization of 12 months may be granted for members who are prescribed zoledronic acid or Zometa for multiple myeloma.

C. **Bone Metastases from a Solid Tumor**

Authorization of 12 months may be granted for members who are prescribed zoledronic acid or Zometa for bone metastases from a solid tumor.

D. Prostate Cancer

Authorization of 12 months may be granted for members with prostate cancer who are prescribed zoledronic acid or Zometa for the treatment or prevention of osteoporosis during androgen deprivation therapy (ADT)

E. Breast Cancer

Authorization of 12 months may be granted for postmenopausal (natural or induced) members who are receiving adjuvant therapy for the treatment of breast cancer and are prescribed zoledronic acid or Zometa to maintain or improve bone mineral density and reduce the risk of fractures.

F. Systemic Mastocytosis

Authorization of 12 months may be granted for members who are prescribed zoledronic acid or Zometa for the treatment of osteopenia or osteoporosis in members with systemic mastocytosis.

III. CONTINUATION OF THERAPY**A. Hypercalcemia of malignancy**

Authorization of 2 months will be granted for continued treatment in members requesting reauthorization for hypercalcemia of malignancy who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

B. All Diagnosis (excluding hypercalcemia of malignancy)

Authorization of 12 months will be granted for continued treatment in members requesting reauthorization for an indication listed in Section II (excluding hypercalcemia of malignancy) who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

IV. REFERENCES

1. Zometa [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; December 2018.
2. Zoledronic acid [package insert]. Memphis, TN: Northstar Rx LLC; May 2018.
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SPECIALTY GUIDELINE MANAGEMENT

ZOLGENSMA (abeparvovec-xioi)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Zolgensma is indicated for the treatment of pediatric patients less than 2 years of age with spinal muscular atrophy (SMA) with bi-allelic mutations in the *survival motor neuron (SMN1)* gene.

Limitations of use:

- The safety and effectiveness of repeat administrations of Zolgensma have not been evaluated.
- The use of Zolgensma in patients with advanced SMA (e.g., complete paralysis of limbs, permanent ventilator dependence) has not been evaluated.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
Genetic testing results demonstrating bi-allelic mutations in the *survival motor neuron 1 (SMN1)* gene

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a physician who specializes in treatment of spinal muscular atrophy.

IV. CRITERIA FOR INITIAL APPROVAL

Spinal muscular atrophy

Authorization of one dose total may be granted for treatment of spinal muscular atrophy when all of the following criteria are met:

1. Member has a genetically confirmed diagnosis of SMA, with documentation of bi-allelic mutations in the *survival motor neuron 1 (SMN1)* gene (deletions or point mutations).
2. Member is less than 2 years of age.
3. Member does not have advanced SMA, including but not limited to any of the following:
 - a. Complete paralysis of limbs
 - b. Invasive ventilatory support (tracheostomy)

Reference number(s)
3093-A

- c. Respiratory assistance for 16 or more hours per day (including non-invasive respiratory support) continuously for 14 or more days in the absence of acute reversible illness (excluding perioperative ventilation)
4. The member has an anti-adeno-associated virus 9 (AAV9) antibody titer less than or equal to 1:50 as determined by Enzyme-linked Immunosorbent Assay (ELISA) binding immunoassay.
5. If the member is on nusinersen (Spinraza), it will be discontinued prior to administration of the requested drug.
6. The member has not received Zolgensma previously.

V. REFERENCES

1. Zolgensma [package insert]. Bannockburn, IL. AveXis, Inc; May 2019.

SPECIALTY GUIDELINE MANAGEMENT

ZOLINZA (vorinostat)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Treatment of cutaneous manifestations in patients with cutaneous T-cell lymphoma who have progressive, persistent, or recurrent disease on or following two systemic therapies

B. Compendial Uses

1. Mycosis fungoides (MF)
2. Sézary syndrome (SS)

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR APPROVAL

Cutaneous T-cell Lymphoma (CTCL)

Authorization of 12 months may be granted for the treatment of CTCL (e.g., MF, SS).

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced disease progression or an unacceptable toxicity.

IV. REFERENCES

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2. The NCCN Drugs & Biologics Compendium™ © 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed January 24, 2019.

SPECIALTY GUIDELINE MANAGEMENT

ZORBTIVE (somatropin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Zorbtive is indicated for the treatment of short bowel syndrome in adult patients receiving specialized nutritional support. Zorbtive should be used in conjunction with optimal management of short bowel syndrome.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Short bowel syndrome (SBS)

Authorization of a lifetime maximum of 4 weeks may be granted to members who depend on intravenous parenteral nutrition support who are prescribed Zorbtive for the treatment of SBS.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Zorbtive [package insert]. Rockland, MA: EMD Serono, Inc.; May 2017.

SPECIALTY GUIDELINE MANAGEMENT

ZULRESSO (brexanolone)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Treatment of postpartum depression (PPD) in adults

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 1 infusion may be granted for treatment of moderate to severe postpartum depression in members 18 years of age or older when all of the following criteria are met:

- A. Member has had a major depressive episode that began no earlier than the third trimester of pregnancy and no later than the first 4 weeks following delivery, documented by standardized rating scales that reliably measure depressive symptoms (e.g., Beck Depression Scale [BDI], Hamilton Depression Rating Scale [HDRS], Montgomery-Asberg Depression Rating Scale [MADRS], etc.)
- B. Diagnosis is verified by a psychiatrist
- C. Member is 6 months postpartum or less
- D. Lactation has ceased or breastmilk produced will not be used for feedings during the infusion and up to 4 days following infusion completion
- E. Member does not have current substance or alcohol use disorder
- F. Member will not receive more than one infusion per pregnancy/childbirth

III. REFERENCES

1. Zulresso [package insert]. Cambridge, MA: Sage Therapeutics, Inc.; March 2019.

SPECIALTY GUIDELINE MANAGEMENT

ZYDELIG (idelalisib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Relapsed chronic lymphocytic leukemia (CLL), in combination with rituximab, in patients for whom rituximab alone would be considered appropriate therapy due to other co-morbidities
2. Relapsed follicular B-cell non-Hodgkin lymphoma (FL) in patients who have received at least two prior systemic therapies
3. Relapsed small lymphocytic lymphoma (SLL) in patients who have received at least two prior systemic therapies

Limitations of use:

Zydelig is not indicated and is not recommended for first-line treatment of any patient.

Zydelig is not indicated and is not recommended in combination with bendamustine and/or rituximab for the treatment of FL.

Accelerated approval for FL and SLL was granted based on overall response rate. Improvement in patient survival or disease related symptoms has not been established. Continued approval for these indications may be contingent upon verification of clinical benefit in confirmatory trials.

B. Compendial Uses

1. Relapsed or refractory CLL/SLL
2. Refractory or relapsed follicular lymphoma
3. Marginal zone lymphomas (nodal, splenic, gastric MALT and non-gastric MALT)

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. **Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL)**

Authorization of 12 months may be granted for treatment CLL/SLL when either of the following criteria are met:

- a. Zydelig will be used as a single agent, or
- b. Zydelig will be used in combination with rituximab.

B. **Follicular B-cell non-Hodgkin lymphoma (FL)**

Authorization of 12 months may be granted for treatment of FL in patients who have received at least two prior systemic therapies for their disease.

Reference number(s)
1706-A

C. Marginal zone lymphomas

Authorization of 12 months may be granted for treatment of marginal zone lymphoma (nodal, splenic, gastric MALT, and non-gastric MALT) in patients who have received at least two prior systemic therapies for their disease.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced disease progression or an unacceptable toxicity.

IV. REFERENCES

1. Zydelig [package insert]. Foster City, CA: Gilead Sciences, Inc.; January 2018.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed April 28, 2019.

SPECIALTY GUIDELINE MANAGEMENT

ZYKADIA (ceritinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Zykadia is indicated for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK)-positive as detected by an FDA-approved test.

B. Compendial Uses

1. NSCLC, recurrent, advanced or metastatic ALK rearrangement-positive or ROS1 rearrangement-positive tumors
2. Inflammatory myofibroblastic tumor (IMT) with ALK translocation
3. Recurrent brain metastases from ALK-positive NSCLC

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: ALK mutation or translocation status or ROS-1 mutation status (where applicable).

III. CRITERIA FOR INITIAL APPROVAL

A. **Non-small cell lung cancer (NSCLC)**

Authorization of 12 months may be granted for treatment of NSCLC when the member meets either of the following criteria:

1. Member has recurrent, advanced or metastatic ALK-positive NSCLC (including brain metastases from NSCLC).
2. Member has recurrent, advanced or metastatic ROS1-positive NSCLC.

B. **Inflammatory myofibroblastic tumor (IMT)**

Authorization of 12 months may be granted for treatment of ALK-positive IMT.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication in Section III who have not experienced disease progression or an unacceptable toxicity.

Reference number(s)
1668-A

V. REFERENCES

1. Zykadia [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corp; March 2019.
2. The NCCN Drugs & Biologics Compendium 2018 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 15, 2019.
3. The NCCN Clinical Practice Guidelines in Oncology Non-Small Cell Lung Cancer (Version 3.2019). 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 14, 2019.
4. The NCCN Clinical Practice Guidelines in Oncology Soft Tissue Sarcoma (Version 2.2019). 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 14, 2019.
5. The NCCN Clinical Practice Guidelines in Oncology Central Nervous System Cancers (Version 1.2019). 2019 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed March 14, 2019.

SPECIALTY GUIDELINE MANAGEMENT

ZYTIGA (abiraterone) abiraterone

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

1. Indicated in combination with prednisone for the treatment of patients with metastatic castration-resistant prostate cancer.
2. Indicated in combination with prednisone for the treatment of patients with metastatic high-risk castration-sensitive prostate cancer.

B. Compendial Uses

Node-positive (N₁), non-metastatic (M₀) prostate cancer

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

Coverage will not be provided if the requested medication is used in combination with a second-generation oral anti-androgen (e.g., apalutamide [Erleada]) or an oral androgen metabolism inhibitor (e.g., abiraterone acetate [Yonsa]).

III. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for the treatment of node positive or metastatic prostate cancer when the member has had a bilateral orchiectomy or will be using the requested medication in combination with a GnRH analog.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES

1. Zytiga [package insert]. Horsham, PA: Janssen Biotech, Inc.; June 2019.

Reference number(s)
1934-A

2. Abiraterone [package insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; September 2018.
3. IBM Micromedex®DRUGDEX® (electronic version). IBM Watson Heath, Greenwood Village, Colorado. Available at <https://www.micromedexsolutions.com>. Accessed July 22, 2019.
4. The NCCN Drugs & Biologics Compendium™ © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org> Accessed July 9, 2019.
5. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology™ Prostate Cancer (Version 2.2019). <https://www.nccn.org>. Accessed July 9, 2019.