Reference number(s)
4463-A

STANDARD MEDICARE PART B 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
   iv. Treatment of pediatric patients 2 years and older with previously untreated high risk classical Hodgkin lymphoma (cHL) in combination with doxorubicin, vincristine, etoposide, prednisone and cyclophosphamide

2. Systemic anaplastic large cell lymphoma (sALCL)
   i. Treatment of systemic anaplastic large cell lymphoma (sALCL) after failure of at least one prior multi-agent chemotherapy regimen
   ii. 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
1. cHL stage I-II unfavorable
2. CD30+ B-Cell Lymphomas
   i. Monomorphic post-transplant lymphoproliferative disorders (B-cell type)
   ii. Monomorphic post-transplant lymphoproliferative disorders (T-cell type)
   iii. Diffuse large B-cell lymphoma
   iv. HIV-Related B-cell lymphomas (CD30+ HIV-related diffuse large B-cell lymphoma, primary effusion lymphoma, and human herpesvirus-8 (HHV8)-positive diffuse large B-cell lymphoma)
   v. High-grade B-Cell lymphomas
   vi. Primary mediastinal large B-cell lymphoma
3. CD30+ Primary Cutaneous Lymphomas
   i. Mycosis Fungoides (MF)/Sezary Syndrome (SS)
   ii. Lymphomatoid papulosis (LyP)

iii. Cutaneous anaplastic large cell lymphoma

4. CD30+ T-Cell Lymphomas
   i. Hepatosplenic T-cell lymphoma
   ii. Adult T-cell leukemia/lymphoma
   iii. Breast implant-associated anaplastic large cell lymphoma (ALCL)
   iv. Peripheral T-cell lymphoma (PTCL)
   v. Extranodal NK/T-cell Lymphoma
   vi. Angioimmunoblastic T-cell lymphoma

All other indications will be assessed on an individual basis. Submissions for indications other than those enumerated in this policy should be accompanied by supporting evidence from Medicare approved compendia.

II. DOCUMENTATION

The following documentation must be available, upon request, for all submissions:
Initial requests: Testing or analysis confirming CD30 expression on the surface of the cell

III. CRITERIA FOR INITIAL APPROVAL

A. Classical Hodgkin lymphoma (cHL)

Authorization of 12 months may be granted for treatment of CD30+ cHL when any of the following are met:

1. The requested drug will be used as a single agent, or
2. The requested drug will be used in combination with doxorubicin, vinblastine, and dacarbazine, or
3. The requested drug will be used in combination with bendamustine for subsequent therapy, or
4. The requested drug will be used in combination with dacarbazine, or
5. The requested drug will be used in combination with nivolumab for subsequent therapy,or
6. The requested drug will be used in combination with gemcitabine for subsequent therapy, or
7. The requested drug will be used in combination with ifosfamide, carboplatin and etoposide for subsequent therapy, or
8. The requested drug will be used in combination with etoposide, prednisone and doxorubicin, or
9. The requested drug will be used in combination with cyclophosphamide, prednisone, and dacarbazine for subsequent therapy, or
10. The requested drug will be used in combination with doxorubicin, vincristine, etoposide, prednisone and cyclophosphamide

B. B-Cell Lymphomas

Authorization of 12 months may be granted for treatment of CD30+ B-cell lymphomas with any of the following subtypes:

1. Monomorphic post-transplant lymphoproliferative disorders (B-cell type) when both of the following are met:
   i. The requested drug will be used for subsequent therapy, and
   ii. The member is not a candidate for transplant
2. Monomorphic post-transplant lymphoproliferative disorders (T-cell type) when the requested drug will be used in combination with cyclophosphamide, doxorubicin, and prednisone.
3. Diffuse large B-cell lymphoma when all of the following are met:
   i. The requested drug will be used as subsequent therapy, and
   ii. The member is not a candidate for transplant.

4. HIV-Related B-cell lymphomas (HIV-related diffuse large B-cell lymphoma, primary effusion lymphoma, and human herpesvirus-8 (HHV8)-positive diffuse large B-cell lymphoma) when both of the following are met:
   i. The requested drug will be used for subsequent therapy, and
   ii. The member is not a candidate for transplant.
5. High-grade B-cell lymphomas when both of the following are met:
   i. The requested drug will be used for subsequent therapy, and
   ii. The member is not a candidate for transplant.
6. Primary mediastinal large B-cell lymphoma when both of the following are met
   i. The requested drug will be used for relapsed or refractory disease, and
   ii. The requested drug will be used in combination with nivolumab or pembrolizumab

C. Primary Cutaneous Lymphomas

Authorization of 12 months may be granted for treatment of CD30+ primary cutaneous lymphomas with any of the following subtypes:

1. Mycosis fungoides (MF)/Sezary syndrome (SS)
2. Lymphomatoid papulosis (LyP) when both of the following are met:
   i. The requested drug will be used as a single agent, and
   ii. The disease is relapsed or refractory.
3. Cutaneous anaplastic large cell lymphoma when either of the following are met:
   i. The requested drug will be used as a single agent, or
   ii. The requested drug will be used in combination with cyclophosphamide, doxorubicin, and prednisone (CHP).

D. T-Cell Lymphomas

Authorization of 12 months may be granted for treatment of CD30+ T-cell lymphomas with any of the following subtypes:

1. Hepatosplenic T-cell lymphoma when either of the following are met:
   i. The requested drug will be used as a single agent after two or more primary treatment regimens, or
   ii. The requested drug will be used in combination with cyclophosphamide, doxorubicin, and prednisone.
2. Adult T-cell leukemia/lymphoma when either of the following are met:
   i. The requested drug will be used as a single agent for subsequent therapy, or
   ii. The requested drug will be used in combination with cyclophosphamide, doxorubicin, and prednisone.
3. Breast implant associated anaplastic large cell lymphoma (ALCL) when either of the following are met:
   i. The requested drug will be used as a single agent, or
   ii. The requested drug will be used in combination with cyclophosphamide, doxorubicin, and prednisone.
4. Peripheral T-cell lymphoma (PTCL) [including the following subtypes: anaplastic large cell lymphoma, peripheral T-cell lymphoma not otherwise specified, angioimmunoblastic T-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 either of the following are met:
   i. The requested drug will be used a single agent for subsequent or palliative therapy, or
   ii. The requested drug will be used in combination with cyclophosphamide, doxorubicin, and prednisone.
5. Extranodal NK/T-cell lymphoma when all of the following are met:
   i. The requested drug will be used as a single agent, and
   ii. The member has relapsed or refractory disease, and

iii. The member has had an inadequate response or contraindication to asparaginase-based therapy (e.g., pegaspargase).

6. Systemic anaplastic large cell lymphoma when either of the following are met:
   i. The requested drug will be used as a single agent, or
   ii. The requested drug will be used in combination with cyclophosphamide, doxorubicin, and prednisone (CHP).

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested agent.

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

A. The member is currently receiving therapy with the requested drug.
B. The requested drug is being used to treat an indication enumerated in Section III.
C. The member is receiving benefit from therapy. Benefit is defined as:
   1. No evidence of unacceptable toxicity while on the current regimen and
   2. No evidence of disease progression while on the current regimen.

V. SUMMARY OF EVIDENCE

The contents of this policy were created after examining the following resources:

1. The prescribing information for Adcetris.
2. The available compendium
   a. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
   b. Micromedex DrugDex
   c. American Hospital Formulary Service- Drug Information (AHFS-DI)
   d. Lexi-Drugs
   e. Clinical Pharmacology
3. NCCN Guideline: Hodgkin lymphoma
4. NCCN Guideline: T-cell lymphomas
5. NCCN Guideline: Pediatric Hodgkin lymphoma
6. NCCN Guideline: Pediatric aggressive mature B-cell lymphomas
7. NCCN Guideline: Primary cutaneous lymphomas
8. NCCN Guideline: B-cell lymphomas

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Adcetris are covered in addition to the following:

1. cHL stage I-II unfavorable
2. CD30+ B-Cell Lymphomas
   i. Monomorphic post-transplant lymphoproliferative disorders (B-cell type)
   ii. Monomorphic post-transplant lymphoproliferative disorders (T-cell type)
   iii. Diffuse large B-cell lymphoma
   iv. HIV-Related B-cell lymphomas (CD30+ HIV-related diffuse large B-cell lymphoma, primary effusion lymphoma, and human herpesvirus-8 (HHV8)-positive diffuse large B-cell lymphoma)
   v. High-grade B-Cell lymphomas
   vi. Primary mediastinal large B-cell lymphoma
3. CD30+ Primary Cutaneous Lymphomas
   i. Mycosis Fungoides (MF)/Sezary Syndrome (SS)
   ii. Lymphomatoid papulosis (LyP)

iii. Cutaneous anaplastic large cell lymphoma

4. CD30+ T-Cell Lymphomas
   i. Hepatosplenic T-cell lymphoma
   ii. Adult T-cell leukemia/lymphoma
   iii. Breast implant-associated anaplastic large cell lymphoma (ALCL)
   iv. Peripheral T-cell lymphoma (PTCL)
   v. Extranodal NK/T-cell Lymphoma
   vi. Angioimmunoblastic T-cell lymphoma

VI. EXPLANATION OF RATIONALE

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Support for cHL stage I-II unfavorable can be found in the NCCN Drugs and Biologics Compendium. Use of information in the NCCN Drugs and Biologics Compendium for off-label use of drugs and biologicals in an anti-cancer chemotherapeutic regimen is supported by the Medicare Benefit Policy Manual, Chapter 15, section 50.4.5 (Off-Label Use of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen).

Support for CD30+ B-cell lymphomas can be found in the NCCN Drugs and Biologics Compendium. Use of information in the NCCN Drugs and Biologics Compendium for off-label use of drugs and biologicals in an anti-cancer chemotherapeutic regimen is supported by the Medicare Benefit Policy Manual, Chapter 15, section 50.4.5 (Off-Label Use of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen).

Support for CD30+ primary cutaneous lymphomas can be found in the NCCN Drugs and Biologics Compendium. Use of information in the NCCN Drugs and Biologics Compendium for off-label use of drugs and biologicals in an anti-cancer chemotherapeutic regimen is supported by the Medicare Benefit Policy Manual, Chapter 15, section 50.4.5 (Off-Label Use of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen).

Support for CD30+ T-cell lymphomas can be found in the NCCN Drugs and Biologics Compendium. Use of information in the NCCN Drugs and Biologics Compendium for off-label use of drugs and biologicals in an anti-cancer chemotherapeutic regimen is supported by the Medicare Benefit Policy Manual, Chapter 15, section 50.4.5 (Off-Label Use of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen).

VII. REFERENCES

1. Adcetris [package insert]. Bothell, WA: Seagen, Inc; November 2022.
2. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org. Accessed April 5, 2023.