Reference number(s)
3061-A

STANDARD MEDICARE PART B 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.
3. Adult Relapsed or Refractory (r/r) Follicular Lymphoma (FL)
   Adult patients with relapsed or refractory (r/r) follicular lymphoma (FL) after two or more lines of systemic therapy.

   Limitation of Use: Kymriah is not indicated for treatment of patients with primary central nervous system lymphoma.

B. Compendial Uses
1. Pediatric B-cell ALL first relapse post hematopoietic stem cell transplant (HSCT)
2. Histologic transformation of indolent lymphomas to DLBCL
3. Human immunodeficiency virus (HIV)-related B-cell lymphomas (including HIV-related diffuse large B-cell lymphoma, primary effusion lymphoma, and human herpesvirus 8 (HHV8)-positive diffuse large B-cell lymphoma, not otherwise specific)
4. Monomorphic post-transplant lymphoproliferative disorder (B-cell type)
5. Ph-negative or Ph-like B-ALL that is minimal residual disease positive (MRD+) after consolidation therapy
6. Ph-positive B-ALL with less than complete response or MRD+ at end of consolidation

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. EXCLUSIONS

Coverage will not be provided for members with any of the following exclusions:
A. Previous treatment course with the requested medication or another CD19-directed chimeric antigen receptor (CAR) T-cell therapy
B. Inadequate and unstable kidney, liver, pulmonary and cardiac function

C. Active or latent hepatitis B, active hepatitis C or any active uncontrolled infection
D. Active graft versus host disease
E. Active inflammatory disorder

III. DOCUMENTATION

The following documentation must be available, upon request, for all submissions:
For all indications: Chart notes, medical record documentation or claims history supporting previous lines of therapy

IV. 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 ALL in members less than 26 years of age when the member meets any of the following:
1. Member has Philadelphia chromosome-negative disease that is refractory or has had 2 or more relapses
2. Member has Philadelphia chromosome-positive disease and meets any of the following:
   i. Member has refractory disease
   ii. Member had 2 or more relapses and has failed at least 2 tyrosine kinase inhibitors (TKIs) (e.g., bosutinib, dasatinib, imatinib, nilotinib, ponatinib).
   iii. Member has relapsed disease and is TKI intolerant
   iv. Member has experienced a relapse post-hematopoietic stem cell transplant (HSCT)
3. Ph-negative or Ph-like B-ALL that is minimal residual disease positive (MRD+) after consolidation therapy
4. Ph-positive B-ALL with less than complete response or MRD+ at end of consolidation

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:
   i. Diffuse large B-cell lymphoma (DLBCL) arising from follicular lymphoma
   ii. Follicular lymphoma
   iii. Histologic transformation of indolent lymphomas to DLBCL
   iv. Diffuse large B-cell lymphoma (DLBCL)
   v. High-grade B-cell lymphomas (including high-grade B-cell lymphoma with translocations of MYC and BCL2 and/or BCL6 [double/triple hit lymphoma], high-grade B-cell lymphoma, not otherwise specified)
   vi. Human immunodeficiency virus (HIV)-related B-cell lymphomas (including HIV-related diffuse large B-cell lymphoma, primary effusion lymphoma, and human herpesvirus 8 (HHV8)-positive diffuse large B-cell lymphoma, not otherwise specific)
   vii. Monomorphic post-transplant lymphoproliferative disorder (B-cell type)
2. The member has received prior treatment with two or more lines of systemic therapy
3. The member does not have primary central nervous system lymphoma.
4. Member has an ECOG performance status of 0 to 2 (member is ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours).

V. SUMMARY OF EVIDENCE

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

1. The prescribing information for Kymriah.
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: Acute lymphoblastic leukemia
4. NCCN Guideline: Pediatric acute lymphoblastic leukemia
5. NCCN Guideline: B-cell lymphomas
6. National Coverage Determination: Chimeric Antigen Receptor (CAR) T-cell Therapy

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

1. Pediatric B-cell ALL first relapse post hematopoietic stem cell transplant (HSCT)
2. Histologic transformation of indolent lymphomas to DLBCL
3. Human immunodeficiency virus (HIV)-related B-cell lymphomas (including HIV-related diffuse large B-cell lymphoma, primary effusion lymphoma, and human herpesvirus 8 (HHV8)-positive diffuse large B-cell lymphoma, not otherwise specific)
4. Monomorphic post-transplant lymphoproliferative disorder (B-cell type)
5. Ph-negative or Ph-like B-ALL that is minimal residual disease positive (MRD+) after consolidation therapy
6. Ph-positive B-ALL with less than complete response or MRD+ at end of consolidation

VI. EXPLANATION OF RATIONALE

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

Support for using Kymriah to treat compendial indications listed in section V 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).

All FDA-approved indications are covered according to the conditions outlined in National Coverage Determination Manual section 110.24 (Chimeric Antigen Receptor [CAR] T-cell Therapy).

VII. REFERENCES

1. Kymriah [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; May 2022.
2. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 17, 2023.
3. NCCN Clinical Practice Guidelines in Oncology® Acute Lymphoblastic Leukemia (Version 1.2022).© 2023 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 17, 2023.
4. NCCN Clinical Practice Guidelines in Oncology® B-Cell Lymphomas (Version 2.2023).© 2023 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 14, 2023.
5. National Coverage Determination (NCD) for Chimeric Antigen Receptor (CAR) T-cell Therapy (110.24-Version 1). https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=374&ncdver=1&DocID=110.24&SearchType=Advanced&bc=EAAAAAIAAAAA&. Accessed April 17, 2023.

6. Maude SL, Laetsch TW, Buechner J, et al. Tisagenlecleucel in Children and Young Adults with B-Cell Lymphoblastic Leukemia. N Engl J Med. 2018;378(5):439-448.
7. Schuster SJ, Bishop MR, Tam CS, et al. Tisagenlecleucel in Adult Relapsed or Refractory Diffuse Large B-Cell Lymphoma. N Engl J Med. 2019;380(1):45-56.