Reference number(s)
2294-A

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)
   Kymriah is indicated for the treatment of 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 (DLBCL)
   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)

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 all indications: Chart notes, medical record documentation or claims history supporting previous lines of therapy.
B. For Acute Lymphoblastic Leukemia:
1. Testing or analysis confirming CD19 tumor expression in bone marrow or peripheral blood.
2. Testing or analysis confirming at least 5% lymphoblasts in the bone marrow.

III. 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

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 all of the following criteria are met:
1. The member has CD19 tumor expression in bone marrow or peripheral blood.
2. The member has at least 5% lymphoblasts in the bone marrow.
3. Member meets either of the following:
    i. Member has Philadelphia chromosome-negative disease that is refractory or has had 2 or more relapses
    ii. Member has Philadelphia chromosome-positive disease and meets any of the following:
        a. Member has refractory disease
        b. Member has had 2 or more relapses and has failed at least 2 tyrosine kinase inhibitors (TKIs) (e.g., bosutinib, dasatinib, imatinib, nilotinib, ponatinib)
        c. Member has relapsed disease and is TKI intolerant
        d. Member has experienced a relapse post-hematopoietic stem cell transplant (HSCT)
4. The member has a Karnofsky (age ≥16 years) or Lansky (age < 16 years) performance status greater than or equal to 50%.

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. 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. 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.
6. 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.