Tisagenlecleucel (Kymriah®)

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the medical policy and a health plan or government program (e.g., TennCare), the express terms of the health plan or government program will govern.

The proposal is to add text/statements in red and to delete text/statements with strikethrough:

POLICY

INDICATIONS

The indications below including FDA-approved indications and compendial 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

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.

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.

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.

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

Compendial Uses

- Pediatric B-cell ALL first relapse post hematopoietic stem cell transplant (HSCT)
- Histologic transformation of indolent lymphomas to DLBCL
- 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)~~
- Monomorphic post-transplant lymphoproliferative disorder (B-cell type)

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

DOCUMENTATION

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

- For all indications: Chart notes or medical record documentation demonstrating failure of ~~or claims history supporting~~ previous lines of therapy.

- For Acute Lymphoblastic Leukemia:
  - Testing or analysis confirming CD19 tumor expression in bone marrow or peripheral blood.
  - Testing or analysis confirming at least 5% lymphoblasts in the bone marrow.

EXCLUSIONS

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

- Previous treatment course with the requested medication or another CD19-directed chimeric antigen receptor (CAR) T-cell therapy
- Inadequate and unstable kidney, liver, pulmonary and cardiac function
- Active or latent hepatitis B, active hepatitis C or any active uncontrolled infection
- Active graft versus host disease
- Active inflammatory disorder

COVERAGE CRITERIA ~~FOR INITIAL APPROVAL~~

Pediatric and Young Adult Relapsed or Refractory (r/r) B-cell Acute Lymphoblastic Leukemia (ALL)

Authorization of 3 months (one dose) 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:

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

Adult B-cell Lymphomas

Authorization of 3 months (one dose) 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:

- Member has any of the following B-cell lymphoma subtypes:
  - Diffuse large B-cell lymphoma (DLBCL) arising from follicular lymphoma
  - Follicular lymphoma
  - Histologic transformation of indolent lymphomas to DLBCL
  - Diffuse large B-cell lymphoma (DLBCL)
  - 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)
  - 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 and plasmablastic lymphoma)
  - Monomorphic post-transplant lymphoproliferative disorder (B-cell type)

- The member has received prior treatment with two or more lines of systemic therapy.
- The member does not have primary central nervous system lymphoma.
- 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).

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

REFERENCES

1. Kymriah [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; December 2024.
2. The NCCN Drugs & Biologics Compendium® © 2025 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 29, 2025.
3. NCCN Clinical Practice Guidelines in Oncology® Acute Lymphoblastic Leukemia (Version 3.2024).© 2025 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 29, 2025.
4. NCCN Clinical Practice Guidelines in Oncology® B-Cell Lymphomas (Version 2.2025).© 2025 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 29, 2025.
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.
7. Clinical Consult: CVS Caremark Clinical Programs Review. Focus on Hematology-Oncology Clinical Programs. September 2021.

EFFECTIVE DATE

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