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DRUG POLICY

Kymriah (tisagenlecleucel)

NOTICE

This policy contains information which is clinical in nature. The policy is not medical advice. The information in this policy is used by Wellmark to make determinations whether medical treatment is covered under the terms of a Wellmark member's health benefit plan. Physicians and other health care providers are responsible for medical advice and treatment. If you have specific health care needs, you should consult an appropriate health care professional. If you would like to request an accessible version of this document, please contact customer service at 800-524-9242.

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This medical policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

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

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.

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

Compendial Use

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
4. Monomorphic post-transplant lymphoproliferative disorder (B-cell type)

POLICY

Required Documentation

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

1. For all indications: Chart notes or medical record documentation demonstrating failure of previous lines of therapy.
2. For Acute Lymphoblastic Leukemia:
 - a. Testing or analysis confirming CD19 tumor expression in bone marrow or peripheral blood.
 - b. 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:

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

Criteria for Initial Approval

A. 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 acute lymphoblastic leukemia (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:
 - a. Member has Philadelphia chromosome-negative disease that is refractory or has had 2 or more relapses
 - b. Member has Philadelphia chromosome-positive disease and meets any of the following:
 - i. Member has refractory disease
 - ii. 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)
 - iii. Member has relapsed disease and is TKI intolerant
 - iv. 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 (one dose) may be granted for the 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
 - b. Follicular lymphoma
 - c. Histologic transformation of indolent lymphomas to DLBCL
 - d. Diffuse large B-cell lymphoma (DLBCL)

- e. 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)
- f. Human immunodeficiency virus (HIV)-related B-cell lymphomas (including HIV-related diffuse large B-cell lymphoma, primary effusion lymphoma, human herpesvirus 8 (HHV8)-positive diffuse large B-cell lymphoma, not otherwise specific and plasmablastic lymphoma)
- g. 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 Eastern Cooperative Oncology Group (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).

Continuation of Therapy

Repeat treatment of Kymriah for any indication is considered investigational, as the safety and efficacy beyond one dose has not been studied. The evidence is insufficient to determine the effects on net health outcomes.

Dosing and Administration

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

Quantity Limits

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

Kymriah will be provided based on the FDA recommended dosing and administration:

- Patients 50kg or less: weight-based dosing at 0.2 to 5.0×10^6 CAR-positive viable T-cells per kg of body weight intravenously
- Patients greater than 50kg: $\leq 2.5 \times 10^8$ total CAR-positive T-cells intravenously

Kymriah approvals will be limited to one treatment per lifetime.

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

- Q2042 – Tisagenlecleucel, up to 600 million CAR-positive viable T-cells, including leukapheresis and dose preparation procedures, per therapeutic dose

REFERENCES

- Kymriah [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; December 2024.
- The NCCN Drugs & Biologics Compendium® © 2025 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed April 29, 2025.
- 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.
- 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.
- 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.
- 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.

- Clinical Consult: CVS Caremark Clinical Programs Review. Focus on Hematology-Oncology Clinical Programs. September 2021.

POLICY HISTORY

Policy #: 05.04.77

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