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. Acquired immunodeficiency syndrome (AIDS)-related B-cell lymphomas (including AIDS-related diffuse large B-cell lymphoma, primary effusion lymphoma, and human herpesvirus 8 (HHV8)-positive diffuse large B-cell lymphoma, not otherwise specified)
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, medical record documentation or claims history supporting 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.

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 one-time 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 not received a previous treatment course of the requested medication or another CD19-directed chimeric antigen receptor (CAR) T-cell therapy.
2. The member has CD19 tumor expression in bone marrow or peripheral blood.
3. The member has at least 5% lymphoblasts in the bone marrow.
4. 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., 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)
5. The member has a Karnofsky (age ≥16 years) or Lansky (age < 16 years) performance status greater than or equal to 50%.
6. The member has adequate and stable kidney, liver, pulmonary and cardiac function as demonstrated by all of the following:
    a. Creatinine clearance ≥ 60 mL/minute
    b. Serum creatinine of ≤ 1.5 times upper limit of normal
    c. Alanine aminotransferase (ALT) ≤ 5 times upper limit of normal for age
    d. Bilirubin ≤ 2.0 mg/dL with the exception of patients with Gilbert-Meulengracht syndrome; patients with Gilbert-Meulengracht syndrome may be included if their total bilirubin is ≤ 3 times the upper limit of normal
    e. Direct bilirubin ≤ 1.5 times upper limit of normal
    f. Hemodynamically stable and left ventricular ejection fraction (LVEF) ≥ 45% confirmed by echocardiogram or multigated acquisition (MUGA) scan
7. The member does not have any active infections including hepatitis B (HBsAG negative) or hepatitis C virus (anti-HCV negative); (a history of hepatitis B or hepatitis C virus is permitted if the viral load is undetectable per quantitative PCR and/or nucleic acid testing).
8. The member does not have active graft versus host disease.
9. The member does not have active inflammatory disorder.

10. The member will receive Kymriah at a treatment center that is certified to administer Kymriah per Kymriah REMS requirements.

B. Adult B-cell Lymphomas

Authorization of 3 months will be granted for a one-time treatment of Kymriah for the treatment of B-cell lymphomas in members 18 years of age or older at the time of infusion 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 (also known as histologic transformation of follicular lymphoma to DLBCL)
   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. Acquired immunodeficiency syndrome (AIDS)-related B-cell lymphomas (including AIDS-related diffuse large B-cell lymphoma, primary effusion lymphoma, and human herpesvirus 8 (HHV8)-positive diffuse large B-cell lymphoma, not otherwise specified)
   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. The member has not received a previous treatment course of the requested medication or another CD19-directed chimeric antigen receptor (CAR) T-cell therapy.
5. 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).
6. The member has adequate and stable kidney, liver, pulmonary and cardiac function.
7. The member does not have any active infections including hepatitis B (HBsAG negative) or hepatitis C virus (anti-HCV negative); (a history of hepatitis B or hepatitis C virus is permitted if the viral load is undetectable per quantitative PCR and/or nucleic acid testing).
8. The member does not have active graft versus host disease.
9. The member does not have an active inflammatory disorder.
10. The member will receive Kymriah at a treatment center that is certified to administer Kymriah per Kymriah REMS requirements.

<u>Continuation of Therapy</u>

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.

<u>Dosing and Administration</u>

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

<u>Quantity Limits</u>

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 $5.0x10^6$ CAR-positive viable T-cells per kg of body weight intraveneously
- Patients greater than 50kg: ≤ 2.5×10^8 total CAR-positive T-cells intraveneously

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; May 2022.
- NCCN Drugs & Biologics Compendium® © 2021 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 14, 2022.
- NCCN Clinical Practice Guidelines in Oncology® Acute Lymphoblastic Leukemia (Version 1.2022).© 2022 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 14, 2022.
- NCCN Clinical Practice Guidelines in Oncology® B-Cell Lymphomas (Version 2.2022).© 2022 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 14, 2022.
- 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.
- Hunger SP, Mullighan CG. Acute lymphoblastic leukemia in children. *N Engl J Med.* Oct 15 2015;373(16):1541-1552. PMID 26465987
- Maude SL, Teachey DT, Porter DL, et al. CD19-targeted chimeric antigen receptor T-cell therapy for acute lymphoblastic leukemia. *Blood.* Jun 25 2015; 125(26)4017-4023. PMID 25999455
- Pui CH, Carroll WL, Meshinchi S, et al. Biology, risk stratification, and therapy of pediatric acute leukemias: an update. *J Clin Oncol.* Feb 10 2011;29(5):551-565. PMID 21220611
- Tallen G, Ratei R, Mann G, et al. Long-term outcome in children with relapsed acute lymphoblastic leukemia after time-point and site-of-relapse stratification and intensified short-course multidrug chemotherapy: results of trial ALL-REZ BFM 90. *J Clin Oncol.* May 10 2010;28(14):2339-2347. PMID 20385996
- Bajwa R, Schechter T, Soni S, et al. Outcome of children who experience disease relapse following allogeneic hematopoietic SCT for hematologic malignancies. *Bone Marrow Transplant.* May 2013;48(5):661-665. PMID 23128573
- Jeha S, Gaynon PS, Razzouk BI, et al. Phase II study of clofarabine in pediatric patients with refractory or relapsed acute lymphoblastic leukemia. *J Clin Oncol.* Apr 20 2006;24(12):1917-1923. PMID 16622268
- von Stackelberg A, Locatelli F, Zugmaier G, et al. Phase I/phase II study of blinatumomab in pediatric patients with relapsed/refractory acute lymphoblastic leukemia. *J Clin Oncol.* Dec 20 2016;34(36):4381-4389. PMID 27998223
- UpToDate. Overview of the Treatment of Acute Lymphoblastic Leukemia in Children and Adolescents. Terzah M. Horton M.D., PhD, C. Philip Steuber M.D. Topic last updated March 1, 2019. Also available at https://www.uptodate.com.
- UpToDate. Treatment of Relapsed or Refractory Acute Lymphoblastic Leukmia in Adults. Richard A. Larson M.D.. Topic last updated April 12, 2019. Also available at https://www.uptodate.com
- UpToDate. Treatment of Relapsed or Refractory Diffuse Large B Cell Lymphoma. Arnold S. Freedman M.D., Jonathan W. Friedberg M.D., Topic last updated October 8, 2019. Also available at https://www.uptodate.com
- UpToDate. Histologic Transformation of Follicular Lymphoma. Arnold S. Freedman M.D., Jonathan W. Friedberg M.D., Topic last updated October 2, 2019. Also available at https://www.uptodate.com

- Immunotherapy for the Preventative and Treatment of Relapse Following Allogeneic Hematopoietic Cell Transplantation. Robert S. Negrin M.D., Topic last updated November 1, 2018. Also available at https://www.uptodate.com
- FDA News Release. FDA Approval Brings First Gene Therapy to the United States. Kymriah (tisagenlecleucel) for certain pediatric and young adult patients with a form or acute lymphoblastic leukemia (ALL). Also available at https://www.fda.gov
- FDA News Release – FDA approves CAR-T cell therapy to treat adults with certain tuypes of large B-cell lymphoma. Also availabe at https://www.fda.gov/NewEvents/Newsroom/PressAnnouncements/ucm581216.htm
- Novartis Press Release: Kymriah (Tisagenlecleucel) receives second FDA approvals to treat appropriate relapsed or refractory patients with large B-cell lymphoma. Also available at https://www.novartis.com
- U.S. FDA Advisory Committee Briefing Document Tisagenlecleucel (CTL019) for the treatment of pediatric and young adult patietns with relapsed/refractory B-cell acute lymphoblastic leukemia. July 12, 2017
- National Comprehensive Cancer Network (NCCN) Pediatric Acute Lymphoblastic Leukemia 1.2022. Also available at https://www.nccn.org
- National Comprehensive Cancer Network (NCCN) Drugs and Biologics Accessed October 2021. Also available at https://www.nccn.org
- ECRI. Panel Providers Guidelines for Managing CAR-T Cell Toxicities. Published November 30, 2017. Also available at https://www.ecri.org
- ECRI. Kymriah (Tisagenlecleucel) (Novartis Pharmaceuticals Corp.) for Treatment Diffuse Large B-Cell Lymphoma. Published June 25, 2018. Also available at https://www.ecri.org
- Friedberg JW. Relapsed/Refractory Diffuse Large B-Cell Lymphoma. Hematology Am Soc Hematol Educ Program. 2011:2011:498-505
- Crump M, Neelapu SS, Farooq U. Outcomes in refractory diffuse large B-cell lymphoma: results from the international SCHOLAR-1 study. Blood 2017 Oct 19:130(16):1800-1808.
- Porter D, Hwang WT, Frey NV, et. al. Chimeric antigen receptor T cells persist and induce sustained remissions in relapsed refractory chronic lymphocytic leukemia Sci. Transl Med 2015 Sep 2:7(303):303ra139. PMID 26333935
- JULIET phase II clinical trial (NCT02445248)
- Lee DW, Santomasso BD, Locke FL, et al. ASTCT Consensus Grading for Cytokine Release Syndrome and Neurologic Toxicity Associated with Immune Effector Cells. Biol Blood Marrow Transplant. Apr 2019; 25(4): 625-638. PMID 30592986

POLICY HISTORY

Policy #: 05.04.77
Original Effective Date: January 1, 2023
Reviewed: August 2023
Revised:
Current Effective Date: January 1, 2023