

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Oncology (Injectable – CAR-T) – Kymriah Utilization Management Medical Policy

- Kymriah® (tisagenlecleucel intravenous infusion – Novartis Oncology)

REVIEW DATE: 03/29/2023

OVERVIEW

Kymriah, a CD19-directed genetically modified autologous T cell immunotherapy, is indicated for the following uses:¹

- **B-cell precursor acute lymphoblastic leukemia (ALL)**, in patients ≤ 25 years of age with disease that is refractory or in second or later relapse.
- **Follicular lymphoma**, in patients ≥ 18 years of age with relapsed or refractory disease after two or more lines of systemic therapy. This indication is approved under accelerated approval based on response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).
- **Large B-cell lymphoma**, in patients ≥ 18 years of age with relapsed or refractory disease after two or more lines of systemic therapy including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, high-grade B-cell lymphoma, and DLBCL arising from follicular lymphoma.

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

Kymriah, a chimeric antigen receptor T-cell (CAR-T) therapy, is supplied as a frozen suspension of genetically modified autologous T cells in infusion bag(s) labeled for the specific recipient.¹ Kymriah is shipped directly to the cell laboratory associated with the infusion center in a liquid nitrogen Dewar. The product and patient-specific labels are found inside the Dewar. Store the infusion bag in the vapor phase of liquid nitrogen (less than or equal to minus 120°C) in a temperature-monitored system. Kymriah should be thawed prior to infusion.

Guidelines

Kymriah is discussed in guidelines from The National Comprehensive Cancer Network (NCCN).

- **ALL, adult:** The NCCN guidelines (version 1.2022 – April 4, 2022) address Kymriah.^{2,3} In Philadelphia chromosome-positive B-cell ALL, Kymriah is cited as a treatment option for patients < 26 years of age and with refractory disease or \geq two relapses and failure of two tyrosine kinase inhibitors (TKIs) [category 2A]. For Philadelphia chromosome-negative B-cell ALL, Kymriah is listed as a therapy option for patients < 26 years of age and with refractory disease or \geq two relapses (category 2A).
- **ALL, pediatric:** The NCCN guidelines (version 2.2023 – March 10, 2023) recommend Kymriah for the treatment of patients with refractory or \geq two relapses, TKI intolerant or refractory disease, or relapse post-hematopoietic stem cell transplantation (category 2A).^{3,5} Kymriah is also recommended for patients who are minimal residual disease positive after consolidation therapy, and in Philadelphia chromosome-positive disease with less than complete response.
- **B-cell lymphoma:** The NCCN guidelines (version 2.2023 – February 8, 2023) recommend Kymriah for the treatment of the following relapsed or refractory disease after at least two course of systemic therapy: DLBCL, DLBCL following transformation from follicular lymphoma or nodal marginal zone lymphoma, follicular lymphoma, high-grade B-cell lymphoma, human immunodeficiency virus (HIV)-related B-cell lymphoma, human herpes virus 8 (HHV8)-positive

DLBCL, primary effusion lymphoma, and post-transplant lymphoproliferative disorders (category 2A).^{3,4}

Safety

Kymriah has a Boxed Warning regarding cytokine release syndrome and neurological toxicities.¹ Due to these risks, Kymriah is only available through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the Kymriah REMS.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Kymriah. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. Due to the specialized skills required for evaluation and diagnosis of patients treated with Kymriah, as well as the monitoring required for adverse events and long-term efficacy, approval requires Kymriah to be prescribed by or in consultation with a physician who specializes in the condition being treated. The approval duration is 6 months to allow for an adequate time frame to prepare and administer 1 dose of therapy.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Kymriah is recommended in those who meet one of the following criteria:

FDA-Approved Indications

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1. **Acute Lymphoblastic Leukemia, B-Cell Precursor.** Approve a single dose if the patient meets the following criteria (A, B, C, D, and E):
 - A) Patient is < 26 years of age; AND
 - B) Patient meets one of the following (i, ii, or iii):
 - i. Patient has disease that is refractory, or in second or later relapse; OR
 - ii. Patient is minimal residual disease positive after consolidation therapy; OR
 - iii. Patient is Philadelphia chromosome-positive and has experienced one of the following (a, b, or c):
 - a) Less than complete response; OR
 - b) Tyrosine kinase inhibitor intolerant or refractory disease; OR
Note: Tyrosine kinase inhibitors include Sprycel (dasatinib tablets), imatinib tablets, Iclusig (ponatinib tablets), Tasigna (nilotinib capsules), and Bosulif (bosutinib tablets).
 - c) Relapse post-hematopoietic stem cell transplantation; AND
 - C) Patient received or plans to receive lymphodepleting chemotherapy prior to Kymriah infusion; AND
 - D) Patient has not been previously treated with chimeric antigen receptor T-cell (CAR-T) therapy; AND
Note: Examples of CAR-T therapy includes Kymriah, Breyanzi (lisocabtagene maraleucel intravenous infusion), Tecartus (brexucabtagene autoleucel intravenous infusion), Yescarta (axicabtagene ciloleucel intravenous infusion), Abecma (idecabtagene vicleucel intravenous infusion) and Carvykti (ciltacabtagene autoleucel intravenous infusion).
 - E) Kymriah is prescribed by or in consultation with an oncologist.

Dosing. Approve one of the following dosing regimens (A or B):

- A) The dose is up to 5.0×10^6 chimeric antigen receptor (CAR)-positive viable T cells per kg body weight intravenously for patients ≤ 50 kg; OR
- B) The dose is up to 2.5×10^8 CAR-positive viable T-cells intravenously for patients > 50 kg.

2. **B-Cell Lymphoma.** Approve a single dose if the patient meets the following criteria (A, B, C, D, E, and F):

- A) Patient is ≥ 18 years of age; AND
- B) Patient has one of the following diagnoses (i, ii, iii, iv, v, vi, vii, viii, ix, or x):
 - i. Large B-cell lymphoma; OR
 - ii. Diffuse large B-cell lymphoma; OR
 - iii. Diffuse large B-cell lymphoma arising from follicular lymphoma; OR
 - iv. Diffuse large B-cell lymphoma arising from nodal marginal zone lymphoma; OR
 - v. Follicular lymphoma; OR
 - vi. High-grade B-cell lymphoma; OR
 - vii. Human immunodeficiency virus (HIV)-related B-cell lymphoma; OR
 - viii. Human Herpes Virus 8-positive diffuse large B-cell lymphoma; OR
 - ix. Primary effusion lymphoma; OR
 - x. Post-transplant lymphoproliferative disorders, B-cell type; AND
- C) Kymriah is being used for disease that is relapsed or refractory after two or more lines of systemic therapy; AND
- D) Patient meets one of the following (i or ii):
 - i. Patient received or plans to receive lymphodepleting chemotherapy prior to Kymriah infusion; OR
 - ii. Patient's white blood cell count is less than or equal to $1 \times 10^9/L$ within 1 week prior to Kymriah infusion; AND
- E) Patient has not been previously treated with chimeric antigen receptor T-cell (CAR-T) therapy; AND
Note: Examples of CAR-T therapy includes Kymriah, Breyanzi (lisocabtagene maraleucel intravenous infusion), Tecartus (brexucabtagene autoleucel intravenous infusion) Yescarta (axicabtagene ciloleucel intravenous infusion), Abecma (idecabtagene vicleucel intravenous infusion) and Carvykti (ciltacabtagene autoleucel intravenous infusion).
- F) Kymriah is prescribed by or in consultation with an oncologist.

Dosing. The dose is up to 6.0×10^8 chimeric antigen receptor (CAR)-positive viable T cells administered intravenously.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Kymriah is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Kymriah™ intravenous infusion [prescribing information]. East Hanover, NJ: Novartis Oncology; May 2022.
2. The NCCN Acute Lymphoblastic Leukemia Clinical Practice Guidelines in Oncology (version 1.2022 – April 4, 2022). © 2022 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on March 20, 2023.

3. The NCCN Drugs and Biologics Compendium. © 2023 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on March 20, 2023. Search term: tisagenlecleucel.
4. The NCCN B-Cell Lymphomas Clinical Practice Guidelines in Oncology (version 2.2023 – February 8, 2023). © 2023 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on March 20, 2023.
5. The NCCN Pediatric Acute Lymphoblastic Leukemia Clinical Practice Guidelines in Oncology (version 2.2023 – March 10, 2023). © 2023 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on March 20, 2023.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	03/23/2022
Selected Revision	B- Cell Lymphoma: Added follicular lymphoma as an additional option for approval.	06/22/2022
Update	08/26/2022: Added: “The approval duration is 6 months to allow for an adequate time frame to prepare and administer 1 dose of therapy.” to the Policy Statement	NA
Annual Revision	B-Cell Lymphoma: Primary effusion lymphoma was added as an additional option for approval. Acquired immune deficiency syndrome (AIDS)-related B-cell lymphoma was changed to human immunodeficiency virus (HIV)-related B-cell lymphoma.	03/29/2023