CARECONTINUUM™

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Oncology (Injectable – CAR-T) – Kymriah Utilization Management Medical Policy
- Kymriah® (tisagenlecleucel intravenous infusion – Novartis Oncology)

REVIEW DATE: 03/05/2025

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 3.2024 – December 20, 2024) 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 ≥ 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 ≥ two relapses (category 2A).
- **ALL, pediatric:** The NCCN guidelines (version 2.2025 – December 16, 2024) recommend Kymriah for the treatment of patients with BCR::ABL1-negative (Philadelphia chromosome-negative) ALL that is refractory or ≥ two relapses; and for BCR::ABL1-positive (Philadelphia chromosome-positive) ALL that is TKI intolerant or refractory, or relapsed 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 BCR::ABL1-positive disease with less than complete response (category 2B).
- **B-cell lymphoma:** The NCCN guidelines (version 2.2025 – February 10, 2025) 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 indolent 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, neurological toxicities, and secondary hematological malignancies.[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 ALL of the following (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: Examples of 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 x 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 x 10^8 CAR-positive viable T-cells intravenously for patients > 50 kg.

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

A) Patient is ≥ 18 years of age; AND

B) Patient meets ONE of the following (i or ii):

i. Patient meets BOTH of the following (a and b):

a) Patient has follicular lymphoma; AND

b) Medication is used for relapsed or refractory disease after two or more lines of systemic therapy; OR

Note: Examples of systemic therapy include CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) + Gazyva (obinutuzumab intravenous infusion) or rituximab products, CVP (cyclophosphamide, vincristine, prednisone) + rituximab products, lenalidimide + rituximab products.

ii. Patient meets BOTH of the following (a and b):

a) Patient has ONE of the following diagnoses [(1), (2), (3), (4), (5), (6), (7), (8), or (9)]:

(1) Large B-cell lymphoma; OR

(2) Diffuse large B-cell lymphoma; OR

(3) Diffuse large B-cell lymphoma arising from indolent lymphoma; OR

(4) High-grade B-cell lymphoma; OR

(5) Human immunodeficiency virus (HIV)-related B-cell lymphoma; OR

(6) HIV-related plasmablastic lymphoma; OR

(7) Human Herpes Virus 8-positive diffuse large B-cell lymphoma; OR

(8) Primary effusion lymphoma; OR

(9) Post-transplant lymphoproliferative disorders, B-cell type; AND

b) Medication is used in ONE of the following situations [(1) or (2)]:

(1) Disease that is relapsed or refractory after two or more lines of systemic therapy; OR

Note: Examples of systemic therapy include RCHOP (rituximab product, cyclophosphamide, doxorubicin, vincristine, prednisone), dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin) + rituximab product, DHA (dexamethasone, cytarabine) + platinum (carboplatin, cisplatin, or oxaliplatin) ± rituximab product.

(2) Disease relapse > 12 months after first-line therapy and partial response to second-line therapy; AND

Note: Examples of systemic therapy include RCHOP (rituximab product, cyclophosphamide, doxorubicin, vincristine, prednisone), dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin) + rituximab product, RCDOP (rituximab product, cyclophosphamide, liposomal doxorubicin, vincristine, prednisone).

C) 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 x 10^9/L within 1 week 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 infusionion) and Carvykti (ciltacabtagene autoleucel intravenous infusion).

E) Kymriah is prescribed by or in consultation with an oncologist.

Dosing. The dose is up to 6.0 x 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; December 2024.
2. The NCCN Acute Lymphoblastic Leukemia Clinical Practice Guidelines in Oncology (version 3.2024 – December 20, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 24, 2025.
3. The NCCN Drugs and Biologics Compendium. © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 24, 2025. Search term: tisagenlecleucel.
4. The NCCN B-Cell Lymphomas Clinical Practice Guidelines in Oncology (version 2.2025 – February 10, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 25, 2025.
5. The NCCN Pediatric Acute Lymphoblastic Leukemia Clinical Practice Guidelines in Oncology (version 2.2025 – December 16, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 24, 2025.

HISTORY

Type of Revision	Summary of Changes	Review Date
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
Annual Revision	**B-Cell Lymphoma:** Follicular was changed to indolent in the option for approval "diffuse large B-cell lymphoma arising from indolent lymphoma." Removed diffuse large B-cell lymphoma arising from nodal marginal zone lymphoma.	03/27/2024
Annual Revision	**B-Cell Lymphoma:** Follicular lymphoma moved to an option for approval if the medication is used for relapsed or refractory disease after two or more lines of systemic therapy. Added Note with examples of systemic therapy. Large B-cell lymphoma, diffuse large B-cell lymphoma, diffuse large B-cell lymphoma arising from indolent lymphoma, high-grade B-cell lymphoma, human immunodeficiency virus (HIV)-related B-cell lymphoma, human herpes virus 8-positive diffuse large B-cell lymphoma, primary effusion lymphoma, post-transplant lymphoproliferative disease, B-cell type moved to new options for approval; if medication is used for disease that is relapsed or refractory after two or more lines of systemic therapy, or disease relapse > 12 months after first-line therapy and partial response to second-line therapy were added as options of approval. Added Notes with examples of systemic therapy. Added HIV-related plasmablastic lymphoma as a new option for approval.	03/05/2025