Drug Coverage Policy

Effective Date 7/1/2024
Coverage Policy Number.....IP0197
Policy Title.....Kymriah

Oncology (Injectable – CAR-T) – Kymriah

- Kymriah® (tisagenlecleucel intravenous infusion – Novartis Oncology)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Cigna Healthcare Coverage Policy

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 4.2023 – February 5, 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 4.2024 – February 7, 2024) recommend Kymriah for the treatment of patients with refractory or ≥ 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 (category 2B).
- **B-cell lymphoma:** The NCCN guidelines (version 1.2024 – January 18, 2024) 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]

Medical Necessity Criteria

Tisagenlecleucel (Kymriah) is considered medically necessary when ONE of the following is met (1 or 2):

FDA-Approved Indications

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 autoleuleucel 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.

2. B-Cell Lymphoma. Approve a single dose if the patient meets ALL of the following (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, or ix):
- **i.** Large B-cell lymphoma; OR
- **ii.** Diffuse large B-cell lymphoma; OR
- **iii.** Diffuse large B-cell lymphoma arising from indolent lymphoma; OR
- **iv.** Follicular lymphoma; OR
- **v.** High-grade B-cell lymphoma; OR
- **vi.** Human immunodeficiency virus (HIV)-related B-cell lymphoma; OR
- **vii.** Human Herpes Virus 8-positive diffuse large B-cell lymphoma; OR
- **viii.** Primary effusion lymphoma; OR
- **ix.** 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 x 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 x 10^8 chimeric antigen receptor (CAR)-positive viable T cells administered intravenously.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven (criteria will be updated as new published data are available).

Coding

1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

CPT® Codes	**Description**
0537T	Chimeric antigen receptor T-cell (CAR-T) therapy; harvesting of blood-derived T lymphocytes for development of genetically modified autologous CAR-T cells, per day
0538T	Chimeric antigen receptor T-cell (CAR-T) therapy; preparation of blood-derived T lymphocytes for transportation (e.g., cryopreservation, storage)
0539T	Chimeric antigen receptor T-cell (CAR-T) therapy; receipt and preparation of CAR-T cells for administration
0540T	Chimeric antigen receptor T-cell (CAR-T) therapy; CAR-T cell administration, autologous

HCPCS Codes	Description
Q2042	Tisagenlecleucel, up to 600 million car-positive viable T cells, including leukapheresis and dose preparation procedures, per therapeutic dose

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 4.2023 – February 5, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 21, 2024.
3. The NCCN Drugs and Biologics Compendium. © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 20, 2024. Search term: tisagenlecleucel.

4. The NCCN B-Cell Lymphomas Clinical Practice Guidelines in Oncology (version 1.2024 – January 18, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 20, 2024.
5. The NCCN Pediatric Acute Lymphoblastic Leukemia Clinical Practice Guidelines in Oncology (version 4.2024 – February 7, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 20, 2024.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Review	**Acute Lymphoblastic Leukemia** **Removed** (1) 'Individual is not being treated for primary central nervous system lymphoma, (2) 'Individual has an Eastern Cooperative Oncology Group (ECOG) performance status of 0-1', (3) Individual has an Eastern Cooperative Oncology Group (ECOG) performance status of 0-1, (4) 'Individual does not have active or latent hepatitis B, active hepatitis C or other active uncontrolled infection', (5) 'Individual does not have an active inflammatory disorder', (6) 'Individual does not have active graft versus host disease, (7) Hematologist as allowable specialist **B-Cell Lymphoma.** **Removed** (1) 'Individual is not being treated for primary central nervous system lymphoma', (2) 'Individual has an Eastern Cooperative Oncology Group (ECOG) performance status of 0-1', (3) 'Individual does not have active or latent hepatitis B, active hepatitis C or other active uncontrolled infection', (4) 'Individual does not have an active inflammatory disorder' (5) Hematologist as allowable specialist **Updated** the following: "follicular" was changed to "indolent" in the option for approval "diffuse large B-cell lymphoma arising from indolent lymphoma." The option of approval of diffuse large B-cell lymphoma arising from nodal marginal zone lymphoma was removed.	7/1/2024

The policy effective date is in force until updated or retired