Effective Date **2/1/2024**
Next Review Date… **2/1/2025**
Coverage Policy Number **IP0197**

Tisagenlecleucel

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Related Coverage Resources

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. 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.

Overview

This policy supports medical necessity review for tisagenlecleucel (Kymriah®).

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

Medical Necessity Criteria

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

1. **Acute Lymphoblastic Leukemia, B-Cell Precursor.** Individual meets **ALL** of the following criteria (A, B, C, D, E, F, G, H, I and J):
    A. Individual is less than 26 years of age
    B. Individual meets **ONE** of the following (i, ii or iii):
        i. Individual has disease that is refractory, or in second or later relapse
        ii. Individual is minimal residual disease positive after consolidation therapy

iii. Individual is Philadelphia chromosome-positive and experienced **ONE** of the following (a, b, or c):
   a. Less than complete response
   b. Tyrosine kinase inhibitor intolerant or refractory

      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

C. Individual has received or plans to receive lymphodepleting chemotherapy (for example, cyclophosphamide and fludarabine) prior to Kymriah infusion
D. Individual has not been previously treated with CAR-T therapy

   Examples of CAR-T therapy include 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. Individual is not being treated for primary central nervous system lymphoma

F. Individual has a Karnofsky (age at least 16 years) or Lansky (age less than 16 years) performance status greater than or equal to 50%

G. Individual does not have active or latent hepatitis B, active hepatitis C or other active uncontrolled infection

H. Individual does not have an active inflammatory disorder

I. Individual does not have active graft versus host disease

J. Medication is prescribed by, or in consultation, with a Hematologist or Oncologist

   Dosing. **ONE** of the following dosing regimens (A or B):[1]
   A. The dose is up to 5.0×10^6 chimeric antigen receptor (CAR)-positive viable T cells per kg body weight intravenously for individuals less than or equal to 50 kg
   B. The dose is up to 2.5×10^8 CAR-positive viable T-cells intravenously for individuals at least 50 kg

2. B-Cell Lymphoma. Individual meets **ALL** of the following criteria (A, B, C, D, E, F and G):
A. Individual is 18 years of age or older
B. Individual has **ONE** of the following diagnoses:
   i. Diffuse large B-cell lymphoma (DLBCL)
   ii. Diffuse large B-cell lymphoma arising from follicular lymphoma
   iii. Diffuse large B-cell lymphoma arising from nodal marginal zone lymphoma
   iv. Follicular lymphoma
   v. High-grade B-cell lymphoma
   vi. Human immunodeficiency virus (HIV)-related B-cell lymphoma
   vii. Human Herpes Virus 8-positive diffuse large B-cell lymphoma
   viii. Large B-cell lymphoma
   ix. Post-transplant lymphoproliferative disorders, B-cell type
   x. Primary effusion lymphoma
C. Kymriah is being used for disease that is relapsed or refractory after two or more lines of systemic therapy

i. If DLBCL arising from follicular lymphoma or nodal marginal zone lymphoma, chemotherapy regimen included at least **ONE** anthracycline or anthracenedione-based regimen, unless contraindicated

D. Individual meets **ONE** of the following (i or ii):
   i. Individual received or plans to receive lymphodepleting chemotherapy (for example, cyclophosphamide and fludarabine) prior to Kymriah infusion
   ii. Individual's white blood cell count is less than or equal to 1 x 10^9/L within 1 week prior to Kymriah infusion

E. Individual has not been previously treated with CAR-T therapy

Examples of CAR-T therapy include 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. Individual is not being treated for primary central nervous system lymphoma

G. Individual has an Eastern Cooperative Oncology Group (ECOG) performance status of 0-1

H. Individual does not have active or latent hepatitis B, active hepatitis C or other active uncontrolled infection

I. Individual does not have an active inflammatory disorder

J. Individual does not have active graft versus host disease

K. Medication is prescribed by, or in consultation with, a Hematologist or Oncologist

Dosing. The dose is up to 6.0 x 10^8 chimeric antigen receptor (CAR)-positive viable T cells administered intravenously.[1]

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.

Reauthorization Criteria

Not applicable for continuation beyond initial approval duration.

Authorization Duration

Authorization is for a single dose.

Conditions Not Covered

Any other use is considered experimental, investigational or unproven.

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

Background

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 ≥ 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 2.2023 – March 10, 2023) 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.
- **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.

Dosing and Product Availability[1]
For autologous use only. For intravenous use only.
Kymriah is provided as a single-dose for infusion containing a suspension of chimeric antigen receptor (CAR) positive viable T cells.

Dosing:
Dosage in Pediatric and Young Adult Relapsed or Refractory (r/r) B-cell Acute Lymphoblastic Leukemia (ALL) - Based on the patient weight reported at the time of leukapheresis:

- Patients 50 kg or less: administer 0.2 to 5.0 x 10^6 CAR-positive viable T cells per kg body weight
- Patients above 50 kg: administer 0.1 to 2.5 x 10^8 CAR-positive viable T cells

Dosage in Adult Relapsed or Refractory (r/r) Diffuse Large B-cell lymphoma (DLBCL) and Follicular Lymphoma (FL)

- For adult patients: administer 0.6 to 6.0 x 10^8 CAR-positive viable T cells

Product Availability:
Pediatric and Young Adult B-cell ALL (up to 25 years of age)

- A single dose of Kymriah contains 0.2 to 5.0 x 10^6 CAR-positive viable T cells per kg of body weight for patients 50 kg or less, or 0.1 to 2.5 x 10^8 CAR-positive viable T cells for patients more than 50 kg, suspended in one to three patient-specific infusion bag(s) for IV infusion.

Adult Relapsed or Refractory Diffuse Large B-cell Lymphoma and Follicular Lymphoma

- A single dose of Kymriah contains 0.6 to 6.0 x 10^8 CAR-positive viable T cells suspended in one to three patient-specific infusion bag(s) for IV infusion.

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.