Overview

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

Medical Necessity Criteria

Tisagenlecleucel (Kymriah) is considered medically necessary when ONE of the following is met (1, 2, or 3):

1. **Acute Lymphoblastic Leukemia, B-Cell Precursor.** Individual meets ALL of the following criteria:
   - Individual is < 26 years of age
   - 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

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

*Note:* CAR-T therapy includes Kymriah, Breyanzi® (lisocabtagene maraleucel injection), Tecartus™ (brexucabtagene autoleucel injection), Yescarta® (axicabtagene ciloleucel injection), and Abecma® (idecabtagene vicleucel injection).

E. Individual is not being treated for primary central nervous system lymphoma
F. Medication is prescribed by, or in consultation, with an oncologist or hematologist

2. **B-Cell Lymphoma.** Individual meets ALL of the following criteria:
A. Individual is ≥ 18 years of age  
B. Individual has ONE of the following diagnoses (i, ii, iii, iv, v, vi, vii, or viii):
   i. Large B-cell lymphoma  
   ii. Diffuse large B-cell lymphoma [DLBCL]
   iii. High-grade B-cell lymphoma
   iv. Diffuse large B-cell lymphoma arising from follicular lymphoma
   v. Diffuse large B-cell lymphoma arising from nodal marginal zone lymphoma
   vi. Acquired immune deficiency syndrome (AIDS)-related B-cell lymphoma
   vii. Human Herpes Virus 8-positive diffuse large B-cell lymphoma
   viii. Post-transplant lymphoproliferative disorders, B-cell type
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 lymphodepleting chemotherapy prior to Kymriah infusion
   ii. Individual’s white blood cell count is less than or equal to 1 x 10⁹/L within 1 week prior to Kymriah infusion
E. Individual has not been previously treated with CAR-T therapy

*Note:* CAR-T therapy includes Kymriah, Breyanzi® (lisocabtagene maraleucel injection), Tecartus™ (brexucabtagene autoleucel injection), Yescarta® (axicabtagene ciloleucel injection), and Abecma® (idecabtagene vicleucel injection).

F. Individual is not being treated for primary central nervous system lymphoma
G. Medication is prescribed by, or in consultation with, an oncologist or hematologist

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.

*Note:* Receipt of sample product does not satisfy any criteria requirements for coverage.
**Reauthorization Criteria**

Not applicable for continuation beyond initial approval duration.

**Authorization Duration**

Authorization is for a single dose.

**Conditions Not Covered**

Tisagenlecleucel (Kymriah) is considered experimental, investigational or unproven for ANY other use.

**Coding / Billing Information**

Note: 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:

<table>
<thead>
<tr>
<th>CPT® Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0537T</td>
<td>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</td>
</tr>
<tr>
<td>0538T</td>
<td>Chimeric antigen receptor T-cell (CAR-T) therapy; preparation of blood-derived T lymphocytes for transportation (e.g., cryopreservation, storage)</td>
</tr>
<tr>
<td>0539T</td>
<td>Chimeric antigen receptor T-cell (CAR-T) therapy; receipt and preparation of CAR-T cells for administration</td>
</tr>
<tr>
<td>0540T</td>
<td>Chimeric antigen receptor T-cell (CAR-T) therapy; CAR-T cell administration, autologous</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q2042</td>
<td>Tisagenlecleucel, up to 600 million car-positive viable T cells, including leukapheresis and dose preparation procedures, per therapeutic dose</td>
</tr>
</tbody>
</table>


**Background**

**OVERVIEW**

Kymriah, a CD19-directed genetically modified autologous T cell immunotherapy, is indicated for the treatment of:

- **B-cell precursor acute lymphoblastic leukemia (ALL)**, in patients ≤ 25 years of age with disease that is refractory or in second or later relapse.

- **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. Regarding this specific indication, Kymriah is not indicated for treatment of patients with primary central nervous system lymphoma.
Kymriah 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 2.2020 – October 23, 2020) 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 2.2021 – October 22, 2020) recommend Kymriah for the treatment of patients with refractory or ≥ 2 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 3.2021 – March 16, 2021) recommend Kymriah for the treatment of the following relapsed or refractory disease after at least two course of systemic therapy: DLBCL following transformation from follicular lymphoma or nodal marginal zone lymphoma, DLBCL, high-grade B-cell lymphoma, AIDS-related B-cell lymphoma, human herpes virus 8 (HHV8)-positive DLBCL, and post-transplant lymphoproliferative disorders (category 2A).3,4

Dosing and Product Availability

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):**

  - 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**
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.

Safety

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

References