

Kymriah(tisagenlecleucel)

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

- Patients up to 25 years of age, with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory, or in second or later relapse.
- Adult patients with relapsed or refractory (r/r) large B-cell lymphoma, 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.

I. Criteria for Initial Approval

Kymriah will be considered for coverage when **ALL** of the criteria below are met, confirmed with supporting medical documentation.

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

- Approved for patients 25 years of age or younger.
- Prescribed by, or in consultation with, a specialist in Oncology.
 - Kymriah is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the KYMRIAH REMS.
 - Provider must be enrolled in the KYMRIAH REMS program.
- The following medical documentation is provided:
 - Documentation that the diagnosis is B-cell precursor ALL that is refractory or in second or later relapse.
 - The patient has been treated with 2 cycles of standard chemotherapy without a complete response or achieved a complete response and experienced multiple relapses following standard chemotherapy (at least 2 cycles).
 - Second or later bone marrow (BM) relapse.
 - Any BM relapse after allogeneic stem cell transplantation (SCT).

- Patient is not eligible for allogeneic SCT; AND
 - Patient has a performance status (Karnofsky/Lansky) ≥ 50 .
- The patient has a confirmed CD19 tumor expression.
- The patient has not previously been treated with gene therapy or Kymriah.
- The patient is Philadelphia Chromosome positive (Ph+) and they have tried and failed, is intolerant to, or has a contraindication to at least two tyrosine kinase inhibitors (TKI) (e.g., imatinib, dasatinib, ponatinib, etc.)
- The patient does not have an active central nervous system (CNS) 3 acute lymphoblastic leukemia.
- The patient has received, or will receive, lymphodepleting chemotherapy fludarabine (30 mg/m² intravenous daily for 4 days) and cyclophosphamide (500 mg/m² intravenous daily for 2 days starting with the first dose of fludarabine)] within two weeks preceding the Kymriah infusion.
- The provider agrees to monitor for:
 - Cytokine Release Syndrome (CRS), including fatal or life-threatening reactions, occurring in patients receiving Kymriah. *Do NOT administer Kymriah to patients with active infection or inflammatory disorders.
 - In case of CRS, the provider agrees to ensure at least two doses of Tocilizumab are available on site prior to the Kymriah infusion.
 - Hypogammaglobulinemia: Monitor and provide replacement therapy until resolution. Assess immunoglobulin levels in newborns of mothers treated with Kymriah.
 - Neurological events after treatment with Kymriah.

Adult Relapsed or Refractory Diffuse Large B-cell Lymphoma

- Approved for patients 18 years of age and older.
- Prescribed by, or in consultation with, a specialist in Oncology.
 - Kymriah is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the KYMRIAH REMS.
 - Provider must be enrolled in the KYMRIAH REMS program.
- Documentation that the patient has been diagnosed with relapsed/refractory B-cell lymphoma.
 - Diffuse large B-cell lymphoma (DLBCL) not otherwise specified; OR
 - High grade B-cell lymphoma; OR
 - Diffuse large B-cell lymphoma (DLBCL) arising from follicular lymphoma.

- The patient has not previously been treated with gene therapy or Kymriah.
- The patient has experienced disease progression following a trial of two or more lines of systemic therapy.
- Previous therapy includes anthracycline chemotherapy agent and an anti-CD20 antibody.
- The patient has received, or will receive, lymphodepleting chemotherapy fludarabine (25 mg/m² intravenous daily for 3 days) and cyclophosphamide (250 mg/m² intravenous daily for 3 days starting with the first dose of fludarabine), or alternate therapy with bendamustine 90 mg/m² intravenous daily for 2 days --for patients unable to receive cyclophosphamide] within two weeks preceding the Kymriah infusion.
 - Lymphodepleting chemotherapy may be omitted if a patient's white blood cell (WBC) count is less than or equal to 1 x 10⁹ /L within 1 week prior to KYMRIAH infusion.
- The patient does not have primary central nervous system lymphoma.
- The patient does not have human immunodeficiency virus (HIV), active Hepatitis B or C, active uncontrolled infection and any autoimmune disease requiring immune suppression.
- The provider agrees to monitor for:
 - Cytokine Release Syndrome (CRS), including fatal or life-threatening reactions, occurred in any patient receiving Kymriah. *Do NOT administer Kymriah to patients with active infection or inflammatory disorders.
 - In case of CRS, the provider agrees to ensure at least 2 doses of Tocilizumab are available on site prior to the Kymriah infusion.
 - Hypogammaglobulinemia: Monitor and provide replacement therapy until resolution. Assess immunoglobulin levels in newborns of mothers treated with Kymriah.
 - Neurological events after treatment with Kymriah.

II. Criteria for Continuation of Therapy

Each request/dosing of Kymriah will require a prior authorization given the toxicities/complexities of this medication.

III. Dosing/Administration

Kymriah must be administered according to the current FDA labeling guidelines for dosage and timing.

IV. Length of Authorization for Initial Therapy

Kymriah will be authorized for 6 months when criteria for initial approval are met.

V. Billing Code/Information

- HCPCS Q2042 – Tisagenlecleucel (Kymriah), up to 600 million car-positive viable t cells, including leukapheresis and dose preparation procedures, per therapeutic dose.

B - Cell Precursor Acute Lymphoblastic Leukemia (ALL)	1 billable unit (1 infusion of up to 250 million CAR-positive viable T-cells)
Large B-Cell Lymphoma	3 billable units (1 infusion of up to 600 million CAR-positive viable T-cells)

Prior authorization of benefits is not the practice of medicine nor the substitute for the independent medical judgment of a treating medical provider. The materials provided are a component used to assist in making coverage decisions and administering benefits. Prior authorization does not constitute a contract or guarantee regarding member eligibility or payment. Prior authorization criteria are established based on a collaborative effort using input from the current medical literature and based on evidence available at the time.

Approved by MDH Clinical Criteria Committee: 12/21/2020

Last Reviewed Date: 12/21/2020