CareSource Rxinnovations

PHARMACY POLICY STATEMENT
Georgia Medicaid

DRUG NAME	Kymriah (tisagenlecleucel)
BENEFIT TYPE	Medical
STATUS	Prior Authorization Required

Kymriah, approved by the FDA in 2017, is an intravenously administered CD19-directed genetically modified autologous T cell immunotherapy indicated for the treatment of: 1) Patients up to 25 years of age with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse; and 2) Adults 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; and 3) Adults with relapsed or refractory follicular lymphoma (FL) after two or more lines of systemic therapy (accelerated approval).

Kymriah (tisagenlecleucel) will be considered for coverage when the following criteria are met:

Acute Lymphoblastic Leukemia (ALL)

For **initial** authorization:

1. Member is up to 25 years of age; AND
2. Member has a documented diagnosis of B-cell ALL; AND
3. Documentation of one of the following:
   a) Philadelphia chromosome negative (Ph-) disease that is refractory or in second or later relapse, or
   b) Philadelphia chromosome positive (Ph+) disease that is refractory or in second or later relapse AND following therapy that has included 2 tyrosine kinase inhibitors (TKI); AND
4. Member has a Karnofsky (age ≥16 years) or Lansky (age < 16 years) performance status ≥ 50; AND
5. Documentation of CD19 tumor expression; AND
6. Bone marrow with ≥ 5% lymphoblasts by morphologic assessment; AND
7. Member does NOT have any of the following:
   a) Prior gene or CAR-T cell therapy
   b) Primary central nervous system (CNS) lymphoma; AND
8. Member has been or will be pre-screened for hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) prior to collection of cells; AND
9. Healthcare facility/provider has enrolled in the Kymriah REMS program; AND
10. Member's weight is documented for dose calculation.
11. **Dosage allowed/Quantity limit:**
    50 kg or less: administer 0.2 to 5.0 x 10^6CAR-positive viable T cells per kg body weight
    More than 50 kg: administer 0.1 to 2.5 x 10^8 total CAR-positive viable T cells (non-weight based)

If all the above requirements are met, the medication will be approved for 3 months.

For **reauthorization**:

1. Kymriah will not be authorized for continued therapy.

Large B-cell Lymphoma

For **initial** authorization:
1. Member is 18 years of age or older; AND
2. Member has a documented diagnosis large B-cell lymphoma including any of the following:
   a) Diffuse large B-cell lymphoma (DLBCL) not otherwise specified (NOS)
   b) High grade B-cell lymphoma (HGBCL)
   c) DLBCL arising from follicular lymphoma (transformation FL; TFL)
   d) Intravascular LBCL
   e) DLBCL associated with chronic inflammation
   f) Fibrin-associated DLBCL
   g) EBV-positive DLBCL, NOS
   h) T-cell/histiocyte-rich LBCL; AND
3. Member has relapsed or refractory disease after 2 or more lines of systemic therapy; AND
4. Member has an Eastern cooperative oncology group (ECOG) performance status of 0 or 1; AND
5. Member does NOT have any of the following:
   a) Primary central nervous system (CNS) lymphoma
   b) Prior allogeneic HSCT
   c) Prior CAR-T therapy; AND
6. Member has been or will be pre-screened for hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) prior to collection of cells; AND
7. Healthcare facility/provider has enrolled in the Kymriah REMS program; AND
8. Member's weight is documented for dose calculation.
9. **Dosage allowed/Quantity limit:** Administer 0.6 to 6.0 x 10^8 CAR-positive viable T cells.

If all the above requirements are met, the medication will be approved for 3 months.

For **reauthorization**:
1. Kymriah will not be reauthorized for continued therapy.

Follicular Lymphoma (FL)

For **initial** authorization:
1. Member is 18 years of age or older; AND
2. Member has a documented diagnosis of relapsed or refractory FL (grade 1, 2, or 3A); AND
3. Member's disease has progressed after 2 or more lines of systemic therapy; AND
4. Member has an Eastern cooperative oncology group (ECOG) performance status of 0 or 1; AND
5. Member does NOT have any of the following:
   a) Primary central nervous system (CNS) lymphoma
   b) Prior allogeneic HSCT
   c) Prior CAR-T therapy
   d) Follicular lymphoma grade 3B; AND
6. Member has been or will be pre-screened for hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) prior to collection of cells; AND
7. Healthcare facility/provider has enrolled in the Kymriah REMS program; AND
8. Member's weight is documented for dose calculation.
9. **Dosage allowed/Quantity limit:** Administer 0.6 to 6.0 x 10^8 CAR-positive viable T cells.

If all the above requirements are met, the medication will be approved for 3 months.

For **reauthorization**:
1. Kymriah will not be reauthorized for continued therapy.

CareSource considers Kymriah (tisagenlecleucel) not medically necessary for the treatment of conditions that are not listed in this document. For any other indication, please refer to the Off-Label policy.

DATE	ACTION/DESCRIPTION
10/24/2017	New policy for Kymriah created.
08/27/2018	New indication of Large B-cell lymphoma was added. Criteria expanded for ALL diagnosis for member's disease history requirement.
08/18/2020	Updated billing code. Amended criteria for both diagnoses. ALL: changed lower age limit from 3 years to 1 year. Added #3, 4. Removed TKI's that were listed but not relevant in this context. B cell lymphoma: minor changes. Removed criterion for premedication. Removed some of the exclusion cut offs that appeared to be arbitrary to the controlled trial environment but not necessary to mandate from a utilization management perspective for the clinical setting.
05/27/2021	B cell lymphoma: Removed life expectancy restriction. Added ECOG score.
06/10/2022	Transferred to new template. Updated references. Added new indication for FL.
12/11/2024	Updated refs. Changed has been screened to has been or will be screened. Added documentation of weight. Changed "active central nervous system malignancy involvement" to "primary central nervous system lymphoma." FL: Simplified prior therapy requirement. Changed measurable disease to has progressed. LBCL: Added more subtypes per NCCN slide MS-105. Simplified prior therapy requirement. ALL: Removed lower age limit to match label. Simplified prior therapy and split between Ph positive or Ph negative to match NCCN. Replaced life expectancy requirement with Karnofsky/Lansky status. Added CNS exclusion.

References:

1. Kymriah [package insert]. East Hanover, NJ; Novartis Pharmaceuticals Corp., 2024.
2. National Comprehensive Cancer Network. Pediatric Acute Lymphoblastic Leukemia. (Version 2.2024). https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf. Accessed December 11, 2024.
3. National Comprehensive Cancer Network. B-Cell Lymphomas. (Version 3.2024). https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed December 11, 2024.
4. Maude SL, Laetsch TW, Buechner J, et al. Tisagenlecleucel in Children and Young Adults with B-Cell Lymphoblastic Leukemia. *N Engl J Med*. 2018;378(5):439-448. doi:10.1056/NEJMoa1709866
5. Laetsch TW, Maude SL, Rives S, et al. Three-Year Update of Tisagenlecleucel in Pediatric and Young Adult Patients With Relapsed/Refractory Acute Lymphoblastic Leukemia in the ELIANA Trial. *J Clin Oncol*. 2023;41(9):1664-1669. doi:10.1200/JCO.22.00642
6. Fowler NH, Dickinson M, Dreyling M, et al. Tisagenlecleucel in adult relapsed or refractory follicular lymphoma: the phase 2 ELARA trial. *Nat Med*. 2022;28(2):325-332. doi:10.1038/s41591-021-01622-0
7. Schuster SJ, Bishop MR, Tam CS, et al. Tisagenlecleucel in Adult Relapsed or Refractory Diffuse Large B-Cell Lymphoma. *N Engl J Med*. 2019;380(1):45-56. doi:10.1056/NEJMoa1804980

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