COLORADO
Department of Health Care Policy & Financing

303 E. 17th Ave.
Denver, CO 80203

Health First Colorado (Colorado's Medicaid Program) Coverage Standards for CAR T-Cell Therapy

November 2023

Coverage Standards will be reviewed and evaluated for any applicable changes due to the evolving nature of factors including disease course, available treatment options and available peer-reviewed medical literature. If request is for use outside of stated coverage standards, support with peer reviewed medical literature and/or subsequent clinical rationale shall be provided and will be evaluated at the time of request.

Chimeric antigen receptor (CAR) T-Cell treatment is a multi-step process including collection, infusion, and recovery. Treatment will only be approved once per member lifetime. CAR-T requests will be evaluated for medical necessity and reviewed on a case-by-case basis for all Health First Colorado Members based on the following:

Breyanzi (lisocabtagene maraleucel)

1. Medical records and treating hematologist/oncologist provide testing and documentation to confirm member has the following diagnoses and prior treatment experience:
    a. Member is 18 years of age or older with a diagnosis of large B-cell lymphoma, including diffuse large B-cell lymphoma not otherwise specified, high-grade B-cell lymphoma, primary mediastinal large B-cell lymphoma, and follicular lymphoma grad 3B who have one of the following:
        i. Refractory disease to first-line chemoimmunotherapy or relapse within 12 months of first-line chemoimmunotherapy OR
        ii. Refractory disease to first-line chemoimmunotherapy or relapse after first-line chemoimmunotherapy and are not eligible for hematopoietic stem cell transplantation due to comorbidities or age OR
        iii. Relapsed or refractory disease after two or more lines of systemic therapy
2. Prior to treatment:
    a. Member will receive lymphodepleting (LD) chemotherapy regimen appropriate for specified diagnosis
        i. Provide LD chemotherapy that member will receive including drug, dose, route frequency and duration prior to treatment with Breyanzi
    b. Member has been screened for hepatitis B virus, hepatitis C, and HIV

   c. Member has been informed of anticipated benefits, risks, and expectations with treatment including but not limited to the following
      i. Remission, post treatment occurrence of secondary malignancy, cytokine release syndrome, neurologic toxicity, and hypogammaglobulinemia
3. Treating and prescribing provider(s) attest to the following:
   a. Provider is a hematologist or oncologist experienced in treating with CAR-T therapy
   b. The hospital or associated clinic where the treatment will occur is specially certified per the drug manufacturer and in compliance with the Breyanzi REMS program for the treatment
      i. Treatment location for administration of requested medication is provided (inpatient or outpatient hospital)
4. Member must *not* have any of the following:
   a. Primary central nervous system lymphoma
   b. Prior treatment with CAR T-cell immunotherapy
   c. Active infection or inflammatory disorder
   d. Administration of live virus vaccination to member at least 6 weeks prior to therapy, during therapy, and until recovery of immune system post-CAR-T therapy

References

1. Breyanzi [package insert]. Bothell, WA; Juno Therapeutics, Inc., 2023.
2. Kamdar, et al. "Lisocabtagene maraleucel versus standard of care with salvage chemotherapy followed by autologous stem cell transplantation as second-line treatment in patients with relapsed or refractory large B-cell lymphoma (TRANSFORM): results from an interim analysis of an open-label, randomised, phase 3 trial." The Lancet, vol 8399, no. 10343, 2022, pp 2294-2308., https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00662-6/fulltext.

Carvykti (ciltacabtagene autoleucel)

1. Medical records and treating hematologist/oncologist provide testing to confirm member has one of the following diagnoses and prior treatment experience has been documented:
    a. Member is 18 years and older with a diagnosis of relapsed or refractory multiple myeloma, after four or more prior lines of therapy, defined by any of the following:
        i. Serum monoclonal paraprotein (M-protein) ≥ 1 g/dL OR
        ii. Urine M-protein level ≥ 200 mg/24 h
        iii. Serum free light chain ≥ 10 mg/dL and abnormal immunoglobulin kappa lambda free light chain ratio
    b. Prior treatment must include ALL the following:
        i. Proteasome inhibitor
        ii. Immunomodulatory agent
        iii. Anti-CD38 monoclonal antibody
2. Treating and prescribing provider(s) attest to the following:
    a. Provider is a hematologist/oncologist experienced in treating with CAR-T therapy
    b. The hospital or associated clinic where the treatment will occur is specially certified per the drug manufacturer and in compliance with the CARVYKTI REMS program for the treatment
        i. Treatment location for administration of requested medication is provided (inpatient, outpatient hospital).
        ii.
3. Prior to treatment
    a. Member will receive lymphodepleting (LD) chemotherapy regimen appropriate for specified diagnosis
        i. Provide LD chemotherapy that member will receive including drug, dose, route frequency and duration prior to treatment with Carvykti.
    b. Member has adequate kidney, liver, cardiac, and pulmonary function (must meet established criteria/measures) to receive full therapy.
    c. Member has been screened for hepatitis B virus, hepatitis C virus, and HIV
    d. Member has been informed of anticipated benefits, risks and expectations with treatment including but not limited to the following
        i. Remission, post treatment occurrence of secondary malignancy, cytokine release syndrome, neurologic toxicity, and hypogammaglobulinemia
4. Member must not have any of the following:
    a. Primary central nervous system lymphoma
    b. Active infection or inflammatory disorder
    c. Administration of live virus vaccination to member at least 6 weeks prior to therapy, during therapy, and until recovery of immune system post-CAR-T therapy
    d. Prior treatment with a therapy targeted to B-cell maturation antigen (BCMA)

References

1. Carvykti [package insert]. Somerset, NJ; Janssen Biotech, Inc., 2023.
2. Berdeja, Jesus G, et al. "Ciltacabtagene Autoleucel, a B-Cell Maturation Antigen-Directed Chimeric Antigen Receptor T-Cell Therapy in Patients with Relapsed or Refractory Multiple Myeloma (Cartitude-1): A Phase 1b/2 Open-Label Study." The Lancet, vol. 398, no. 10297, 2021, pp. 314–324., https://doi.org/10.1016/s0140-6736(21)00933-8.

Kymriah (tisagenlecleucel)

1. Medical records and treating hematologist/oncologist provide testing to confirm member has one of the following diagnoses and prior treatment experience has been documented:
    a. For member age 18 years and older, Large B-cell lymphoma relapsed or refractory (r/r) disease after two or more lines of systemic therapy (including an anti-CD20 antibody and an anthracycline), including one of the following (i.-iii.), OR relapsed after autologous hematopoietic stem cell transplantation (HSCT)
        i. Diffuse large B-cell lymphoma (DLBCL), not otherwise specified
        ii. High grade B-cell lymphoma
        iii. DLBCL arising from follicular lymphoma
    b. For member age less than age 26 years B-cell precursor acute lymphoblastic leukemia (ALL), refractory or in second or later relapse

2. Prior to treatment:
    a. Member will receive Lymphodepleting (LD) chemotherapy:
        i. Provide LD chemotherapy that member will receive including drug, dose, route frequency and duration prior to treatment with Kymriah.
    b. Member's parent or caretaker/guardian has been informed of anticipated benefits, risks and expectations with treatment including, but not limited to the following:
        i. Remission, Cytokine Release Syndrome (CRS), neurological toxicities, serious infections, hypogammaglobulinemia, prolonged cytopenia, and manufacturing failure
    c. Member has adequate organ, cardiac, and pulmonary function (must meet established criteria/measures) to receive full therapy
    d. Member has been screened for hepatitis B virus, hepatitis C virus, and HIV

3. Treating and prescribing provider(s) attest to the following:
    a. Provider is a hematologist/oncologist experienced in treating with CAR-T therapy
    b. The hospital or associated clinic where the treatment will occur is specially certified per the drug manufacturer and in compliance with the KYMRIAH REMS program for the treatment (including immediate on-site access to tocilizumab)
    c. Member has appropriate labs completed prior to Kymriah treatment for monitoring during and after treatment

4. Treatment location for administration of requested medication is provided (inpatient or outpatient hospital).

5. Member must *not* have any of the following:
    a. For adult members with Large B-cell lymphoma r/r, member does not have active central nervous system malignancy

References:

1. 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.
2. 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.
3. ClinicalTrials.gov. Study of Efficacy and Safety of CTL019 in Pediatric ALL Patients (ENSIGN). 2020; https://clinicaltrials.gov/ct2/show/study/NCT02228096. Accessed December 16, 2020.
4. Kymriah [package insert]. East Hanover, NJ; Novartis. May 2018.

Tecartus (axicabtagene ciloleucel)

1. Medical records and treating hematologist/oncologist provide testing to confirm member meets the following diagnosis specific criteria:
    a. Diagnosis for member aged 18 years and older
        i. Relapsed or refractory mantle cell lymphoma (MCL).
        (This indication is approved under accelerated approval based on overall response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial)
            1. Prior treatment must include ALL of the following:
                a. Anthracycline or bendamustine-containing chemotherapy AND
                b. Anti-CD20 monoclonal antibody therapy (e.g., ,rituximab) AND
                c. Bruton's tyrosine kinase (BTK) inhibitor (e.g., Ibrutinib, acalabrutinib, zanubrutinib)

            AND
            2. Member has at least one measurable lesion AND
            3. Member has adequate bone marrow reserve defined by all the following:
                a. Absolute neutrophil count (ANC) ≥ 1000 cells/μL
                b. Absolute lymphocyte count (ALC) ≥ 100 cells/μL
                c. Platelet count ≥ 75,000/μL
        ii. Relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL) defined as one of the following
            1. Primary refractory disease
            2. First relapse if first remission ≤ 12 months
            3. Relapsed or refractory disease after 2 or more lines of systemic therapy
            4. Relapsed or refractory disease after allogeneic transplant provided individuals is at least 100 days from stem cell transplant at the time of enrollment

2. Prior to treatment:
    a. Member will receive lymphodepleting (LD) chemotherapy regimen appropriate for specified diagnosis
        i. Provide LD chemotherapy that member will receive including drug, dose, route frequency and duration prior to treatment with Tecartus.
    b. Member has adequate kidney, liver, cardiac, and pulmonary function (must meet established criteria/measures) to receive full therapy.
    c. Member has been screened for hepatitis B virus, hepatitis C virus, and HIV
    d. Member has been informed of anticipated benefits, risks and expectations with treatment including but not limited to the following

i. Remission, post treatment occurrence of secondary malignancy, cytokine release syndrome, neurologic toxicity, and hypogammaglobulinemia

3. Treating and prescribing provider(s) attest to the following:
    a. Provider is a hematologist/oncologist experienced in treating with CAR-T therapy
    b. The hospital facility or associated clinic where the treatment will occur is specially certified per the drug manufacturer and in compliance with the YESCARTA and TECARTUS REMS program for the treatment (including immediate on-site access to tocilizumab)
        i. Treatment location for administration of requested medication is provided (inpatient or outpatient hospital).
    c. Member will be monitored at the certified healthcare facility daily for at least seven days for patients with MCL and at least 14 days for patients with ALL following infusion for signs and symptoms of Cytokine Release Syndrome (CRS) and neurologic events.

4. Member must not have any of the following:
    a. Active infection or inflammatory disorder
    b. History of a seizure disorder, cerebrovascular ischemia/hemorrhage, dementia, cerebellar disease, cerebral edema, posterior reversible encephalopathy syndrome, or any autoimmune disease with central nervous system (CNS) involvement
    c. History of prior allogeneic HSCT
    d. History of primary central nervous system lymphoma

References:

1. Tecartus [package insert]. Santa Monica, CA; Kite Pharma, Inc. 2021.
2. Shah, Bijal, et al. "KTE-X19 Anti-CD19 CAR T-Cell Therapy in Adult Relapsed/Refractory Acute Lymphoblastic Leukemia: ZUMA-3 Phase 1 Results." *Blood*, vol. 138, no. 1, July 2021, pp. 11–22, www.ncbi.nlm.nih.gov/pmc/articles/PMC9999039/.
3. Wang, Michael L., et al. "KTE-X19, an Anti-CD19 Chimeric Antigen Receptor (CAR) T Cell Therapy, in Patients (Pts) with Relapsed/Refractory (R/R) Mantle Cell Lymphoma (MCL): Results of the Phase 2 ZUMA-2 Study." *Blood*, vol. 134, no. Supplement_1, Nov. 2019, pp. 754–54, doi:https://doi.org/10.1182/blood-2019-126064.

Yescarta (axicabtagene ciloleucel)

1. Medical records and treating hematologist/oncologist provide testing to confirm member has one of the following diagnoses and prior treatment experience:
    a. Diagnosis for member age 18 years and older:
        i. Relapsed or refractory disease after two or more lines of systemic therapy
            1. diffuse large B-cell lymphoma (DLBCL), not otherwise specified
            2. primary mediastinal large B-cell lymphoma
            3. high grade B-cell lymphoma
            4. DLBCL arising from follicular lymphoma
        ii. Large B-cell lymphoma that is refractory to first-line chemoimmunotherapy or that relapses within 12 months of first-line chemoimmunotherapy
    b. Treatment regimens:
        i. The lymphoma has not responded to first line chemotherapy
        ii. The lymphoma has not responded to second or greater lines of chemotherapy, or
        iii. The lymphoma has relapsed within 12 months of an autologous hematopoietic stem cell transplant (HSCT)

2. Prior to treatment:
    a. Member will receive Lymphodepleting (LD) chemotherapy:
        i. Provide LD chemotherapy that member will receive including drug, dose, route frequency and duration prior to treatment with Yescarta.
    b. Member's parent or caretaker/guardian has been informed of anticipated benefits, risks and expectations with treatment including but not limited to the following
        i. Remission, post treatment occurrence of secondary malignancy, cytokine release syndrome, neurologic toxicity, and hypogammaglobulinemia
    c. Member has adequate liver, kidney, cardiac, and pulmonary function (must meet established criteria/measures) to receive full therapy.
    d. Member has been screened for hepatitis B virus, hepatitis C virus, and HIV

3. Treating and prescribing provider(s) attest to the following:
    a. Provider is a hematologist/oncologist experienced in treating with CAR-T therapy
    b. The hospital facility or associated clinic where the treatment will occur is specially certified per the drug manufacturer and in compliance with the YESCARTA and TECARTUS REMS program for the treatment (including immediate on-site access to tocilizumab)
        i. Treatment location for administration of requested medication is provided (inpatient, outpatient hospital).
    c. Member has appropriate labs completed prior to Yescarta treatment for monitoring during and after treatment

4. Member must *not* have any of the following:
    a. History of primary central nervous system lymphoma
    b. Administration of live virus vaccination to member at least 6 weeks prior to therapy, during therapy, and until recovery of immune system post-CAR-T therapy

c. Active infection or inflammatory disorder
d. History of prior allogeneic HSCT

References:

1. Locke FL, Ghobadi A, Jacobson CA, et al. Long-term safety and activity of axicabtagene ciloleucel in refractory large B-cell lymphoma (ZUMA-1): a single-arm, multicentre, phase 1-2 trial. *Lancet Oncology.* 2019;20(1):31-42. doi: https://dx.doi.org/10.1016/S1470-2045(18)30864-7.

2. Yescarta [package insert]. Santa Monica, CA; Kite Pharma, Inc. 2019.