Quartz

CAR T Cell Therapy

Last Revision/Review Date: November 18, 2020 **P&P # C.6.30**

Policy

The Medical Management Department reviews referral requests for prior authorization of FDA approved CAR-T Cell therapy to include Kymriah™ (Tisagenlecleucel) and Yescarta™ (axicabtagene ciloleucel) for FDA approved indications.

NOTE: Final approval determinations for CAR T cell therapy must be made by the Medical Director.

This Medical Policy does not constitute medical advice. When deciding coverage, the enrollee's specific plan document must be referenced. The terms of an enrollee's plan document (Certificate of Coverage (COC) or Summary Plan Description (SPD)) may differ from this Medical Policy. In the event of a conflict, the enrollee's specific benefit plan document supersedes this Medical Policy. All reviewers must first identify enrollee eligibility, any federal or state regulatory requirements, and the plan benefit coverage prior to use of this Medical Policy. Other Policies and Coverage Determination Guidelines may apply. Quartz reserves the right, in its sole discretion, to modify its Policies and Guidelines as necessary.

Procedure

I. **CAR T-cell therapy with use of Yescarta™** (Axicabtagene ciloleucel)**:**

A. Documentation Required:
In order to facilitate the authorization process, referral requests must include the following:

1. Documentation of a B-cell lymphoma diagnosis;
2. Documentation that the patient's disease is relapsed or refractory after two or more lines of systemic therapy;
3. Documentation that patient does not have current, active, serious infection including hepatitis B (HBV), hepatitis C (HCV), and human immunodeficiency virus (HIV) prior to collection of cells (leukapheresis);
4. Patient is without a diagnosed active inflammatory disorder (e.g., active autoimmune hepatitis, vasculitis, inflammatory bowel disease, connective tissue disease)
5. Documentation regarding prior allogeneic hematopoietic stem cell transplantation;
6. Patient has adequate organ and bone marrow functioning;
7. Documentation of the lack of central nervous system malignancy involvement;
8. Documentation of patient's current performance status, (e.g., ambulatory activity level, ability to work, lack of confinement to bed);
9. No prior CAR T-cell therapy;
10. Documentation that the health care facility is an Authorized Treatment Center for the specific

B. **Criteria for Medical Necessity of CAR T-cell therapy Yescarta™**

Yescarta™ is considered medically necessary for the treatment of large B-cell lymphoma if **ALL** of the following criteria are met:

1. Age 18 years and older; **AND**
2. Disease is relapsed or refractory with documented failure of two or more lines of systemic therapy; **AND**
3. Systemic therapy must have included anthracycline as well as an anti-CD20 monoclonal antibody unless the tumor is CD20-negative; **AND**
4. Disease is **ANY ONE** of the following:
    i. Diffuse large B-cell lymphoma not otherwise specified (DLBCL, NOS)
    ii. Diffuse large B-cell lymphoma arising from follicular lymphoma
    iii. Primary mediastinal large B-cell lymphoma
    iv. High grade B-cell lymphoma; **AND**
5. Documentation that the patient is without a current, active, serious infection including HBV, HCV and HIV; **AND**
6. Patient is without an active inflammatory disorder (e.g., active autoimmune hepatitis, vasculitis, inflammatory bowel disease, connective tissue disease); **AND**
8. Patient is without central nervous system malignancy involvement; **AND**
9. Patient has not had a prior allogeneic hematopoietic stem cell transplantation; **AND**
10. Patient must have adequate organ and bone marrow function; **AND**
11. Patient has an adequate performance status (e.g., ambulatory, able to complete all ADLs, and not bed confined); **AND**
12. The individual has not received prior CAR-T therapy; **AND**
13. If patient has a history of an allogeneic hematopoietic stem cell transplant there is no evidence of active Graft vs. Host disease requiring treatment; **AND**
14. The facility requesting approval is an Approved Yescarta Treatment Center https://www.yescarta.com/authorized-treatment-centers/.

C. Conditions considered experimental and investigational for treatment with Yescarta™ (not an all-inclusive list):

1. Use in non-FDA approved conditions or conditions not listed in the medical criteria noted above, including: (not an all-inclusive list)
    - Acute lymphoblastic leukemia (ALL)
    - Follicular lymphoma
    - Indolent non-Hodgkin lymphoma (NHL)
    - Mantle cell lymphoma
    - Marginal zone lymphoma
2. Patients who have had prior CAR T-cell therapy;
3. Use in patients under the age of 18 years or over the age of 65 years;
4. Prior allogeneic hematopoietic stem cell transplantation;
5. Presence of central nervous system malignancy involvement;
6. Inadequate organ or bone marrow functioning;
7. History or presence of a CNS disorder such as a seizure disorder, cerebrovascular ischemia/hemorrhage, dementia, cerebellar disease or any autoimmune disease with CNS involvement;
8. Current, active, serious infection including HBV, HCV or HIV;

9. Patient has an active inflammatory disorders (e.g., active autoimmune hepatitis, vasculitis, inflammatory bowel disease, connective tissue disease);
10. Patients with an inadequate performance status (e.g., non-ambulatory, unable to do ADLs, bed confined);
11. Patient with a current, active, serious infection including HBV, HCV and HIV;
12. Patients without refractory or relapsed disease;
13. Treatment at a facility that is not an approved Yescarta Treatment Center.

II. CAR T-cell therapy with use of Kymriah™ (tisagenlecleucel)

A. Documentation Required:

In order to facilitate the authorization process, referral requests must include the following:

1. Documentation of CD19 positive B-cell acute lymphoblastic leukemia (B-ALL) diagnosis and Philadelphia chromosome status;
2. Documentation of previous systemic therapy including patient response;
3. Documentation of Tyrosine kinase inhibitor use for patients with Philadelphia chromosome-positive B-ALL OR documentation of a hypersensitivity, intolerance or contraindication to their use in this patient;
4. Documentation that the patient's disease is refractory to the most recent therapy or has relapsed disease;
5. Patient has adequate organ and bone marrow function;
6. Documentation of any central nervous system malignancy involvement;
7. Documentation that the patient is without current, serious infection including HBV, HCV and HIV;
7. Patient is without a diagnosed inflammatory disorder (e.g., active autoimmune hepatitis, vasculitis, inflammatory bowel disease, connective tissue disease);
8. Documentation of patient's current performance status, (e.g., ambulatory activity level, ability to work, lack of confinement to bed);
9. No prior CAR T-cell therapy;
10. Documentation that the health care facility is a Kymriah Authorized Treatment Center.

B. Criteria for Medical Necessity of CAR T-cell therapy with Kymriah™

Kymriah™ is considered medically necessary for the treatment of B-ALL if **ALL** of the following criteria are met:

1. Age ≤ 25 years old; **AND**
2. Disease is refractory to treatment **OR** patient has had two or more relapses. For adolescents and young adult patients with Philadelphia chromosome-positive B-cell precursor acute lymphoblastic leukemia (B-ALL), they must have failed treatment with 2 tyrosine kinase inhibitors (TKIs);
   AND
3. Must have adequate organ and bone marrow function; **AND**
4. Absence of current, active, uncontrolled, serious infection including HBV, HCV, and HIV; **AND**
5. Patient is without an active inflammatory disorder (e.g., active autoimmune hepatitis, vasculitis, inflammatory bowel disease, connective tissue disease); **AND**
6. Patient has an adequate performance status (e.g.,Karnofsky or Lansky score greater than or equal to 50); **AND**
7. No prior CAR T-cell therapy; **AND**

8. If patient has a history of an allogeneic hematopoietic stem cell transplant there is no evidence of active Graft vs. Host disease requiring treatment; **AND**
9. Treatment will be provided by a Kymriah™ Authorized Treatment Center. https://www.us.kymriah.com/acute-lymphoblastic-leukemia-children/interested-in/where-to-get-treatment/

Kymriah™ is considered medically necessary for treatment of large B-cell lymphoma if **ALL** of the following criteria are met:

1. Age 18 years and older; **AND**
2. Disease is relapsed or refractory with documented failure of two or more lines of systemic therapy **OR** any relapse after prior autologous stem cell transplant regardless of prior therapy; **AND**
3. Disease is **ANY ONE** of the following:
    v. Diffuse large B-cell lymphoma not otherwise specified (DLBCL, NOS),
    vi. Diffuse large B-cell lymphoma arising from follicular lymphoma,
    vii. Primary mediastinal large B-cell lymphoma,
    viii. High grade B-cell lymphoma; **AND**
4. Documentation that the patient is without a current, active, serious infection including HBV, HCV and HIV; **AND**
5. Patient is without a diagnosed inflammatory disorder (e.g., active autoimmune hepatitis, vasculitis, inflammatory bowel disease, connective tissue disease); **AND**
6. Patient is without central nervous system malignancy involvement; **AND**
7. Patient with relapse after prior allogeneic hematopoietic stem cell transplantation only if they meet the following:
    i. experienced graft rejection, **AND**
    ii. no active GVHD and no required immunosuppression, **AND**
    iii. is greater than 6 months from transplant; **AND**
8. Patient must have adequate organ and bone marrow function; **AND**
9. Patient has an adequate performance status (e.g., ambulatory, able to complete all ADLs, and not bed confined); **AND**
10. Patient is not currently taking systemic corticosteroids (recent or current use of inhaled steroids is not exclusionary); **AND**
11. The individual has not received prior CAR-T therapy; **AND**
12. If patient has a history of an allogeneic hematopoietic stem cell transplant there is no evidence of active Graft vs. Host disease requiring treatment; **AND**
13. The facility requesting approval is an Approved Kymriah™ Treatment Center.

C. Conditions considered experimental and investigational for treatment with Kymriah™ (not an all-inclusive list):

1. Use in patients > 25 years of age with acute lymphoblastic leukemia (ALL);
2. Prior CAR T-cell treatment;
3. Presence of active central nervous system malignancy involvement in patients with lymphoma;
4. Inadequate organ or bone marrow function;
5. Patient diagnosed with active inflammatory disorders (e.g., active autoimmune hepatitis, vasculitis, inflammatory bowel disease, connective tissue disease);
6. Patients with an inadequate performance status (e.g., non-ambulatory, unable to do ADLs, bed confined);

7. Patients who are pregnant or lactating;
8. Patient with a current, active, uncontrolled, serious infection including HBV, HCV and HIV;
9. Patients without refractory or relapsed disease;
10. Use in non-FDA approved conditions, conditions not listed in the medical criteria noted above or one of the following:
    a. Acute myeloid leukemia (AML)
    b. Chronic lymphocytic leukemia (CLL)
    c. Hodgkin lymphoma (HL)
    d. Plasma cell disorders (e.g., multiple myeloma (MM))
    e. Solid tumors (e.g., glioma, glioblastoma and neuroblastoma)
    f. T-cell leukemia/lymphoma (e.g., acute T-cell leukemia, adult T-cell leukemia/lymphoma, anaplastic large-cell lymphoma, and cutaneous T cell lymphoma)

III. CAR T-cell therapy with use of Tecartus™ (brexucabtagene autoleucel)

A. Documentation Required:

In order to facilitate the authorization process, referral requests must include the following:

1. Documentation mantle cell lymphoma diagnosis and CD19 status;
2. Documentation of previous systemic therapy including patient response;
3. Documentation that the patient's disease is refractory to the most recent therapy or has relapsed disease;
4. Patient has adequate organ and bone marrow function;
5. Documentation of any central nervous system malignancy involvement;
6. Documentation that the patient is without current, serious infection including HBV, HCV and HIV;
7. Patient is without a diagnosed inflammatory disorder (e.g., active autoimmune hepatitis, vasculitis, inflammatory bowel disease, connective tissue disease);
8. Documentation of patient's current performance status, (e.g., ambulatory activity level, ability to work, lack of confinement to bed);
9. No prior CAR T-cell therapy;
10. Documentation that the health care facility is a Tecartus™ Authorized Treatment Center.

B. Criteria for Medical Necessity of CAR T-cell therapy with Tecartus™

Tecartus™ is considered medically necessary for the treatment of Mantle Cell Lymphoma if **ALL** of the following criteria are met:

1. Age 18 years or older; **AND**
2. Diagnosis of Mantle Cell Lymphoma that is relapsed or refractory to first line systemic treatment including chemoimmunotherapy and a BTK inhibitor; **AND**
3. Must have adequate organ and bone marrow function; **AND**
4. Absence of current, active, uncontrolled, serious infection including HBV, HCV, and HIV; **AND**
5. Patient is without an active inflammatory disorder (e.g., active autoimmune hepatitis, vasculitis, inflammatory bowel disease, connective tissue disease); **AND**
6. Patient has an adequate performance status (e.g.,Karnofsky or Lansky score greater than or equal to 50); **AND**
7. No prior CAR T-cell therapy; **AND**
8. Treatment will be provided by a Tecartus™ Authorized Treatment Center.

C. Conditions considered experimental and investigational for treatment with Tecartus™ (not an all-inclusive list):

1. Use in patients under age 18;
2. Prior CAR T-cell treatment;
3. Presence of active central nervous system malignancy involvement in patients with lymphoma;
4. Inadequate organ or bone marrow function;
5. Patient diagnosed with active inflammatory disorders (e.g., active autoimmune hepatitis, vasculitis, inflammatory bowel disease, connective tissue disease);
6. Patients with an inadequate performance status (e.g., non-ambulatory, unable to do ADLs, bed confined);
7. Patients who are pregnant or lactating;
8. Patient with a current, active, uncontrolled, serious infection including HBV, HCV and HIV;
9. Patients without refractory or relapsed disease;
10. Use in non-FDA approved conditions or conditions not listed in the medical criteria noted above.

CPT Codes

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
Q2041	Axicabtagene ciloleucel, up to 200 million autologous anti-CD19 CAR T Cells, including leukapheresis and dose preparation procedures, per infusion
Q2042	Tisagenlecleucel, up to 600 million car-positive viable t cells, including leukapheresis and dose preparation procedures, per therapeutic dose
J3490	Unclassified drugs
J3590	Unclassified biologics
J9999	Not otherwise classified, antineoplastic drugs

References

Institute for Clinical and Economic Review. Chimeric antigen reception t-cell therapy for b-call cancers: effectiveness and value. Final evidence report. March 23, 2018. Available at: https://icer-review.org/wp-content/uploads/2017/07/ICER_CAR_T_Final_Evidence_Report_032318.pdf
Accessed August 15, 2018.

Jain T, Bar M, Kansagra AJ, et al. Utilization of Chimeric Antigen Receptor (CAR) T Cell Therapy in Clinical Practice for Relapsed/Refractory Aggressive B cell non-Hodgkin Lymphoma: An Expert Panel Opinion from the American Society for Transplantation and Cellular Therapy. Biol Blood Marrow Transplant. 2019 Aug 22. pii: S1083-8791(19)30529-4. doi: 10.1016/j.bbmt.2019.08.015. [Epub ahead of print]

National Comprehensive Cancer Network® (NCCN) Clinical Practice Guidelines in Oncology.

- Acute Lymphoblastic Leukemia (Adult and AYA). V1.2020. Accessed September 2, 2020.
- B-Cell Lymphomas. V4.2020.. Accessed September 2, 2020.
- Pediatric Acute Lymphoblastic Leukemia. V2.2020. Accessed September 2, 2020.

OPTUM. Chimeric Antigen Receptor T-cell Therapy. Clinical Guideline. Version 1.0. Effective September 1, 2020. Accessed September 2, 2020.

Schuster SJ, Bishop MR, Tam CS, et al. Tisagenlecleucel in Adult Relapsed or Refractory Diffuse Large B-Cell Lymphoma. N Engl J Med. 2019;380:45-56.

Schuster SJ, Svoboda J, Chong EA, et al. Chimeric antigen receptor T cells in refractory B-cell lymphomas. N Engl J Med. 2017;377:2545-54.

Wang M, Munoz J, Goy A, et al. KTE-X19 CAR T-cell Therapy in Relapsed or Refractory Mantle Cell Lymphoma. N Engl J Med. 2020;382(14):1331-1342.