oscar

Clinical Guideline

Guideline Number: Yescarta (axicabtagene ciloleucel) (CG063, Ver. 5)

Yescarta (axicabtagene ciloleucel)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

The Plan members who have certain types of treatment-resistant lymphoma or leukemia may be eligible for chimeric antigen receptor (CAR) T-cell therapy. CAR T-cell treatment involves genetically modifying a patient's white blood cells to specifically target the cancer cells in the body. This type of therapy is also known as adoptive immunotherapy. The process starts by filtering the white blood cells from the patient's blood. The filtered cells are then genetically modified to target the tumor receptors and expanded to a greater quantity. The patient's existing immune system is then depleted, often with chemotherapy, prior to infusion in order to allow for a more effective environment for the CAR T-cells to function.

As there are potentially serious side effects, treatment should only be performed when the benefits outweigh the risks, under the care of a licensed physician and in an inpatient facility that is certified to administer CAR T-cell therapy. The facility must provide adequate inpatient monitoring during the infusion or extremely close outpatient monitoring with transplant or CAR T-cell experience. The facility must also have at least two doses of tocilizumab immediately available should a severe adverse reaction occur. Patients are also expected to be available and within appropriate proximity of the treatment location to be monitored for 4 weeks after treatment. Yescarta can only be accessed at specific treatment centers. To obtain more information, contact the REMS Call Center at 1-844-454-KITE (5483) or visit www.YescartaTecartusREMS.com.

This guideline does not address adoptive T-cell therapy for metastatic prostate cancer: Sipuleucel-T (Provenge™). For sipuleucel-T (Provenge™), please review the criteria outlined in MCG Sipuleucel-T (A-0661).

Definitions:

"AIDS" stands for Acquired Immunodeficiency Syndrome. It is a condition caused by the Human Immunodeficiency Virus (HIV), which attacks the immune system and weakens its ability to fight off infections and diseases. AIDS is considered the most advanced stage of HIV infection and is characterized by severe immune deficiency, leading to life-threatening opportunistic infections, cancers, and neurological disorders.

"Allogeneic Stem Cell Transplant" is a treatment where donor stem cells are harvested and transferred into patients with cancer or disorders (after their own immune system has been depleted using chemotherapy or total body irradiation) to repopulate their entire bone marrow with healthy cells.

"Autologous Stem Cell Transplant" is similar to allogeneic stem cell transfer, except the patient's own stem cells are used instead of a matched donor.

"B-cell lymphomas" refer to a group of non-Hodgkin's lymphomas developing from cancerous white blood cells (specifically B-lymphocytes), often involving lymph nodes or other extranodal tissues. This group of lymphomas includes, but is not limited to, the following:

- Burkitt lymphoma
- Diffuse large B-cell lymphoma (DLBCL)
- Primary mediastinal B-cell lymphoma (PMBCL)
- Mantle cell lymphoma
- Marginal zone lymphomas
- Transformed follicular lymphoma

"CAR T-cell" or "Chimeric Antigen Receptor T-cell" therapy is a type of adoptive immunotherapy where a patient's white blood cells (specifically T-lymphocytes) are genetically engineered to specifically target the receptors on the cancer cells (CD19 receptor in the case of B-cell lymphomas and leukemias), B-cell maturation antigen (BCMA) or prostatic acid phosphatase (PAP) in the case of prostate cancer).

"CAR-T cell-related encephalopathy syndrome" (CRES) is another inflammatory immune response that can occur with CAR-T treatment and is treated in the same way as CRS.

"Cytokine release syndrome" (CRS) is an inflammatory immune response that may occur with CAR T-cell treatment. It often manifests as fever, hypotension, nausea, and other symptoms, and is an emergent condition that may require prompt treatment with tocilizumab (treatment binds to and inhibits IL-6 to reduce inflammatory and immune excessive response) and/or corticosteroids.

"ECOG score" (Eastern Cooperative Oncology Group) is a measure of a patient's general well-being and ability to participate in activities of daily living. The score ranges from 0 (fully active with restrictions) to 5 (dead) and is available at https://ecog-acrin.org/resources/ecog-performance-status.

"HHV8 (Human herpesvirus 8)", also known as Kaposi's sarcoma-associated herpesvirus (KSHV), is a virus that can cause several types of cancers including Kaposi sarcoma, primary effusion lymphoma, and multicentric Castleman disease.

"Leukemia" refers to a type of malignancy affecting the bone marrow and circulating cells in the bloodstream. Acute lymphoid leukemia (ALL) is one example.

"MALT" stands for mucosa-associated lymphoid tissue, which is a type of tissue found in various mucosal surfaces of the body.

"Metastatic Castrate-Resistant Prostate Cancer" is prostate cancer that has metastasized or spread outside of the pelvis. Castrate-resistant refers to the state of the cancer not responding to medications or systemic agents that typically inhibit progression by blocking hormonal signals.

"Relapsed" refers to a lymphoma or leukemia that had previously responded to treatment with remission, but has returned after a period since the last treatment.

"Refractory" refers to a lymphoma or leukemia that has not responded, has progressed, or has not achieved remission.

Medical Necessity Criteria for Authorization

The Plan considers a single dose of YESCARTA® (axicabtagene ciloleucel) medically necessary when ALL the following criteria are met:

1. Prescribed by or in consultation with a hematologist-oncologist; *AND*
2. The member is 18 years of age or older; *AND*
3. Treatment is for ONE of the following histologically confirmed CD19-positive large B-cell lymphomas, under the following conditions:
    a. If the patient has had prior treatment with first-line chemoimmunotherapy and has any of the following B-cell lymphoma subtypes[#a]:
        i. AIDS-related B-cell lymphomas; *or*
        ii. Diffuse large B-cell lymphoma (DLBCL); *or*
        iii. Monomorphic post-transplant lymphoproliferative disorder (B-cell type); *or*
        iv. Other high-grade B-cell lymphomas; *or*
        v. Primary mediastinal large B-cell lymphoma; *or*

b. If the patient has had prior treatment with two or more lines of systemic therapy and has any of the following B-cell lymphoma subtypes[#a]:
    i. AIDS-related B-cell lymphomas; *or*
    ii. Diffuse large B-cell lymphoma (DLBCL); *or*
    iii. DLBCL arising (histologic transformation) from follicular lymphoma or nodal marginal zone lymphoma[#b]; *or*
    iv. Follicular lymphoma; *or*
    v. Gastric MALT lymphoma; *or*
    vi. Non-gastric MALT lymphoma; *or*
    vii. HHV8-positive diffuse large B-cell lymphoma; *or*
    viii. Monomorphic post-transplant lymphoproliferative disorder (B-cell type); *or*
    ix. Nodal marginal zone lymphoma; *or*
    x. Other high-grade B-cell lymphomas; *or*
    xi. Primary mediastinal large B-cell lymphoma; *or*
    xii. Splenic marginal zone lymphoma; *AND*

    [#a] For members with CD20-positive tumors, previous chemoimmunotherapy regimens should have included an anti-CD20 monoclonal antibody (e.g., Rituxan or rituximab biosimilars), unless contraindicated.

    [#b] for diffuse large B-cell lymphoma arising from follicular lymphoma or nodal marginal zone lymphoma, treatment should have included at least one anthracycline or anthracenedione-based regimen, unless contraindicated.

4. Documented evidence of ALL of the following:
    a. The member is is scheduled for and can safely undergo lymphodepleting therapy (including chemotherapy and/or total body irradiation) before CAR T-cell treatment; *and*
    b. The healthcare facility administering Yescarta is enrolled and adheres to the Yescarta REMS (Risk Evaluation and Mitigation Strategy), which includes:
        i. Immediate, on-site availability of tocilizumab; *and*
        ii. Provision of a minimum of two tocilizumab doses per patient, ensuring administration within 2 hours after Yescarta infusion if required for cytokine release syndrome treatment; *and*
        iii. Healthcare providers involved in prescribing, dispensing, or administering Yescarta are trained in managing cytokine release syndrome and neurological side effects; *and*
    c. The member has undergone screening and does NOT have any of the following:
        i. Active uncontrolled infection or inflammatory disorders; *or*
        ii. Active or latent hepatitis B; *or*
        iii. Active hepatitis C; *or*

        NOTE: history of hepatitis B or C is acceptable if the viral load is currently non-detectable.
        iv. A positive Human Immunodeficiency Virus (HIV) test; *or*

v. Previous treatment with Yescarta or any other CD19-targeted CAR T-cell therapy; *AND*

5. No contraindications (listed in "Experimental or Investigational / Not Medically Necessary" exclusions) are present.

Length of Stay

Initial Inpatient Admission - Up to 7 days

Extension Stay Criteria

Additional inpatient hospital days after 7 days are medically necessary when:

1. Patient has cytokine release syndrome (CRS); *or*
2. Patient has neurotoxicity, CAR-T Related Encephalopathy Syndrome (CRES); *or*
3. Patient has developed any adverse reaction continuing after infusion that include, but are not limited to, fever, hypoxia, hypotension, tachycardia, hypersensitive reactions, hypogammaglobulinemia, infections-pathogen unspecified, bleeding episodes, diarrhea, nausea, vomiting, headache, acute kidney injury, edema, and delirium; *or*
4. Patient is not stable for discharge, as outlined in the general recovery course and discharge criteria in MCG General Recovery Care > Problem Oriented General Recovery Guidelines >Medical Oncology GRG (PG-ONC).

Experimental or Investigational / Not Medically Necessary

CAR T-cell therapy for any other indication is considered experimental, investigational, or unproven. Non-covered indications and contraindications include, but are not limited to, the following:

- Any lymphoma subtype not mentioned above, including primary CNS lymphoma and Mantle cell lymphoma; *or*
- Any leukemia; *or*
- Any other cancer type or condition not included in the Clinical Indications criteria above; *or*
- When any other newly diagnosed malignancy or other malignancy that is under active treatment or not currently in remission is present; *or*
- Patients with an ECOG score of 3-4, as the efficacy and evidence for use in patients with poor performance status is limited; *or*
- Any of the following contraindications:
    - Live vaccination within 6 weeks of planned treatment date; *or*
    - Current pregnancy; *or*
    - Active, severe systemic infection including but not limited to those currently requiring IV antibiotics; *or*
    - Active HIV; *or*
    - Hepatitis B or Hepatitis C with detectable viral load; *or*

- Uncontrolled central nervous system disease, including but not limited to brain metastases, positive CSF disease, seizure disorder, dementia, history of stroke, cerebellar disease, or autoimmune CNS disease.

Applicable Billing Codes (HCPCS/CPT Codes)

CPT/HCPCS Codes considered medically necessary if criteria are met:	
Code	*Description*
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 (eg, 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
96365 - 96368	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug)
96413 - 96417	Chemotherapy administration, intravenous infusion technique
Q2041	Axicabtagene ciloleucel, up to 200 million autologous anti-CD19 CAR positive T cells, including leukapheresis and dose preparation procedures, per therapeutic dose
ICD-10 codes considered medically necessary if criteria are met for Axicabtagene ciloleucel (Yescarta™):	
Code	*Description*
B20	Human immunodeficiency virus [HIV] disease
C82.00 - C82.99	Follicular lymphoma
C83.00 - C83.09	Small cell B-cell lymphoma
C83.30 - C83.39	Diffuse large B-cell lymphoma
C83.80-C83.89	Other non-follicular lymphoma
C83.90-C83.99	Non-follicular (diffuse) lymphoma, unspecified
C85.10 - C85.19	Unspecified B-cell lymphoma

C85.20 - C85.29	Mediastinal (thymic) large B-cell lymphoma
C85.80 - C85.89	Other specified types of non-Hodgkin lymphoma
C88.4	Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue [MALT-lymphoma]
D47.Z1	Post-transplant lymphoproliferative disorder (PTLD)
ICD-10 codes considered experimental or investigational for Axicabtagene ciloleucel (Yescarta™):	
C83.10 - C83.19	Mantle cell lymphoma
C83.70- C83.79	Burkitt lymphoma

References

1. ACTEMRA(R) intravenous, subcutaneous injection, tocilizumab intravenous, subcutaneous injection. Genentech Inc (per FDA), South San Francisco, CA, 2021.
2. Axicabtagene: New Drugs: Australian Prescriber. December 2021 Volume 44 Number 6. Retrieved from: https://www.nps.org.au/assets/AP/pdf/December-44-6-32pp-v2.pdf
3. Burstein DS, Maude S, Grupp S, et al. Cardiac profile of chimeric antigen receptor T cell therapy in children: A single-institution experience. Biol Blood Marrow Transplant. 2018; 24(8):1590-1595.
4. Chavez JC, Bachmeier C, Kharfan-dabaja MA. CAR T-cell therapy for B-cell lymphomas: clinical trial results of available products. Ther Adv Hematol. 2019;10:2040620719841581.
5. Denlinger, N., Bond, D., & Jaglowski, S. (2021). CAR T-cell therapy for B-cell lymphoma. Current Problems in Cancer, 100826.
6. El-Galaly, T. C., Cheah, C. Y., Kristensen, D., Hutchison, A., Hay, K., Callréus, T., & Villa, D. (2020). Potentials, challenges and future of chimeric antigen receptor T-cell therapy in non-Hodgkin lymphomas. Acta Oncologica, 59(7), 766-774. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/32189546/
7. Grupp S, Laetsch T, Buechner J, et al. Analysis of a global registration trial of the efficacy and safety of CTL019 in pediatric and young Adults with relapsed/refractory acute lymphoblastic leukemia (ALL). Blood. 2016; 128(22):221.
8. Halford, Z., Anderson, M. K., Bennett, L. L., & Moody, J. (2021). Tisagenlecleucel in Acute Lymphoblastic Leukemia: A Review of the Literature and Practical Considerations. Annals of Pharmacotherapy, 55(4), 466-479. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/32762363/
9. Kaplan LD & Ai W. HIV-related lymphomas: Treatment of systemic lymphoma. UpToDate. Last updated March 15, 2021.
10. Kite Pharma, Inc. Authorized treatment centers for Yescarta (axicabtagene ciloleucel). Available at: https://www.yescarta.com/authorized-treatment-centers/. Accessed on April 17, 2020.
11. Kochenderfer JN, Dudley ME, Kassim SH, et al. Chemotherapy-refractory diffuse large B-cell lymphoma and indolent B-cell malignancies can be effectively treated with autologous T cells expressing an anti-CD19 chimeric antigen receptor. J Clin Oncol 2015; 33:540.
12. Kymriah [Product Information], Novartis Pharmaceuticals Corporation, East Hanover, NJ; May 2018. Available at: https://www.fda.gov/media/107296/download. Accessed on April 17, 2020.
13. Lamprecht M, Dansereau C. CAR T-Cell Therapy: Update on the State of the Science. Clin J Oncol Nurs. 2019;23(2):6-12.
14. Locke FL, Ghobadi A, Jacobson CA, et al. Long-term study and activity of axicabtagene ciloleucel in refractory long B-cell lymphoma (ZUMA-1): a single-arm, multicenter, phase 1-2 trial. Lancet Oncol. 2019; 20:21-42.

15. Locke FL, Neelapu SS, Bartlett NL, et al. Phase 1 Results of ZUMA-1: A Multicenter Study of KTE-C19 Anti-CD19 CAR T Cell Therapy in Refractory Aggressive Lymphoma. Mol Ther. 2017;25(1):285-295.
16. Locke FL, Rossi J, Xue X, et al. Abstract CT020: immune signatures of cytokine release syndrome and neurologic events in a multicenter registrational trial (ZUMA-1) in subjects with refractory diffuse large B cell lymphoma treated with axicabtagene ciloleucel (KTE-C19). In: Proceedings of the AACR Annual Meeting, 1–5 April 2017 Washington, DC.
17. Maude SL, Frey N, Shaw PA, et al. Chimeric antigen receptor T cells for sustained remissions in leukemia. N Engl J Med. 2014; 371(16):1507-1517.
18. 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.
19. National Comprehensive Cancer Network. Dictionary. https://www.nccn.org/patients/resources/dictionary/default.aspx Accessed 1/25/2021.
20. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines)® B-Cell Lymphomas Version 2.2023 — February 8, 2023. Accessed on March 4th, 2023.
21. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines)® B-Cell Lymphomas Version 5.2021 - September 22, 2021. © 2021National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed on April 17, 2020.
22. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines)® Pediatric Aggressive Mature B-Cell Lymphomas Version 3.2022 — October 19, 2022. Accessed on March 4th, 2023.
23. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology® (NCCN) Management of Immunotherapy-Related Toxicities. https://www.nccn.org/professionals/physician_gls/pdf/immunotherapy.pdf Published Dec 16,2019.
24. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology® (NCCN). © 2019 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org/index.asp. Accessed on April 17, 2020.
25. National Library of Medicine (U.S.). (2017, April -). A Phase 2 Multicenter Study of Axicabtagene Ciloleucel in Subjects With Relapsed/Refractory Indolent Non-Hodgkin Lymphoma (ZUMA-5). Identifier: NCT03105336. https://clinicaltrials.gov/ct2/show/study/NCT03105336
26. Neelapu SS, Locke FL, Bartlett NL, et al. Axicabtagene Ciloleucel CAR T-Cell Therapy in Refractory Large B-Cell Lymphoma. N Engl J Med 2017; 377:2531.
27. Ogbda N, Arwood NM, Bartlett NL, et al. Chimeric Antigen Receptor T-Cell Therapy. JNCCN. 2018;16(9). doi:https://doi.org/10.6004/jnccn.2018.0073
28. Pongas, G., & Cheson, B. (2021). Recent advances in the management of patients with relapsed/refractory follicular lymphoma. Blood and Lymphatic Cancer: Targets and Therapy, 11, 55.
29. Schepisi G, Cursano MC, Casadei C, et al. CAR-T cell therapy: a potential new strategy against prostate cancer. Journal for ImmunoTherapy of Cancer 2019;7:258. doi: 10.1186/s40425-019-0741-7
30. Schuster SJ, Bishop MR, Tam C, et al. Sustained disease control for adult patients with relapsed or refractory diffuse large B-Cell lymphoma: an updated analysis of Juliet, a global pivotal phase 2 trial of tisagenlecleucel. Blood 2018; 132: 1684.
31. 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.
32. Sharma P, King GT, Shinde SS, Purev E, Jimeno A. Axicabtagene ciloleucel for the treatment of relapsed/refractory B-cell non-Hodgkin's lymphomas. Drugs Today. 2018;54(3):187-198.
33. Yescarta (axicabtagene ciloleucel) [prescribing information]. Santa Monica, CA: Kite Pharma Inc; November 2022.
34. Zhang C, Kasi A. Chimeric Antigen Receptor (CAR) T-Cell Therapy. [Updated 2019 Feb 6]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2019 Jan.

Clinical Guideline Revision / History Information

Original Date: 5/5/2020 Reviewed/Revised: 03/11/2021,12/01/2021, 03/17/2022, 3/23/2023