Clinical Policy: CAR T-Cell Therapy

Reference Number: NC.CP.MP.500
Effective Date: 11/15/2022
Last Review Date: 02/2024

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Engineered T cell–based antitumor immunotherapy uses gene transfer of tumor antigen-specific T-cell receptors (TCR) or synthetic chimeric antigen receptors (CAR). CAR T-Cells are prepared from the beneficiary's peripheral blood mononuclear cells, which are obtained via a standard leukapheresis procedure. The blood is sent to the manufacturer where the mononuclear cells are enriched for T cells. The T cells are expanded in cell culture, washed, and formulated into a suspension, which then is cryopreserved. This process may take several weeks. The product is then infused into the beneficiary. This technique has shown very encouraging results in clinical trials for treatment of types of leukemias and lymphomas.

Definitions:

A. Rescue Transplant: a method of replacing blood-forming stem cells that were destroyed by treatment with high doses of anticancer drugs or radiation therapy. The stem cells help the bone marrow recover and make healthy blood cells. A rescue transplant may allow more chemotherapy or radiation therapy to be given so that more cancer cells are killed. It is usually done using the patient's own stem cells that were saved before treatment. Also called stem cell rescue.

United States Food & Drug Administration (U.S. FDA): the Food and Drug Administration is responsible for protecting the public health by ensuring the safety, efficacy, and security of human and veterinary drugs, biological products, and medical devices; and by ensuring

FDA Requirements

Due to the risk of cytokine release syndrome (CRS) and neurological toxicities, CAR T-Cell Therapies are only available through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS). A REMS is a program to manage known or potential serious risks associated with a drug product and is required by the U.S. Food & Drug Administration (U.S. FDA) to ensure that the benefits of the drug outweigh its risks. The U.S. FDA has required a REMS for CAR T-Cell Therapies. Each CAR T-Cell Therapy has a respective REMS Program.

The goals of the REMS are to mitigate the risks of CRS and neurological toxicities by:

a. Ensuring that hospitals and their associated clinics that dispense CAR T-Cell Therapies are specially certified and have on-site, immediate access to tocilizumab; and
b. Ensuring those who prescribe, dispense, or administer CAR T-Cell Therapies are aware of how to manage the risks of cytokine release syndrome and neurological toxicities.

**Note: All hospitals and their associated clinics must be certified and enrolled in the therapy's respective REMS to be able to infuse CAR T-Cell Therapy.*

Background: The below grid outlines current FDA approved agents for CAR T-Cell Therapy.

CAR T-Cell Therapy Agent/Description	FDA Approved Indications

Axicabtagene ciloleucel (Yescarta™): CD19-directed, genetically modified, autologous T-cell immunotherapy.	Yescarta is indicated for the treatment of adult patients with
	• Relapsed or refractory large B-cell lymphoma (LBCL):
	  ○ After two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma
	  ○ That is refractory to first-line chemoimmunotherapy or that relapses within 12 months of first-line chemoimmunotherapy
	  ○ Limitation of use: Yescarta is not indicated for the treatment of patients with primary central nervous system (CNS) lymphoma.*
	• Relapsed or refractory follicular lymphoma (FL) after two or more lines of systemic therapy
	  ○ This indication is approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s)
	
	**Efficacy of Yescarta has not been established in patients with a history of or current CNS lymphoma (see Appendix D)*

Tisagenlecleucel (Kymriah™): CD19-directed, genetically modified, autologous T-cell immunotherapy	Kymriah is 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 large B-cell lymphoma (LBCL) 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 • Adult patients with relapsed or refractory follicular lymphoma (FL) after two or more lines of systemic therapy^ Limitation(s) of use: Kymriah is not indicated for treatment of patients with primary central nervous system (CNS) lymphoma.* ** Efficacy of Kymriah for the treatment of LBCL has not been established in patients with active CNS disease (see Appendix D).* *^ This indication is approved under accelerated approval based on response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.*
Brexucabtagene autoleucel (Tecartus®) is a CD19-directed chimeric antigen receptor (CAR) T cell therapy	Tecartus is indicated for the treatment of: • Adult patients with relapsed or refractory mantle cell lymphoma (MCL)* • Adult patients with relapsed or refractory B-cell precursor acute lymphoblastic lymphoma (ALL) **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.*

CAR T-Cell Therapy Agent/Description	FDA Approved Indications
Idecabtagene vicleucel (Abecma®) is an anti-B cell maturation antigen (BCMA) chimeric antigen receptor (CAR) T-cell immunotherapy	Abecma is indicated for the treatment of adult patients with relapsed or refractory multiple myeloma after four or more prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody
Ciltacabtagene autoleucel (Carvykti™) is a B-cell maturation antigen (BCMA)-directed chimeric antigen receptor T cell (CAR-T) therapy	Caryvkti is indicated for the treatment of adults with relapsed and/or refractory multiple myeloma (MM) after four or more prior lines of therapy, including a proteasome inhibitor (PI), an immunomodulatory drug (IMiD), and an anti-CD38 monoclonal antibody.
Lisocabtagene maraleucel (Breyanzi®) is a CD19-directed genetically modified autologous T-cell immunotherapy.	Breyanzi is indicated for the treatment of adult patients with large B-cell lymphoma (LBCL), including diffuse large B-cell lymphoma (DLBCL) not otherwise specified (including DLBCL arising from indolent lymphoma), highgrade B-cell lymphoma, primary mediastinal large B-cell lymphoma, and follicular lymphoma grade 3B, who have: • Refractory disease to first-line chemoimmunotherapy or relapse within 12 months of first-line chemoimmunotherapy • Refractory disease to first-line chemoimmunotherapy or relapse after first-line chemoimmunotherapy and are not eligible for hematopoietic stem cell transplantation (HSCT) due to comorbidities or age • Relapsed or refractory disease after two or more lines of systemic therapy Limitation of use: Breyanzi is not indicated for the treatment of patients with primary central nervous system (CNS) lymphoma

Policy/Criteria

I. Specific criteria covered:
   a. the CAR T-Cell Therapy has received approval from the United States Food & Drug Administration (U.S. FDA);
   b. the CAR T-Cell Therapy is administered per U.S. FDA approved guidelines regarding:
      i. indications and usage;
      ii. dosage and administration;
      iii. dosage forms and strengths; and
      iv. warnings and precautions;
   c. c. the CAR T-cell Therapy is administered at a certified healthcare facility that has enrolled in the therapy's Risk Evaluation and Mitigation Strategies (REMS) and training has been given to providers on the management of cytokine release syndrome (CRS) and neurological toxicities

II. The provider must submit the following when requesting authorization for CAR T-Cell Therapy

a. Letter of medical necessity signed by the attending physician, which documents past chemotherapy regimens and dates, the clinical and social history, and indications for treatment with CAR T-Cell therapy;
b. Copy of contract between administering facility and manufacturer of the requested CAR T-Cell therapy;
c. Serologies (less than three months old) to include Human Immunodeficiency Virus (HIV) and Hepatitis panel (positive serology results may be reported that are greater than three months old);
d. All diagnostic and procedure results;
e. Other diagnostic tests may be requested as appropriate; and
f. Complete Psychological and social evaluation to include:
    i. beneficiary's medical compliance;
    ii. beneficiary's support network;
    iii. post-treatment care plan, with identification of primary and secondary care providers; and
    iv. history of mental health issues, substance use, or legal issues.

Specific Criteria NOT Covered

I. It is the policy of Carolina Complete Health that CAR T-Cell Therapy shall not be covered for ANY of the following:
    a. the CAR T-Cell Therapy has not received approval from the U.S. FDA;
    b. the CAR T-Cell Therapy is being administered outside U.S. FDA guidelines regarding:
        i. indications and usage;
        ii. dosage and administration; or
        iii. dosage forms and strengths;
    c. the CAR T-Cell Therapy is being administered at a facility that has not enrolled in that therapy's Risk Evaluation and Mitigation Strategy (REMS);
    d. repeat treatment in beneficiaries who have received another CAR T-Cell Therapy previously;
    e. when the beneficiary's psychosocial history limits the beneficiary's ability to comply with pre- and post-infusion medical care; or
    f. when there is current beneficiary or caretaker non-compliance that would make compliance with a disciplined medical regime improbable.

II. CAR T-Cell Therapy shall not cover concurrent rescue transplant with infusion of any CAR T-Cell Therapy as this is considered experimental.

**Note: Carolina Complete Health, in accord with North Carolina Medicaid standards, anticipates coverage of all FDA approved CAR-T therapies for their given and approved indications: each new agent will be reviewed thoroughly at the time of formal release of approval to the market.*

References:

1. Approved Cellular and Gene Therapy Products: Available at: https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/approved-cellular-and-gene-therapy-products; Accessed 11/01/2022
2. Yescarta Prescribing information. Santa Monica, CA: Kite Pharma, Inc.; April 2022. Available at www.yescarta.com. Accessed April 4, 2022.
3. Data on File. Kite Pharma - Yescarta: Primary Results of the Pivotal ZUMA-1 Phase 2 Study. MRC-00038. October 2017.
4. National Comprehensive Cancer Network. B-cell Lymphomas Version 5.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed July 19, 2022.
5. National Comprehensive Cancer Network Drug and Biologics Compendium. Available at http://www.nccn.org/professionals/drug_compendium. Accessed June 9, 2022.
6. National Comprehensive Cancer Network. Central Nervous System Cancers Version 2.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cns.pdf. Accessed October 19, 2021.
7. Kymriah Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; May 2022. Available at: https://www.us.kymriah.com/. Accessed June 7, 2022.
8. Data on File. Novartis Pharmaceuticals Corporation; East Hanover, NJ. November 2020.
9. Abecma Prescribing Information. Summit, NJ: Celgene Corporation; March 2021. Available at: https://www.abecma.com. Accessed February 1, 2022.
10. Carvykti Prescribing Information. Horsham, PA: Janssen Biotech, Inc.; February 2022. Available at: https://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/CARVYKTI-pi.pdf . Accessed March 2, 2022.
11. Breyanzi Prescribing Information. Bothell, WA: Juno Therapeutics, Inc.; June 2022. Available at: https://packageinserts.bms.com/pi/pi_breyanzi.pdf. Accessed July 7, 2022.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

Rev Code	Description
0636	Pharmacy - Drugs Requiring Detailed Coding

HCPCS Codes	Description
C9399	Unclassified drugs or biologicals (if the CAR T-Cell Therapy has been approved by the VDA but has not yet been assigned a product-specific code)

HCPCS Codes	Description
Q2040	Tisagenlecleucel, up to 250 million car-positive viable t cells, including leukapheresis and dose preparation procedures, per infusion
Q2041	Axicabtagene Ciloleucel, up to 200 million autologous anti-CD19 CAR positive viable T Cells, including leukapheresis and dose preparation procedures, per therapeutic dose
Q2042	Tisagenlecleucel, up to 600 million car-positive viable t cells, including leukapheresis and dose preparation procedures, per therapeutic dose
Q2053	Brexucabtagene autoleucel, up to 200 million autologous anti-cd19 car positive viable t cells, including leukapheresis and dose preparation procedures, per therapeutic dose
Q2054	Lisocabtagene maraleucel, up to 110 million autologous anti-CD 19 CAR-positive viable T cells, including leukapheresis and dose preparation procedures, per therapeutic dose
Q2055	Idecabtagene vicleucel, up to 460 million autologous B-cell maturation antigen (BCMA) directed CAR-positive T cells, including leukapheresis and dose preparation procedures, per therapeutic dose
Q2056	Ciltacabtagene autoleucel, up to 100 million autologous B-cell maturation antigen (BCMA) directed CAR-positive T cells, including leukapheresis and dose preparation procedures, per therapeutic dose
J9999	Not otherwise classified, antineoplastic drugs

Reviews, Revisions, and Approvals	Date	Approval Date
Policy Developed	11/2022	11/2022
Revision to remove: "**Note: For Medicaid members**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy." as this is a Medicaid only policy.	02/2023	02/2023
Annual Review with no revisions	02/2024	02/2024

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in

developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.