CLINICAL GUIDELINES FOR MEDICAL NECESSITY

MEDICAL POLICY

Ciltacabtagene Autoleucel (Carvykti®)

Version: 2.1

EFFECTIVE DATE: 6/27/2025

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For Medicare members/enrollees, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Please refer to the CMS website at http://www.cms.gov for additional information.

For Medicaid members/enrollees, circumstances when state Medicaid coverage provisions conflict with the coverage provisions within 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.

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Ciltacabtagene Autoleucel (Carvykti®)

Discussion

Ciltacabtagene autoleucel is a is a B-cell maturation antigen (BCMA)-directed chimeric antigen receptor (CAR) T-cell therapy. T-cells are collected from the patient and re-engineered in the laboratory to produce proteins on their surface called chimeric antigen receptors, or CARs. The CARs recognize and bind to specific proteins, or antigens, on the surface of cancer cells. Once reinfused back into the patient, the CAR-T cells will continue to multiply in the patient's body and, with guidance from their engineered receptor, recognize and kill any cancer cells that harbor the target antigen on their surfaces.[1,2]

The most common nonlaboratory adverse reactions (incidence greater than 20%) are pyrexia, cytokine release syndrome, hypogammaglobulinemia, hypotension, musculoskeletal pain, fatigue, infections-pathogen unspecified, cough, chills, diarrhea, nausea, encephalopathy, decreased appetite, upper respiratory tract infection, headache, tachycardia, dizziness, dyspnea, edema, viral infections, coagulopathy, constipation, and vomiting. The most common Grade 3 or 4 laboratory adverse reactions (incidence greater than or equal to 50%) include lymphopenia, neutropenia, white blood cell decreased, thrombocytopenia, and anemia. Clinically significant adverse events included increased early mortality, cytokine release syndrome (CRS), neurologic toxicities, hemophagocytic lymphohistiocytosis (HLH)/macrophage activation syndrome (MAS), prolonged and recurrent cytopenias, infections, hypogammaglobulinemia, hypersensitivity reactions, and secondary malignancies.[1]

Ciltacabtagene autoleucel is approved by the Food and Drug Administration (FDA) and endorsed by the National Comprehensive Cancer Network (NCCN) for multiple myeloma.[3]

Definitions

- **Cytokine release syndrome (CRS) -** A systemic inflammatory response triggered by infections and certain drugs. CRS can present with a range of symptoms from mild, flu-like symptoms to severe, life-threatening manifestations, including high fever, hypotension, and multi-organ system failure. It is commonly associated with T cell-engaging therapies like CAR T cells and bispecific T-cell engaging (BiTE) antibody constructs.[4]
- **Food and Drug Administration (FDA)** - The FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation.[5]
- **Hemophagocytic Lymphohistiocytosis (HLH)/Macrophage Activation Syndrome (MAS)** - A rare, life-threatening state of immune hyperactivation that arises in the setting of genetic mutations and infectious, inflammatory, or neoplastic triggers. Sustained, aberrant activation of cytotoxic $CD8^+$ T cells and resultant inflammatory cytokine release are core pathogenic mechanisms.[6]

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- **Hypogammaglobulinemia** - A disorder caused by low serum immunoglobulin or antibody levels. Immunoglobulins are the main components of the humoral immune response and can recognize antigens to trigger a biological response and eradicate the infectious source.[7]
- **National Comprehensive Cancer Network (NCCN)** - An alliance of more than 30 leading cancer centers devoted to patient care, research, and education. The NCCN guidelines are utilized for Radiation Therapy and Medical Oncology standards. NCCN consensus clinical standards are periodically updated and Nant Health, Inc. reviews these and updates its policies within a timely manner.[8]

Policy

Coverage will be considered for FDA approved indications and for NCCN category 1, 2A, or 2B recommendations when all criteria are met:

Multiple Myeloma

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **FDA** criteria coverage:

3. Relapsed or refractory disease who have received at least 1 prior line of therapy, including a proteasome inhibitor and an immunomodulatory agent, and are refractory to lenalidomide;[1] OR

For **NCCN** criteria coverage:

4. Previously treated disease for relapsed/refractory disease in patients who have received at least one of the following:
   a) 1 prior line of therapy, including an immunomodulatory agent and a proteasome inhibitor if lenalidomide refractory
   b) 3 prior lines of therapy.[3]

Dosage:

1. Administer a lymphodepleting regimen of cyclophosphamide and fludarabine before infusion of ciltacabtagene autoleucel.
2. The recommended dose range is 0.5-1.0×106 CAR-positive viable T cells per kg of body weight, with a maximum dose of 1×108 CAR-positive viable T cells per single infusion.[1]

Authorization Period and Renewal Criteria

Ciltacabtagene autoleucel is a one-time dose therapy and will not be renewed.

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(CPT®, ICD 10 and HCPCS)

Procedure codes appearing in medical policy documents are only included as a general reference. This list may not be all-inclusive and is subject to updates. In addition, the codes listed are not a guarantee of payment. CPT codes are available through the AMA.

Code	Description
C90	Multiple myeloma and malignant plasma cell neoplasms
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

Revision and Review History

No.	Description	Date(s)
1	Original Effective Date:	1/1/2024
2	Policy Annual Review Dates:	5/28/2024, 6/7/2024, 6/13/2025
3	Department Owner:	Medical Affairs
4	NH Advisory Committee Approval Dates:	5/11/2023, 6/7/2023, 6/18/2024, 6/27/2025, 7/11/2025
5	Revision Changes:	6/13/2025 Updated discussion section, definitions, dosage, and coding; removed policy criteria not endorsed by FDA or NCCN; v2.0 7/11/2025 Removed any mention of the REM requirement due to recent FDA update; 2.1

References

[1] Carvykti (ciltacabtagene autoleucel) [package insert]. https://www.fda.gov/media/156560/download?attachment. Accessed June 13, 2025.

[2] Cancer Institute. CAR T Cells: Engineering Patients' Immune Cells to Treat Their Cancers. https://www.cancer.gov/about-cancer/treatment/research/car-t-cells. Accessed June 13, 2025.

[3] National Comprehensive Cancer Network. NCCN Guidelines: Multiple Myeloma. https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed June 13, 2025.

[4] Shimabukuro-Vornhagen A, Gödel P, Subklewe M, et al. Cytokine release syndrome. *J Immunother Cancer*. 2018;6(1):56. Published 2018 Jun 15.https://pmc.ncbi.nlm.nih.gov/articles/PMC6003181/. Accessed June 13, 2025.

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[5] U.S. Food & Drug Administration. https://www.fda.gov/about-fda/what-we-do. Accessed June 13, 2025.

[6] Griffin G, Shenoi S, Hughes GC. Hemophagocytic lymphohistiocytosis: An update on pathogenesis, diagnosis, and therapy. *Best Pract Res Clin Rheumatol.* 2020;34(4):101515. https://pubmed.ncbi.nlm.nih.gov/32387063/. Accessed June 13, 2025.

[7] Huq ME, Bhatnagar NK, Hostoffer RW. Hypogammaglobulinemia. [Updated 2023 Jun 5]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan. https://www.ncbi.nlm.nih.gov/books/NBK563134/. Accessed June 13, 2025.

[8] National Comprehensive Cancer Network. https://www.nccn.org/home. Accessed June 13, 2025.

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