CLINICAL GUIDELINES FOR MEDICAL NECESSITY

MEDICAL POLICY

Ciltacabtagene Autoleucel (Carvykti®)

Version: 1.0

EFFECTIVE DATE: 1/1/2024

NantHealth® | Eviti®

Please note the following:

Ciltacabtagene Autoleucel (Carvykti®)

Note: 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.

Note: 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.

Ciltacabtagene Autoleucel (Carvykti): Discussion

Multiple myeloma (MM) is a malignant neoplasm of plasma cells that accumulate in the bone marrow, leading to bone destruction and marrow failure. The American Cancer Society (ACS) estimated an incidence of multiple myeloma to be 32,270 new cases in the US in 2020 with an estimated 12,830 deaths. MM accounts for 1.8% of hematologic malignancies in the United States. The median age of patients with MM is 69 years. [1]

Ciltacabtagene autoleucel is a B-cell maturation antigen (BCMA)-directed genetically modified autologous T cell immunotherapy. Ciltacabtagene autoleucel is made by collecting T cells from the patient and re-engineering them in the laboratory to produce proteins on their surface called chimeric antigen receptors, or CARs. The CARs recognize and bind to the specific proteins, or antigens, on the surface of cancer cells. After the revamped T cells are "expanded" into the millions in the laboratory, they're infused back into the patient. Approved by the FDA in 2022, ciltacabtagene autoleucel is indicated for the treatment of relapsed or refractory multiple myeloma (RRMM) after four or more prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody. [2,3]

Due to the complications from CAR-T therapies of cytokine release syndrome (CRS) hemophagocytic lymphohistiocytosis/macrophage activation syndrome (HLH/MAS) and neurologic deficits, all providers/healthcare facilities involved in the treatment of patients getting CAR-T therapy, must be registered in the Ciltacabtagene Autoleucel Risk Evaluation and Mitigation Strategy (REMS) Program. [3,4]

Ciltacabtagene Autoleucel: Definitions

- **Cytokine release syndrome (CRS) -** A life-threatening complication of CAR-T therapy that occurred in 95% of patients with 5% having grade 3 or over toxicity. The most common clinical manifestations of CRS included pyrexia (96%), hypotension (51%), tachycardia (27%), chills (33%), hypoxia (12%), fatigue (47%), and headache (27%). The median time to onset of CRS is 7 days. The median duration of CRS is 4 days. [3,4]
- **Carvykti -** Ciltacabtagene autoleucel
- **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.
- **Hemophagocytic lymphohistiocytosis/macrophage activation syndrome (HLH/MAS) -** The manifestations of HLH/MAS include hypotension, hypoxia, diffuse alveolar damage, multiple organ dysfunction, renal dysfunction (7%), coagulopathy (22%) and cytopenia. HLH/MAS is potentially life-threatening if not recognized early and treated. [3,4]
- **National Comprehensive Cancer Network (NCCN) -** An alliance of 32 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 NantHealth, Inc. reviews these and updates its policies within a timely manner.
- **Neurologic Toxicities -** Can be severe and life-threatening. These can occur in combination with CRS. The median onset of neurotoxicity from the start of CAR-T therapy was 2 days. The most frequent manifestations of CAR-T cell-associated neurotoxicity include encephalopathy (30%), dizziness (23%), motor dysfunction (16%), tremors (6%), aphasia (8%), ataxia (8%) peripheral neuropathy (6%), and delirium (5%). Monitoring of patients for neurotoxicity should be done daily for 7 days at a REMS-certified facility and should continue for 4 weeks and should be treated promptly. [3,4]
- **Risk Evaluation and Mitigation Strategy (REMS) -** A REMS program is a drug safety program to manage known or potential risk associated with a drug and is required by the US Food and Drug Administration (FDA) to ensure that the benefits of a drug outweigh its risks. Ciltacabtagene autoleucel is only available through this restricted program. The program ensures that hospitals and their associated clinic(s) that dispense ciltacabtagene autoleucel are specially certified and have on-site immediate access to tocilizumab. The program also ensures that those who prescribe, dispense, or administer ciltacabtagene autoleucel are aware of how to manage the risks of CRS and neurologic toxicities. Those involved in the program must successfully complete the knowledge assessment and submit it to the REMS Program. [3,4]

Ciltacabtagene Autoleucel: Policy

Ciltacabtagene Autoleucel will be considered for coverage when the following criteria are met:

Multiple Myeloma:

For authorization:

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND
3. Healthcare facility/provider has enrolled in the Ciltacabtagene Autoleucel REMS program; AND
4. Member has a diagnosis of relapsed or refractory multiple myeloma; AND
5. Member has received 4 or more lines of therapy including ALL the following:
   a) An immunomodulatory agent (e.g., Revlimid)
   b) A proteasome inhibitor (e.g., Velcade)
   c) An anti-CD38 monoclonal antibody (e.g., Darzalex); AND
6. Member has an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1; AND
7. Member does not have any of the following:
   a) Prior treatment with CAR-T therapy (directed at any target)
   b) Prior therapy that targeted BCMA (e.g., Blenrep)
   c) History of an allogeneic stem cell transplant in the past 6 months
   d) History of an autologous stem cell transplant in the past 12 weeks
   e) Known active or prior history of central nervous system involvement

Dosage:

Dosage allowed/Quantity limit: $0.5\text{-}1.0\times10^{6}$ CAR-positive viable T cells per kg of body weight, with a maximum dose of 1×10^{8} CAR-positive viable T cells per single infusion.

For reauthorization:

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

Note: Coverage of ciltacabtagene autoleucel will be provided for FDA-approved indications or National Comprehensive Cancer Network (NCCN) guidelines when it is a Category 1, 2A, or 2B recommendation or when all criteria are met.

Ciltacabtagene Autoleucel: References

1. National Comprehensive Cancer Network. Multiple Myeloma (Version 3.2023). https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed April 21, 2023.
2. CAR T Cells: Engineering Patients' Immune Cells to Treat Their Cancers. https://www.cancer.gov/about-cancer/treatment/research/car-t-cells/. Accessed April 21, 2023.
3. Ciltacabtagene Autoleucel (Carvykti) Package Insert. https://www.fda.gov/media/156560/download. Accessed April 21, 2023.
4. CARVYKTI® Risk Evaluation and Mitigation Strategy (REMS). https://carvyktirems.com. Accessed April 21, 2023.
5. Berdeja JG, Madduri D, Usmani SZ, 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 [published correction appears in Lancet. 2021 Oct 2;398(10307):1216]. Lancet. 2021;398(10297):314-324. doi:10.1016/S0140-6736(21)00933-8. Accessed April 21, 2023.

Ciltacabtagene Autoleucel: Coding (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
C90.00	Multiple Myeloma not having achieved remission
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
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

XW033A7	Introduction of ciltacabtagene autoleucel into peripheral vein, percutaneous approach, new technology group 7
WX043A7	Introduction of ciltacabtagene autoleucel into central vein, percutaneous approach, new technology group 7
0871	Cell Collection w/CPT code 0537T
0872	Specialized Biologic Processing and Storage – Prior to Transport w/CPT 0538T
0873	Storage and Processing after Receipt of Cells from Manufacturer w/CPT 0539T
0874	Infusion of Modified Cells w/CPT 0540T
0891	Special Processed Drugs – FDA Approved Cell Therapy – Charges for Modified cell therapy

Ciltacabtagene Autoleucel: Revision and Review History

No.	Description	Date(s)
1	Original Effective Date:	1/1/2024
2	Policy Review Dates:	5/8/2023
3	Policy Revision Dates:	
4	Department Owner:	Medical Affairs
5	NH Advisory Committee Approval Dates:	5/11/2023 TA, 6/7/2023
6	Revision Changes:	