CLINICAL GUIDELINES FOR MEDICAL NECESSITY

MEDICAL ONCOLOGY

Idecabtagene Vicleucel (Abecma®)

Version: 2.0

EFFECTIVE DATE: 1/1/2024

NantHealth® | Eviti®

Please note the following:

Idecabtagene Vicleucel (Abecma®)

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.

Idecabtagene Vicleucel (Abecma): Discussion

Multiple myeloma (MM) is a malignant neoplasm of plasma cells that accumulate in bone marrow, leading to bone destruction and marrow failure. The American Cancer Society (ACS) estimated an incidence of multiple myeloma to be 35,730 new MM cases in the US in 2023 with an estimated 12,590 deaths. MM accounts for about 1.8% of all cancers and 18% of hematologic malignancies in the United States. In the United States, the average lifetime risk of getting multiple myeloma is about 1 in 103 for men and about 1 in 131 for women. The median age of patients with MM is 69 years.[1,2]

Idecabtagene vicleucel is a B-cell maturation antigen (BCMA)-directed, genetically modified autologous chimeric antigen receptor T-cell (CAR-T) immunotherapy. A patient's own T cells are harvested and genetically modified outside of the body. The re-engineered cells are injected back into the patient and will recognize the BCMA on the malignant plasma cells to target and kill them. Idecabtagene vicleucel was approved in March 2021 and is indicated for the treatment of relapsed or refractory multiple myeloma after two or more prior lines of therapy including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody.[3]

Adverse Reactions include cytokine release syndrome (CRS) which is a life-threatening complication of CAR-T therapy that occurred in 89% of patients, ≥ grade 3 toxicity of 7% and Grade 5 CRS in 0.9%. The most common clinical manifestations of CRS included pyrexia (87%), hypotension (30%), tachycardia (26%), chills (19%), and hypoxia (16. The median duration of CRS was 6-7 days.) Another major adverse effect is hemophagocytic lymphohistiocytosis and macrophage activation syndrome (HLH/MAS)**.** In clinical trials, occurred in 2.9% of patients (10/349). All events of HLH/MAS occurred within 10 days of receiving Idecabtagene Vicleucel, with a median onset of 6.5 days, and occurred in the setting of ongoing or worsening CRS. The manifestations of HLH/MAS include hypotension, hypoxia, multiple organ dysfunction, renal dysfunction, and cytopenia. HLH/MAS is a potentially life-threatening condition with a high mortality rate if not recognized early and treated. Treatment of HLH/MAS should be

administered per institutional standards. Another adverse effect is Neurologic Toxicities which can be severe and life-threatening. These can occur concurrently with CRS, after CRS resolution, or in the absence of CRS following treatment with idecabtagene vicleucel. The most frequent manifestations of CAR-T cell-associated neurotoxicity include encephalopathy (21%), headache (15%), dizziness (8%), tremors (6%), and delirium (6%). In clinical trials, the median time to onset of neurotoxicity was 2 days with a median duration of 8 days. Monitoring of patients for neurotoxicity should be done daily for 7 days at a REMS-certified facility, should continue for 4 weeks after infusion, and should be treated promptly. Other major adverse effects include prolonged cytopenia with bleeding and infection, and T cell malignancies.

Due to the complications from CAR-T therapy of Cytokine Release Syndrome (CRS) as well as 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 Risk Evaluation and Mitigation Strategy (REMS) program.[3,4]

Idecabtagene Vicleucel: Definitions

- **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.
- **National Comprehensive Cancer Network (NCCN) -** An alliance of more than thirty 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.
- **Risk Evaluation and Mitigation Strategy (REMS) -** A REMS program is a drug safety program to manage known or potential risks 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. Idecabtagene vicleucel is only available through this restricted program. The program ensures that hospitals and their associated clinic(s) that dispense idecabtagene vicleucel are specially certified and have on-site immediate access to tocilizumab. The program also ensures that those who prescribe, dispense, or administer idecabtagene vicleucel are aware of how to manage the risks of cytokine release syndrome and neurologic toxicities. Those involved in the program must successfully complete the knowledge assessment and submit it to the REMS Program.[3,4]

Idecabtagene Vicleucel: Policy

Note: Coverage of idecabtagene vicleucel 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.

Idecabtagene vicleucel will be considered for coverage when the following criteria are met:

Multiple Myeloma:

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 Idecabtagene Vicleucel REMS program; AND
4. Diagnosis of relapsed or refractory multiple myeloma (RRMM); AND
5. Persistent disease after treatment with 2 or more prior lines of therapy, including all of 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. An Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1; AND
7. No history of an allogeneic hematopoietic stem cell transplantation (HSCT) or treatment with any gene therapy-based therapeutic for cancer; AND
8. Screened for cytomegalovirus (CMV), hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV); AND
9. Prior to idecabtagene vicleucel therapy, the patient will receive a lymphodepleting therapy of fludarabine and cyclophosphamide at the discretion of the physician.

Dosage:

Dosage allowed/Quantity limit: A single dose for infusion containing a suspension of chimeric antigen receptor (CAR)- positive T cells in one or more infusion bags. The recommended dose range is 300 to 510 x 10^6 CAR-positive T cells.

Note:
An anti-myeloma bridging treatment is allowed at the discretion of the physician for disease control while idecabtagene vicleucel is being manufactured.[3]

For reauthorization:

Idecabtagene vicleucel is a one-time dose and will not be renewed.

Idecabtagene Vicleucel: References

1. National Comprehensive Cancer Network. Multiple Myeloma. https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed May 30, 2024.
2. American Cancer Society. Cancer Facts & Figures 2024. Atlanta: American Cancer Society; 2024. https://www.cancer.org/cancer/types/multiple-myeloma/about/key-statistics.html. Accessed June 3,2024
3. Idecabtagene vicleucel (Abecma) Package Insert. www.fda.gov/media/147055/download. Accessed June 3, 2024.
4. Abecma Risk Evaluation and Mitigation Strategy. http://www.abecmarems.com. Accessed June 3, 2024.
5. 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, 2024.
6. Lee DW, Gardner R, Porter DL, et al. Current concepts in the diagnosis and management of cytokine release syndrome. Blood 2014; 124(2): 188-95. Errata in Blood: 2015;126(8):1048. and 2016;128(11):1533.
7. Miao L, Zhang Z, Ren Z, Li Y. Reactions related to CAR-T cell therapy. Frontiers in Immunology 2021;12: Online. DOI: 10.3389/fimmu.2021.663201. https://pubmed.ncbi.nlm.nih.gov/33995389/. Accessed April 21, 2024.
8. Munshi et al, N Engl J Med 384:705-16;2021, Idecabtagene Vicleucel in Relapsed and Refractory Multiple Myeloma. https://pubmed.ncbi.nlm.nih.gov/33626253/. Accessed April 21, 2024.

Idecabtagene Vicleucel: 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
C90.02	Multiple myeloma in relapse
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. NOTE-For all payers and sites of care: 1 billing unit
XW033K7	Introduction of idecabtagene vicleucel into a peripheral vein, percutaneous approach, new technology group 7

XW043K7	Introduction of idecabtagene vicleucel immunotherapy into a central vein, percutaneous approach, new technology group 7
Z00.6	Encounter for examination for normal comparison and control in clinical research program (only reported for clinical trial cases).
Z51.12	Encounter for antineoplastic immunotherapy
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
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

Idecabtagene Vicleucel: Revision and Review History

No.	Description	Date(s)
1	Original Effective Date:	1/1/2024
2	Policy Review Dates:	5/8/2023, 6/3/2024
3	Policy Revision Dates:	6/3/2024
4	Department Owner:	Medical Affairs
5	NH Advisory Committee Approval Dates:	6/16/2023, 6/18/2024
6	Revision Changes:	6/3/2024: Statistics updated, references (added reference no. 2), Dosage (Max dose from 460 to 510), added adverse effects, prior lines of therapy (changed from 4 to 2).