Medical Drug Clinical Criteria

Subject:	Carvykti (ciltacabtagene autoleucel)		
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Overview

This document addresses the use of Carvykti (ciltacabtagene autoleucel), a B-cell maturation antigen (BCMA)-directed genetically modified autologous T cell immunotherapy indicated for the treatment of adult patients with relapsed or refractory multiple myeloma, who have received at least 1 prior line of therapy, including a proteasome inhibitor and an immunomodulatory agent, and are refractory to lenalidomide.

Ciltacabtagene autoleucel is prepared from the patient's peripheral blood mononuclear cells (obtained via leukapheresis), which are enriched for T cells. When infused back into the patient, the anti-BCMA CAR T cells recognize and eliminate BCMA-expressing target cells. In addition to T cells, ciltacabtagene autoleucel may contain natural killer (NK) cells.

Carvykti has a black box warning for life-threatening or fatal cytokine release syndrome (CRS), neurologic toxicities, Parkinsonism and Guillian-Barrė syndrome, Hemophagocytic Lymphohistiocytosis/Macrophage Activation Syndrome HLH/MAS, prolonged and/or recurrent cytopenia, and secondary hematological malignancies, including myelodysplastic syndrome and acute myeloid leukemia. Due to these black box warnings, Carvykti is only available through a Risk Evaluation and Mitigation Strategy (REMS) program

The National Comprehensive Cancer Network® (NCCN) provides additional recommendations with a category 2A level of evidence for the following uses:

- Multiple Myeloma

Definitions and Measures

Chemotherapy: Medical treatment of a disease, particularly cancer, with drugs or other chemicals.

Disease Progression: Cancer that continues to grow or spread.

Refractory Disease: Illness or disease that does not respond to treatment.

Relapse or recurrence: After a period of improvement, during which time a disease (for example, cancer) could not be detected, the return of signs and symptoms of illness or disease. For cancer, it may come back to the same place as the original (primary) tumor or to another place in the body.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Carvykti (ciltacabtagene autoleucel)

Requests for Carvykti (ciltacabtagene autoleucel) may be approved if the following criteria are met:

I. Individual is 18 years of age or older; **AND**
II. Individual has a diagnosis of relapsed or refractory multiple myeloma; **AND**
III. If individual has a history of an allogeneic stem cell transplant, there are no current signs of active graft versus host disease (GVHD); **AND**
IV. Individual has adequate bone marrow reserve defined by all of the following:
    A. Absolute neutrophil count (ANC) ≥ 1000 cells/uL; **AND**

B. Platelet count ≥ 50,000 cells/uL; **AND**

V. Individual has an Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 1; **AND**

VI. Individual has not received prior CAR T-cell or B-cell maturation antigen (BCMA) targeted therapy; **AND**

VII. Individual is using as a one-time, single administration treatment.

Carvykti (ciltacabtagene autoleucel) may not be approved for the following (Berdeja 2021):

I. Repeat administration; **OR**

II. Active presence or history of central nervous system involvement with myeloma; **OR**

III. Using in combination with other chemotherapy agents (not including the use of lymphodepleting chemotherapy prior to infusion); **OR**

IV. Presence of plasma cell leukemia, Waldenstrom's macroglobulinemia, POEMS syndrome, or primary AL amyloidosis; **OR**

V. Individual has active GVHD; **OR**

VI. History of autologous stem cell transplant less than or equal to 12 weeks before apheresis; **OR**

VII. If prescribed in combination with other CAR T-cell immunotherapy (e.g. Abecma, Breyanzi, Kymriah, Tecartus, Yescarta); **OR**

VIII. History of cardiac conditions, such as New York Heart Association (NYHA) stage III or IV congestive heart failure, myocardial infarction or coronary artery bypass graft (CABG) within the past 6 months, history of clinically significant ventricular arrhythmia or unexplained syncope, not believed to be vasovagal in nature or due to dehydration, or history of severe non-ischemic cardiomyopathy; **OR**

IX. Left ventricular ejection fraction (LVEF) less than 45% (scan performed withing 8 weeks of apheresis); **OR**

X. Active hepatitis B, active hepatitis C, human immunodeficiency virus (HIV) positive, or other active, uncontrolled infection; **OR**

XI. When the above criteria are not met, and for all other indications.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

CPT

38225	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 [Carvyki]
38226	Chimeric antigen receptor T-cell (CAR-T) therapy; preparation of blood-derived T lymphocytes for transportation (eg, cryopreservation, storage) [Carvykti]
38227	Chimeric antigen receptor T-cell (CAR-T) therapy; receipt and preparation of CAR-T cells for administration [Carvykti]
38228	Chimeric antigen receptor T-cell (CAR-T) therapy; CAR-T cell administration, autologous [Carvykti]

HCPCS

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 [Carvykti]

ICD-10 Procedure

XW033A7	Introduction of Ciltacabtagene Autoleucel into Peripheral vein, Percutaneous Approach, New Technology Group 7 [Carvykti]
XW043A7	Introduction of Ciltacabtagene Autoleucel into Central vein, Percutaneous Approach, New Technology Group 7 [Carvykti]

ICD-10 Diagnosis

C90.00	Multiple myeloma not having achieved remission
C90.02	Multiple myeloma in relapse

Document History

Revised: 11/15/2024

Document History:

- 12/17/2024 – Coding update only: Added CPT codes 38225, 38226, 38227, 38228 effective 1/1/25.

- 11/15/2024 – Annual Review: No changes to criteria. Coding Reviewed: No changes.
- 9/18/2024 – Coding Reviewed: Added ICD-10 PCS codes XW033A7 and XW043A7.
- 11/19/2023 – Annual Review: Clarify RN III criteria to state "no current signs of active graft versus host disease (GVHD)." Change "OR to "AND" to ensure appropriate use of CAR-T therapy in RN VI. Clarify RN IX may not be approved criteria to ensure scan is performed within 8 weeks of apheresis. Coding Reviewed: No changes.
- 11/18/2022 – Annual Review: Simplify criteria for diagnosis to relapsed/refractory multiple myeloma; added clarifying criteria for those with a history of an allogeneic stem cell transplant, added criteria for those who have received prior CAR T-cell or B-cell maturation antigen targeted therapy. In the may not be approved criteria, added criteria around CNS disease with myeloma, added active GVHD, and combination use with another CAR T cell therapy. Deleted in the may not be approved criteria: history of allogeneic stem cell transplant, or history of CAR T therapy or other genetically modified T cell therapy. Coding Reviewed: No changes.
- 03/14/2022– Select Review: Add new clinical criteria for Carvykti (Ciltacabtagene autoleucel). Coding reviewed: Added HCPCS J3490, J3590, C9399. All diagnoses pend. Effective 7/1/2022 Added HCPCS C9098. Removed HCPCS C9399. Added ICD-10-CM C90.00, C90.02. Remove All diagnoses pend. Removed C90.0-C90.3. Effective 10/1/2022 Added HCPCS Q2056. Removed HCPCS J3490, J3590, C9399, C9098.

References

1. 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. Lancet. Vol 398:10297:314-324. 24 July 2021. Accessed on September 24, 2024.
2. Madduri D, Berdeja JG, Usmani SZ, et al. CARTITUDE-1: phase 1b/2 study of ciltacabtagene autoleucel, a B-cell maturation antigen-directed chimeric antigen receptor T cell therapy, in relapsed/refractory multiple myeloma. Presented at the 62nd ASH Annual Meeting and Exposition 2020 Dec 5-8. Presented orally 2020 Dec 5. Available at: https://ash.confex.com/ash/2020/webprogram/Paper136307.html. Accessed on September 24, 2024.
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6. San-Miguel, J, Dhakal B, Yong K, et al. Cilta-cel or Standard Care in Lenalidomide-Refractory Multiple Myeloma. The New England Journal of Medicine. Vol 389:335-347. 27 July 2023. Accessed on September 25, 2024.