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, after four or more prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody.

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

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 multiple myeloma; **AND**
III. Individual has measurable disease defined by any of the following:
    A. Serum monoclonal paraprotein (M-protein) level more than or equal to 1 g/dL; **OR**
    B. Urine M-protein level greater than or equal to 200 mg per 24 hours; **OR**
    C. Serum immunoglobulin free light chain greater than or equal to 10 mg/dL and abnormal serum immunoglobulin kappa lambda free light chain ratio; **AND**
IV. Individual has relapsed or refractory disease, defined progression after four (4) or more lines of systemic therapy (which may or may not include therapy supported by hematopoietic stem cell transplant), ***or*** individual is double-refractory to proteasome inhibitor and immunomodulatory drug; **AND** prior therapy includes *all* of the following (Berdeja 2021):
    A. Anti-CD38 antibody (for example isatuximab or daratumumab); **AND**

B. Proteasome inhibitor (for example, ixazomib, bortezomib, or carfilzomib); **AND**
C. An immunomodulatory drug (for example, thalidomide, pomalidomide, or lenalidomide); **AND**

V. 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**

VI. Individual has an Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 1; **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. Presence or history of central nervous system involvement; **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. History of allogeneic stem cell transplant within 6 months before apheresis; **OR**
VI. History of autologous stem cell transplant less than or equal to 12 weeks before apheresis; **OR**
VII. History of chimeric antigen receptor therapy or other genetically modified T-cell therapy; **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 ≤ 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.

HCPCS

J3490	Unclassified drugs (when specified as [Carvykti] (Ciltacabtagene autoleucel))
J3590	Unclassified biologics (when specified as [Carvykti] (Ciltacabtagene autoleucel))
C9399	Unclassified drugs or biologics (when specified as [Carvykti] (Ciltacabtagene autoleucel))

ICD-10 Diagnosis

	All diagnoses pend

Document History

New: 03/14/2022
Document History:

- 03/14/2022– Select Review: Add new clinical criteria for Carvykti (Ciltacabtagene autoleucel). Coding reviewed: Added HCPCS J3490, J3590, C9399. All diagnoses pend.

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 March 9, 2022.
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 March 4, 2022.

3. NCCN Clinical Practice Guidelines in Oncology™. © 2020 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on March 4, 2022.
    a. Multiple Myeloma. V4.2022. Revised December 14, 2021.
4. NCT03548207. ClinicalTrials.gov. U.S. National Library of Medicine. Available https://clinicaltrials.gov/ct2/show/NCT03548207?term=nct03548207&draw=2&rank=1. Accessed on March 4, 2022.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.