Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Ciltacabtagene autoleucel (Carvykti®)	MP-RX-FP-113-23	☒ MMM MA ☒ MMM Multihealth

Service Category

☐ Anesthesia
☐ Surgery
☐ Radiology Procedures
☐ Pathology and Laboratory Procedures
☐ Medicine Services and Procedures
☐ Evaluation and Management Services
☐ DME/Prosthetics or Supplies
☒ Part B Drug

Service Description

This document addresses the use of Ciltacabtagene autoleucel (Carvykti®), a B-cell maturation antigen (BCMA)-directed genetically modified autologous T cell immunotherapy approved by the Food and Drug Administration (FDA) 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.

Background Information

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, 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.

Approved Indications

Carvycti is indicated by the FDA 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.

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Other Uses

None

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

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

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Medical Necessity Guidelines

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.

Ciltacabtagene autoleucel (Carvykti®)

A. Criteria For Initial Approval (*Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met **all** approval criteria.)*

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 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.

B. Criteria For Continuation of Therapy

i. Further treatment with Carvykti will not be authorized since it is designated for a single-dose administration as per its indication.

C. Authorization Duration

i. Initial Approval Duration: 3 months (1 dose only, tocilizumab (Actemra) will be approved if requested)
ii. Reauthorization Approval Duration: Not applicable

D. **Conditions Not Covered**

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

<u>Carvykti (ciltacabtagene autoleucel) may not be approved for the following (Berdeja 2021):</u>

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 ≤ 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.

Limits or Restrictions

1. Therapeutic Alternatives

The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.

i. N/A

2. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

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Drug	Recommended Dosing Schedule
Ciltacabtagene autoleucel (Carvykti®)	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-dose infusion.

Additional Information

- Carvycti is designated for autologous administration via intravenous infusion solely within a certified healthcare setting.
- **Pretreatment**: Carvycti should be initiated 2 to 4 days after completing lymphodepleting chemotherapy regimen with cyclophosphamide 300 mg/m^2/day intravenously (IV) and fludarabine 30 mg/m^2/day IV for 3 days.
- **Premedication** should include acetaminophen (650 – 1000 mg orally) and diphenhydramine (25 to 50 mg orally, or another H1-antihistamine) approximately 30 to 60 minutes before infusion of Carvycti. Prophylactic use of dexamethasone or other systemic corticosteroids should be avoided, as the use may interfere with the activity of Carvycti.
- **Post-medication**: Tocilizumab plays an important role in the treatment of patients receiving CAR T-cell therapy such as Carvycti. It manages and mitigates cytokine release syndrome (CRS), which can occur after CAR T-cell infusion. Tocilizumab should be available to the patient prior to infusion and during the recovery period.

Reference Information

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 October 7, 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 October 7, 2022.
3. NCCN Clinical Practice Guidelines in Oncology™. © 2022 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on October 7, 2022
    a. Multiple Myeloma. V1.2023. Revised September 14, 2022.
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 October 7, 2022.

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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.

Policy History

Revision Type	Summary of Changes	P&T Approval Date	MPCC Approval Date
Policy Inception	Adopted from Elevance	N/A	12/22/2023
Select Review	Update statement for criteria for initial approval: Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met all approval criteria.	Click or tap to enter a date.	Click or tap to enter a date.

Revised: 11/30/2023