Molina Clinical Policy
Carvykti™ (ciltacabtagene autoleucel)
Policy No. 413
Last Approval: 06/11/2025
Next Review Due By: June 2026

DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. Policies are not a supplementation or recommendation for treatment; Providers are solely responsible for the diagnosis, treatment, and clinical recommendations for the Member. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (e.g., will be paid for by Molina) for a particular Member. The Member's benefit plan determines coverage – each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their Providers will need to consult the Member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid Members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP and provide the directive for all Medicare members. References included were accurate at the time of policy approval and publication.

POLICY DESCRIPTION

To define and describe the accepted indications for Carvykti (ciltacabtagene autoleucel) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

INDICATIONS

A. Continuation requests for a not-approvable medication shall be exempt from this policy provided:
1. The member has not experienced disease progression on the requested medication **AND**
2. The requested medication was used within the last year without a lapse of more than 30 days of having an active authorization **AND**
3. Additional medication(s) are not being added to the continuation request.

B. Multiple Myeloma

1. Carvykti (ciltacabtagene autoleucel) may be used for adult members with relapsed / refractory multiple myeloma who have received at least 1 prior line of therapy, including a proteasome inhibitor (e.g., bortezomib, carfilzomib, ixazomib) and an immunomodulatory agent (e.g., lenalidomide, thalidomide, pomalidomide), and are refractory to lenalidomide.

CONTRAINDICATIONS/WARNINGS

US Boxed Warning

- Cytokine release syndrome (CRS), including fatal or life-threatening reactions, occurred in patients following treatment with ciltacabtagene autoleucel. Do not administer ciltacabtagene autoleucel to patients with active infection or inflammatory disorders. Treat severe or life-threatening CRS with tocilizumab or tocilizumab and corticosteroids.
- Immune effector cell-associated neurotoxicity syndrome (ICANS), which may be fatal or life-threatening, occurred following treatment with ciltacabtagene autoleucel, including before CRS onset, concurrently with CRS, after CRS resolution, or in the absence of CRS. Monitor for neurologic events after treatment with ciltacabtagene autoleucel. Provide supportive care and/or corticosteroids as needed. . Parkinsonism and

Guillain-Barré syndrome (GBS) and their associated complications resulting in fatal or life-threatening reactions have occurred following treatment with ciltacabtagene autoleucel.

- Hemophagocytic lymphohistiocytosis/macrophage activation syndrome (HLH/MAS), including fatal and life-threatening reactions, occurred in patients following treatment with ciltacabtagene autoleucel. HLH/MAS can occur with CRS or neurologic toxicities.
- Prolonged and/or recurrent cytopenias with bleeding and infection and requirement for stem cell transplantation for hematopoietic recovery occurred following treatment with ciltacabtagene autoleucel.
- Secondary hematological malignancies, including myelodysplastic syndrome and acute myeloid leukemia, have occurred in patients following treatment with ciltacabtagene autoleucel. T-cell malignancies have occurred following treatment of hematologic malignancies with BCMA- and CD19-directed genetically modified autologous T-cell immunotherapies, including ciltacabtagene autoleucel.
- Ciltacabtagene autoleucel is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the CARVYKTI REMS Program.

EXCLUSIONS CRITERIA

- Disease progression on or after Carvykti (ciltacabtagene autoleucel) or prior treatment with chimeric antigen receptor T (CAR-T) therapy towards CD19 antigen (e.g., Abecma (idecabtagene vicleucel).
- Concurrent use with other anti-myeloma therapy.
- Member does **NOT** have measurable disease defined as any of the following:
  - Serum monoclonal paraprotein (M-protein) level more than or equal to 1.0 g/dL or urine M-protein level ≥ 200 mg/24hr; **OR**
    Light chain multiple myeloma without measurable disease in the serum or the urine: Serum immunoglobulin free light chain 10 mg/dL and abnormal serum immunoglobulin kappa lambda free light chain ratio.
- Does not exceed duration limit as one time administration.
- Dosing exceeds single dose limit of Carvykti (ciltacabtagene autoleucel) 1×10^8 CAR-positive viable T cells per single-dose infusion.
- Investigational use of Carvykti (ciltacabtagene autoleucel) with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:
  - Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
  - Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
  - Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definition of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of < 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
  - Whether the experimental design, considering the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).
  - That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
  - That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.

- That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

MEDICATION MANAGEMENT

A. Please refer to the FDA label/package insert for details regarding these topics.

APPLICABLE CPT / HCPCS PROCEDURE CODES

CPT (Current Procedural Terminology)

Code	Description
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
38226	Chimeric antigen receptor T-cell (CAR-T) therapy; preparation of blood-derived T lymphocytes for transportation (e.g., cryopreservation, storage)
38227	Chimeric antigen receptor T-cell (CAR-T) therapy; receipt and preparation of CAR-T cells for administration
38228	Chimeric antigen receptor T-cell (CAR-T) therapy; CAR-T cell administration, autologous

HCPCS (Healthcare Common Procedure Coding System)

Code	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

AVAILABLE DOSAGE FORMS: Maximum of 1 x 10^8 CAR-positive viable T cells per infusion bag of 5% dimethyl sulfoxide (DMSO)

CODING DISCLAIMER. Codes listed in this policy are for reference purposes only and may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry standard coding practices for all submissions. When improper billing and coding is not followed, Molina has the right to reject/deny the claim and recover claim payment(s). Due to changing industry practices, Molina reserves the right to revise this policy as needed.

APPROVAL HISTORY

06/11/2025	Policy reviewed. No changes to coverage criteria. US Boxed Warning added to policy.
06/12/2024	Criteria revised to include treatment of adult patients with relapsed or refractory multiple myeloma who have received at least one prior line of therapy, including a proteasome inhibitor and an immunomodulatory agent, and are refractory to lenalidomide.
04/10/2024	Changes to inclusion criteria include removal of the Preferred Medication Guidance for Initial Request, addition of section for continuation requests for a not-approvable medication; multiple myeloma clarified inclusion criteria by combining the definition of refractory disease and removing measurable disease or evidence of disease progression from the last line of therapy. Changes to exclusion criteria include removing the following conditions: member not having adequate bone marrow reserve, member not having adequate renal, hepatic, and cardiac function, and history or presence of CNS disorder.
08/09/2023	Criteria revised to include “and there is no Health Plan PDL applicable” to criteria A3 along with addition of criteria B3. Updated references. Added code Q2056 and removed codes C9399, J3490, J3590, and J9999.
08/10/2022	Adopted NCH policy and retired MCP.

REFERENCES

1. San-Miguel J, et al. Cilta-cel or Standard Care in Lenalidomide-Refractory Multiple Myeloma. N Engl J Med. 2023 Jul 27;389(4):335-347. doi: 10.1056/NEJMoa2303379.
2. Berdeja JG, 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. 2021 Jul 24;398(10297):314-324. doi: 10.1016/S0140-6736(21)00933-8.
3. Carvykti prescribing information. Janssen Biotech, Inc. Horsham, PA 2024.
4. Clinical Pharmacology Elsevier Gold Standard 2025.
5. Micromedex® Healthcare Series: Micromedex Drugdex Ann Arbor, Michigan 2025.
6. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2025.
7. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2025.
8. Ellis LM, et al. American Society of Clinical Oncology perspective: Raising the bar for clinical trials by defining clinically meaningful outcomes. J Clin Oncol. 2014 Apr 20;32(12):1277-80.
9. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf.
10. Current and Resolved Drug Shortages and Discontinuations Reported to the FDA: http://www.accessdata.fda.gov/scripts/drugshortages/default.cfm.