Mass General Brigham
Health Plan

# Medical Policy
# Carvykti™ (ciltacabtagene autoleucel)

**Policy Number:** 061

| | Commercial and Qualified Health Plans* | Mass General Brigham ACO** | Medicare Advantage | One Care | Senior Care Options (SCO) |
|---|---|---|---|---|---|
| Authorization required | X | X | X | X | X |
| No Prior Authorization | | | | | |

**Prior authorization for Carvykti for Commercial and Qualified Health Plan members is managed by Prime Therapeutics. See Prime Therapeutics policy for Carvykti for more information.*

***Prior authorization for Carvykti for Mass General Brigham ACO members is managed by the MassHealth Drug Utilization Review Program. See the MassHealth Variation below for more information.*

Carvykti is a chimeric antigen receptor T cell therapy (CAR-T), designed to harness the power of the patient's immune system to recognize and attack their cancer cells. CAR-T is a type of treatment where white blood cells (T cells) are modified in a laboratory to add a gene that helps the patient's own T cells target their cancer.

**FDA-Approved Indication**
Carvykti is a B-cell maturation antigen (BCMA)-directed genetically modified autologous T cell immunotherapy 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, OR
- 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.

**Criteria**

1. Criteria for Initial Approval

   Authorization of a single treatment may be granted to patients 18 years of age or older for treatment of MM when ALL of the following criteria are met:

   A. The member meets one of the following two criteria:
      - 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, OR
      - Relapsed or refractory multiple myeloma, after at least 1 prior line of therapy, including a proteasome inhibitor, and an immunomodulatory agent, and refractory to lenalidomide.

   B. The member has not received any prior FDA approved CAR-T cell therapy directed against B-cell maturation antigen (BCMA).

   C. The patient will receive lymphodepleting chemotherapy (cyclophosphamide and fludarabine) prior to infusion of Carvykti.

D. The patient has stable and adequate kidney, liver, pulmonary, and cardiac function as determined by the treating oncologist or hematologist.

E. The patient does not have clinically significant active infectious or inflammatory disorders.

F. The patient does not have active graft versus host disease.

G. The member has an Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 2. Any performance status above 2 can be considered on a case-by-case basis.

H. The healthcare facility that dispenses and administers Carvytki must be enrolled and comply with the Carvytki Risk Evaluation and Mitigation Strategy known as REMS.

I. The healthcare facility must have tocilizumab available on site for management of Cytokine Release Syndrome.

2. Required Documentation
   - Documentation of prior lines of therapy
   - Provider/patient REMS certification/enrollment
3. Duration of Therapy
   - Single treatment course
   - Additional courses of therapy are considered experimental/investigational.

**Medicare Variation**
Mass General Brigham Health Plan uses guidance from the Centers for Medicare and Medicaid Services (CMS) for medical necessity determinations for its Medicare Advantage plan members. National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), Local Coverage Articles (LCAs), and documentation included in the Medicare manuals are the basis for medical necessity determinations. When there is no guidance from CMS for the requested service, Mass General Brigham Health Plan's medical policies are used for medical necessity determinations. **At the time of Mass General Brigham Health Plan's most recent policy review, Medicare had:**

- **NCD for Chimeric Antigen Receptor (CAR) T-cell Therapy (110.24)**
- **Medicare Benefit Policy Manual Chapter 15: Covered Medical and Other Health Services**

When NCDs and LCDs lack sufficient specificity to ensure consistent medical review and coverage decisions, Mass General Brigham Health Plan applies additional coverage criteria to clarify medical necessity of the requested service. Mass General Brigham Health Plan coverage criteria align with the latest clinical evidence and accepted standards of practice, without contradicting existing determinations, and enhance the clarity of medical necessity criteria, documentation requirements, and clinical indications. Because NCD 110.24 lacks sufficient specificity to ensure consistent medical review and coverage determinations, Mass General Brigham Health Plan uses both the NCD and the criteria described in this policy to review requests for Carvykti.

**MassHealth Variation**
Prior authorization requests for Carvykti for Mass General Brigham ACO members should be submitted to the MassHealth Drug Utilization Review Program. Criteria for Carvykti are found in Table 75: T-Cell Immunotherapies.

**One Care and SCO Variation**

Mass General Brigham Health Plan uses guidance from CMS for medical necessity determinations for its One Care and SCO plan members. NCDs, LCDs, LCAs, and documentation included in the Medicare manuals are the basis for medical necessity determinations. When there is no guidance from CMS for the requested service, Mass General Brigham Health Plan uses medical necessity guidelines from MassHealth. When there is no guidance from CMS or from MassHealth, Mass General Brigham Health Plan's medical policies are used for medical necessity determinations.

**Codes**

**The following codes are included below for informational purposes only; inclusion of a code does not constitute or imply coverage.**

| Authorized CPT/HCPCS Codes | 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 (eg, 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 |
| 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 |

**Summary of Evidence**

Berdeja et al. (2021) reported on the CARTITUDE-1 study, a groundbreaking phase 1b/2 open-label trial evaluating ciltacabtagene autoleucel (Carvykti, cilta-cel), a B-cell maturation antigen (BCMA)-directed chimeric antigen receptor (CAR) T-cell therapy in patients with relapsed or refractory multiple myeloma. Enrolled patients were heavily pretreated, having failed ≥3 prior therapies, including resistance to proteasome inhibitors, immunomodulatory drugs, and anti-CD38 monoclonal antibodies. Patients received a single cilta-cel infusion 5-7 days after lymphodepletion. The trial demonstrated an impressive 97.7% overall response rate (ORR), 82.5% stringent complete response (sCR) rate, 70.4% overall survival (OS) rate, and 54.9% progression-free survival (PFS) rate, indicating exceptional clinical outcomes. Patients typically achieved their first response within one month post-infusion, highlighting the therapy's rapid therapeutic potential. Clinical efficacy was particularly notable, with the median progression-free survival not reached after median follow-up (MFU) of 27.7 months.

The researchers evaluated multiple subgroups, including patients aged 65 years or older, Black/African American patients, those who failed ≥3 prior therapies, individuals with penta-drug refractory disease, high cytogenetic risk patients, those with International Staging System (ISS) stage III disease, high tumor burden cases, and patients with bone or extramedullary plasmacytomas. These analyses demonstrated the treatment's potential to address the complex and varied nature of multiple myeloma across different patient populations.

Subsequent analysis by Martin et al. (2022) demonstrated significant improvements using validated instruments like EORTC QLQ-C30 and EQ-5D-5L. Patients reported clinically meaningful reductions in health-related quality of life (HRQoL) measures including pain and fatigue, with improvements observable as early as Day 29 post-infusion and sustained through follow-up with median follow-up (MFU) 16·9 months.

Outcomes in a Japanese cohort of CARTITUDE-1 was by Ri et al., 2022 with identical study design, inclusion/exclusion criteria, and subgroup analyses. The primary outcome in the Japanese cohort was similar to that in the cohort reported by Berdeja, with 100% ORR. However, the sCR rate was much lower at 25%, with most patients (62.5%) achieving very good partial response. Differences in outcomes may be attributed to small sample size, lack of baseline tumor BCMA expression, and a median follow-up (MFU) of only 8.5 months, since depth of response was observed to increase over time.

The CARTIFAN-1 study protocol was also similar to that of CARTITUDE-1, but in a Chinese population and in the Chinese health delivery system (Mi et al. 2022). Outcomes were likewise similar to those in CARTITUDE-1.

Safety profiles remained manageable with a favorable risk/benefit profile. Grade 3-4 cytokine release syndrome (CRS) was common. Immune effector cell-associated neurotoxicity (ICANS), movement and neurocognitive toxicities (MNTs), and cytopenias were also observed. CARTITUDE-1 (Berdeja et al., 2021) had no deaths within the first 30 days post-infusion or for the entire duration of the Japanese cohort (Ri et al., 2022).

Meta-analysis of several indirect treatment comparisons based on the CARTITUDE-1 trial suggests that cilta-cel for relapsed/refractory may be superior to physician's choice of treatment with respect to OS, PFS, and time to next treatment (Costa et al. 2022).

Two other major trials of cilta-cel are in progress. CARTITUDE-2 is a phase 2 trial that includes one cohort (A) of patients with lenolidamide-refractory MM following 1-3 prior lines of therapy, and another cohort (B) with early relapse ≤12 months after autologous stem cell transplant or start of anti-myeloma treatment. Preliminary outcomes following 28-30 months of follow-up suggest excellent ORR, with large majorities achieving sCR, and excellent PFS and OS rates, with safety profiles similar to prior studies (Hillengass et al. 2023). CARTITUDE-4 is a large, phase 3, randomized, open-label trial of cilta-cel versus physician's choice of effective standard care in patients with lenalidomide-refractory MM following 1-3 prior lines of therapy (San-Miguel et al. 2023). Following median 15.9 months of follow-up, median PFS was not reached in the cilta-cel group, and was 11.8 months in the standard care group (hazard ratio, 0.26 [95% CI 0.18-0.38, p<0.001). Benefits were also observed in secondary outcomes of OR, complete response or better, and absence of minimal residual disease.

On the basis of the CARTITUDE-4 study, the FDA granted authorization for the second indication of lenalidomide-refractory MM following 1-3 prior lines of therapy. National Comprehensive Cancer Network (2024) guidelines have incorporated cilta-cel as a recommended option for relapsed/refractory multiple myeloma following 3 prior lines of therapy, and for lenalidomide-refractory MM following at least 1 prior line of therapy including an IMiD and a PI.

These references collectively underscore ciltacabtagene autoleucel's role in addressing relapsed/refractory multiple myeloma, presenting a comprehensive narrative of robust clinical trial data, patient-reported outcomes, and supportive regulatory frameworks that establish its significant utility in contemporary oncological treatment. Consistent with NCCN guidelines and FDA labeling, MGB Health Plan considers this therapy to be medically necessary for members with MM who meet inclusion criteria based on the various CARTITUDE studies.

**Effective**
January 2026: Ad hoc update. Updated prior authorization table and added variation for One Care and SCO members. Fixed formatting and code disclaimer.
April 2025: Ad hoc update. MassHealth variation updated to include new prior authorization process.

March 2025: Ad hoc update. Clarified Medicare variation. Summary of evidence added. References updated.
February 2025: Annual update. Codes updated. Updated criteria per NCCN guidelines. Updated references.
September 2024: Ad hoc update. Added MassHealth variation.
February 2024: Annual update.
February 2023: Annual update. Added Medicare Advantage to table. Added age language under FDA-approved indication. Medicare variation language added. References updated.
October 2022: Ad hoc update. Coding updated.
July 2022: Effective Date.

**References**


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 [published correction appears in Lancet. 2021 Oct 2;398(10307):1216]. *Lancet.* 2021;398(10297):314-324.

Centers for Medicare & Medicaid Services. National Coverage Determination (NCD): Chimeric Antigen Receptor (CAR) T-cell Therapy (110.24). Implementation Date: 09/20/2021. Updated November 2020. Available: https://www.cms.gov/medicare-coverage-database/search.aspx

Costa LJ, Hari P, Berdeja J. Meta-analysis of ciltacabtagene autoleucel versus physician's choice therapy for the treatment of patients with relapsed or refractory multiple myeloma. *Current Medical Research and Opinion* 2022;38(10):1759-67.

Einsele H, Cohen AD, Delforge M, et al. Biological correlative analyses and updated clinical data of ciltacabtagene autoleucel, a BCMA-directed CAR-T cell therapy, in lenalidomide-refractory patients with progressive multiple myeloma after 1–3 prior lines of therapy: CARTITUDE-2, cohort A. Presented at the American Society of Clinical Oncology Annual Meeting, Chicago, June 3–7, 2022. abstract.

Hillengass J, Cohen AD, Agha M, et al. The phase 2 Cartitude-2 trial: Updated efficacy and safety of ciltacabtagene autoleucel in patients with multiple myeloma and 1-3 prior lines of therapy (Cohort A) and with early relapse after first line treatment (Cohort B). Abstract. *Transplantation and Cellular Therapy* 2024;30(2S):S36-37.

Janssen Biotech, Inc. Carvykti (ciltacabtagene autoleucel) suspension for intravenous infusion. Prescribing Information. Horsham, PA; Janssen Biotech: revised February 2022.

Martin T, Lin Y, Agha M. et al. Health-related quality of life in patients given ciltacabtagene autoleucel for relapsed or refractory multiple myeloma (CARTITUDE-1): a phase 1b-2, open-label study. *Lancet Haematol* 2022 Dec;9(12):e897-e905. doi: 10.1016/S2352-3026(22)00284-8. Epub 2022 Oct 7. PMID: 36215989.

Martin T, Usmani SZ, Berdeja JG, et al. Ciltacabtagene autoleucel, an anti-B-cell maturation antigen chimeric antigen receptor T-cell therapy, for relapsed/refractory multiple myeloma: CARTITUDE-1 2-year follow-up. *J Clin Oncol* 2023;41:1265-1274.

Mi JQ, Zhao W, Jing H, et al. Phase II, open-label study of ciltacabtagene autoleucel, an anti-B-cell maturation antigen chimeric antigen receptor-T-cell therapy, in Chinese patients with relapsed/refractory multiple myeloma (CARTIFAN-1). *J Clin Oncol* 2022;41:1275-84.

National Comprehensive Cancer Network (NCCN). Multiple Myeloma. NCCN Clinical Practice Guidelines in Oncology, Version 1.2025. NCCN, September 17, 2024.

Ri M, Suzuki K, Ishida T, Kuroda J. et al. Ciltacabtagene autoleucel in patients with relapsed/refractory multiple myeloma: CARTITUDE-1 (phase 2) Japanese cohort. *Cancer Sci* 2022 Dec;113(12):4267-4276. doi: 10.1111/cas.15556. Epub 2022 Oct 7. PMID: 36052883; PMCID: PMC9746030.

San-Miguel J, Dhakal B, Yong K, et al. Cilta-cel or standard care in lenalidomide-refractory multiple myeloma. *NEJM* 2023;389(4):335-347.

van de Donk NWCJ, Agha M, Cohen AD, et al. Ciltacabtagene autoleucel (cilta-cel), a BCMA-directed CAR-T cell therapy, in patients with multiple myeloma (MM) and early relapse after initial therapy: CARTITUDE-2 cohort B 18-month follow-up. *Blood* 2022;140:7536-7537.