MEDICAL COVERAGE POLICY	
SERVICE:	**Ciltacabtagene autoleucel (Carvykti™)**
Policy Number:	**298**
Effective Date:	**09/01/2025**
Last Review:	**06/09/2025**
Next Review:	**06/09/2026**

Important note: *Unless otherwise indicated, medical policies will apply to all lines of business. Medical necessity as defined by this policy does not ensure the benefit is covered. This medical policy does not replace existing federal or state rules and regulations for the applicable service or supply. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan documents. See the member plan specific benefit plan document for a complete description of plan benefits, exclusions, limitations, and conditions of coverage. In the event of a discrepancy, the plan document always supersedes the information in this policy.*

SERVICE: Ciltacabtagene autoleucel (Carvykti™)

PRIOR AUTHORIZATION: Required

POLICY: Please review the plan's EOC (Evidence of Coverage) or Summary Plan Description (SPD) for details.

For Medicare plans, please refer to Medicare NCD 110.24 Chimeric Antigen Receptor (CAR) T-cell Therapy

For Medicaid plans, please confirm coverage as outlined in the Texas Medicaid Provider Procedures Manual | TMHP (TMPPM). Texas Mandate HB154 is applicable for Medicaid plans.

Baylor Scott & White Health Plan (BSWHP) may consider ciltacabtagene autoleucel (Carvykti™) medically necessary when documentation is submitted showing ALL of the following criteria are met:

1. Member has a diagnosis relapsed or refractory multiple myeloma (RRMM); **AND**
2. Member is ≥ 18 years of age; **AND**
3. Ciltacabtagene is prescribed by or in consultation with a board-certified hematologist or oncologist; **AND**
4. Ciltacabtagene will be dosed and administered according to FDA approved labeling**; AND**
5. Ciltacabtagene will be used as monotherapy; **AND**
6. Provider attests member will receive ciltacabtagene at a REMS-certified healthcare facility; **AND**
7. Member has an Eastern Cooperative Oncology Group (ECOG) performance status between 0 and 1; **AND**
8. Member has adequate bone marrow, renal, hepatic, and cardiac function; **AND**
9. Member has been assessed by a hematologist/oncologist to be an appropriate candidate for apheresis; **AND**
10. Member has *lenalidomide-refractory* multiple myeloma, receiving one or more prior lines of therapy (regimens) that include all of the following:
    a. One immunomodulatory agent (ex., daratumumab, elotuzumab, isatuximab, lenalidomide, pomalidomide, thalidomide); **AND**
    b. One proteasome inhibitor (ex., bortezomib, carfilizomib, ixazomib)

    AND
11. Member has Not previously been treated with CAR-T cell therapy; **AND**

12. Member has Not received prior B-cell maturation antigen (BCMA) targeted therapy (ex., teclistamab, elranatamab); **AND**
13. Member does Not have any of the following:
    a. Active infection (including hepatitis B, hepatitis C, or HIV infection)
    b. Inflammatory disorder
    c. History of allogeneic stem cell transplant within 6 months before apheresis
    d. History of autologous stem cell transplant less than or equal to 12 weeks before apheresis
    e. Known active, or prior history of central nervous system (CNS) involvement or exhibits clinical signs of meningeal involvement of multiple myeloma

BSWHP considers only ONE treatment per lifetime is medically necessary as repeat administration of ciltacabtagene autoleucel (Carvykti™) is experimental and investigational because the effectiveness of this strategy has not been established.

BSWHP considers ciltacabtagene autoleucel (Carvykti™) for the treatment of all other indications to be experimental and investigational because the effectiveness of this strategy has not been established.

All requests will be reviewed by a clinical pharmacist and medical director.

BACKGROUND:

Chimeric antigen receptor (CAR) T cells and genetically engineered T-cell receptor (TCR T) cells are manufactured by collecting lymphocytes from a patient or donor and modifying them using gene transfer techniques. Viral vectors are introduced that express cell receptors that are highly specific for tumor antigens. CAR T and TCR T cells are then infused back into the patient where they direct a targeted immune response to cancerous tissue. CAR T cells express a hybrid receptor with an extracellular single-chain antibody fragment, a transmembrane domain, and at least 1 intracellular signaling domain. CAR T cells are most often used to treat hematological malignancies.

Multiple myeloma (MM) is a rare hematologic cancer arising from plasma cells in the bone marrow. Malignant plasma cells produce abnormal monoclonal paraproteins that cause organ damage. According to the American Cancer Society (ACS), an estimated 34,920 new cases of MM will be diagnosed, and 12,410 people will die from the disease in the U.S. in 2021. The median age at diagnosis is 69 years, and almost all cases of MM (95%) are diagnosed after the cancer has metastasized. The treatment landscape for MM has evolved over the past 15 years, delivering many new options for improved management of the disease. Despite these advances, MM remains incurable. Almost all patients eventually relapse and develop relapsed/refractory MM (RRMM). The overall 5-year survival rate for MM is 53.9%.

The U.S. Food and Drug Administration (FDA) approved ciltacabtagene autoleucel (Carvykti™) on February 28, 2022, which is 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. The boxed warning includes information that ciltacabtagene is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) because of the risk of cytokine release syndrome (CRS), neurologic toxicities, hemophagocytic lymphohistiocytosis/macrophage activation syndrome (HLH/MAS), prolonged and recurrent cytopenia, and secondary hematological malignancies

The FDA approval of ciltacabtagene was supported by results from the Phase 1b/2 CARTITUDE-1 trial, in which a single treatment of ciltacabtagene was administered to 97 patients with RRMM who had received a median of six prior treatment regimens, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody. An overall response rate (ORR) of 97.9% was demonstrated in the study, with 78.4% of patients achieving a stringent complete response (sCR). At a median of 18 months' follow-up, the median duration of response was 21.8 months. The most common Grade 3 or 4 nonlaboratory adverse reactions were infections-pathogen unspecified (17%), pneumonia (11%), febrile neutropenia (10%), and hypotension (10%). Serious adverse reactions occurred in 55% of patients.

The CARTITUDE-4 trial is a randomized, open-label, multicenter controlled study in patients with RRMM who previously received at least 1 prior line of therapy including a proteasome inhibitor and an immunomodulatory agent. 419 patients were randomized 1:1 to ciltacabtagene or standard therapy. After a median follow-up of 15.9 months, median PFS was not estimable for ciltacabtagene, sCR 65.9%, and ORR 84.6%. PFS rate at 12 months was 75.9% for ciltacabtage. A numerically higher percentage of early deaths occurred in the ciltacabtagene treatment arm (29/208; 14%) compared to control (24/211; 12%). Of the ciltacabtagene deaths, 10 occurred prior to infusion all due to disease progression and 19 after. 3 occurred due to disease progression and 19 due to adverse events, the most common being infection. The most common Grade 3 or 4 nonlaboratory adverse reactions (≥20%) included pyrexia, CRS, hypogammaglobulinemia, musculoskeletal pain, fatigue, diarrhea, upper respiratory tract infection, viral infections, headache, hypotension, and nausea. Serious adverse reactions occurred in 34% of patients.

CODES:

Important note: *Due to the wide range of applicable diagnosis codes and potential changes to codes, an inclusive list may not be presented, but the following codes may apply. Inclusion of a code in this section does not guarantee that it will be reimbursed, and patient must meet the criteria set forth in the policy language.*

CPT Codes:	0540T - Chimeric antigen receptor T cell (CAR-T) therapy; CAR-T cell administration, autologous 96409 - Chemotherapy administration; intravenous, push technique, single or initial substance/drug 96413 - Chemotherapy administration; intravenous infusion technique; up to 1 hour, single or initial substance/drug

HCPCS Codes:	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
ICD10 codes:	C90.00 Multiple myeloma not having achieved remission C90.01 Multiple myeloma in relapse Z51.12 Encounter for antineoplastic immunotherapy
ICD10 Not covered:	

POLICY HISTORY:

Status	Date	Action
New	05/26/2022	New policy
Updated	10/27/2022	Removed language with CMS LCD since NCD applies. Updated HCPCS code. Removed Texas Mandate HB1584 language from main policy section as the policy is compliant. Minor formatting update.
Reviewed	10/09/2023	Updated HCPCS code section. Applied new layout and format.
Updated	06/10/2024	Updated criteria for 2nd line therapy and background
Updated	06/09/2025	Updated beginning note to align with standard language, Updated criteria #1-4 language to align with standard language, Added “Ciltacabtagene will be used as monotherapy”, Updated treatment center criteria to attestation only, Updated criteria to include examples of immunomodulators/proteasome inhibitors/BCMA targeted therapy, Removed cardiac conditions/LVEF/cumulative dose of corticosteroids exclusion criteria, Updated ending note section to algin with business entity changes, Updated drug name in background.

REFERENCES:

The following scientific references were utilized in the formulation of this medical policy. BSWHP will continue to review clinical evidence related to this policy and may modify it at a later date based upon the evolution of the published clinical evidence. Should additional scientific studies become available, and they are not included in the list, please forward the reference(s) to BSWHP so the information can be reviewed by the Medical Coverage Policy Committee (MCPC) and the Quality Improvement Committee (QIC) to determine if a modification of the policy is in order.

1. Carvykti (Ciltacabtagene autoleucel) [prescribing information]. Horsham, PA: Janssen Biotech, Inc.; April 2024.
2. U.S. National Library of Medicine. A Study of JNJ-68284528, a Chimeric Antigen Receptor T Cell (CAR-T) Therapy Directed Against B-Cell Maturation Antigen (BCMA) in Participants With Relapsed or Refractory Multiple Myeloma (CARTITUDE-1). Available at https://clinicaltrials.gov/ct2/show/NCT03548207. Accessed on April 12, 2022.
3. Almåsbak H, Aarvak T, Vemuri MC. CAR T cell therapy: a game changer in cancer treatment. J Immunol Res. 2016;2016:5474602.

4. American Cancer Society. Key Statistics About Multiple Myeloma. Available at: https://www.cancer.org/cancer/multiple-myeloma/about/key-statistics.html. Accessed April 12, 2022.
5. Brentjens RJ. Are chimeric antigen receptor T cells ready for prime time? Clin Adv Hematol Oncol. 2016;14(1):17-19.
6. Children's Hospital of Philadelphia (CHOP). What to Expect: CAR T-cell Therapy Process. 2017. Available at: http://www.chop.edu/centers-programs/cancer-immunotherapy-program/your-experience.
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8. Harris DT, Kranz DM. Adoptive T cell therapies: a comparison of T cell receptors and chimeric antigen receptors. Trends Pharmacol Sci. 2016;37(3):220-230.
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11. Leukemia and Lymphoma Society (LLS). Chimeric Antigen Receptor (CAR) T-Cell Therapy. 2017. Available at: https://www.lls.org/treatment/types-of-treatment/immunotherapy/chimeric-antigen-receptor-car-t-cell-therapy. Accessed April 12, 2022.
12. Locke FL, Davila ML. Regulatory challenges and considerations for the clinical application of CAR-T cell anti-cancer therapy. Expert Opin Biol Ther. 2017;17(6):659-661.
13. Maus MV, Nikiforow S. The why, what, and how of the new fact standards for immune effector cells. J Immunother Cancer. 2017;5:36.
14. NIH National Cancer Institute. Cancer Stat Facts: Myeloma. Available at: https://seer.cancer.gov/statfacts/html/mulmy.html. Accessed April 12, 2022.
15. San-Miguel, Jesús et al. "Cilta-cel or Standard Care in Lenalidomide-Refractory Multiple Myeloma." The New England journal of medicine vol. 389,4 (2023): 335-347. doi:10.1056/NEJMoa2303379
16. Ye B, Stary CM, Gao Q, et al. Genetically modified T-cell-based adoptive immunotherapy in hematological malignancies. J Immunol Res. 2017;2017:5210459.

***Note**:*
Health Maintenance Organization (HMO) products are offered through Scott and White Health Plan dba Baylor Scott & White Health Plan, and Scott & White Care Plans dba Baylor Scott & White Care Plan. Insured PPO and EPO products are offered through Baylor Scott & White Insurance Company. Scott and White Health Plan dba Baylor Scott & White Health Plan serves as a third-party administrator for self-funded employer-sponsored plans. Baylor Scott & White Care Plan and Baylor Scott & White Insurance Company are wholly owned subsidiaries of Scott and White Health Plan. These companies are referred to collectively in this document as Baylor Scott & White Health Plan.

RightCare STAR Medicaid is offered through Scott and White Health Plan in the Central Texas Medicaid Rural Service Area (MRSA); FirstCare STAR is offered through SHA LLC dba FirstCare Health Plans (FirstCare) in the Lubbock and West MRSAs; and FirstCare CHIP is offered through FirstCare in the Lubbock Service Area.