MEDICAL COVERAGE POLICY	
SERVICE:	**Ciltacabtagene autoleucel (Carvykti™)**
Policy Number:	**291**
Effective Date:	**1/1/2024**
Last Review:	**10/09/2023**
Next Review:	**10/09/2024**

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.

BSWHP may consider **ciltacabtagene autoleucel (Carvykti™)** medically necessary when the following criteria are met:

1. The member has a diagnosis relapsed or refractory multiple myeloma (RRMM); **AND**
2. The member is ≥ 18 years of age; **AND**
3. Member diagnosed by a hematologist or oncologist; **AND**
4. One-time, single administration treatment**; AND**
5. Member will be using ciltacabtagene autoleucel at a REMS-certified healthcare facility; **AND**
6. Member has an Eastern Cooperative Oncology Group (ECOG) performance status between 0 and 1; **AND**
7. Member has adequate bone marrow, renal, hepatic, and cardiac function; **AND**
8. Member has relapsed or refractory disease and received four or more prior lines of systemic therapy including:
    a. Immunomodulatory agent
    b. Proteasome inhibitor
    c. Anti-CD38 monoclonal antibody

    AND
9. Member has or will receive lymphodepleting chemotherapy regimen: cyclophosphamide 300 mg/m^2 intravenously (IV) and fludarabine 30 mg/m^2 IV daily for 3 days.
    a. Administer ciltacabtagene autoleucel infusion 2 to 4 days after the completion of the lymphodepleting chemotherapy regimen.

    AND

10. Member will NOT be treated with more than 1×10^8 CAR-positive viable T cells per single-dose infusion; **AND**
11. The individual has NOT previously been treated with CAR-T cell therapy; **AND**
12. The individual has NOT received any therapy that is targeted to B-cell maturation antigen (BCMA); **AND**
13. The 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. 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
    f. Left ventricular ejection fraction (LVEF) less than 45% (scan performed ≤ 8 weeks of apheresis)

    AND
14. The member has NOT received a cumulative dose of corticosteroids equivalent to >= 70 mg of prednisone within the 7 days prior to apheresis; **AND**
15. The member does NOT have known active, or prior history of central nervous system (CNS) involvement or exhibits clinical signs of meningeal involvement of multiple myeloma; **AND**
16. Member has been assessed by a hematologist/oncologist to be an appropriate candidate for apheresis

BSWHP considers repeat administration of **ciltacabtagene autoleucel** experimental and investigational because the effectiveness of this strategy has not been established.

BSWHP considers **ciltacabtagene autoleucel** to be experimental and investigational for all other indications.

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 autoleucel 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), and prolonged cytopenia.

The FDA approval of ciltacabtagene autoleucel (Carvykti™) was supported by results from the Phase 1b/2 CARTITUDE-1 trial, in which a single treatment of ciltacabtagene autoleucel 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 of 97.9% was demonstrated in the study, with 78.4% of patients achieving a stringent complete response. 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.

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.

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 make modifications 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 2022.
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.
7. Fitzgerald JC, Weiss SL, Maude SL, et al. Cytokine release syndrome after chimeric antigen receptor T cell therapy for acute lymphoblastic leukemia. Crit Care Med. 2017;45(2):e124-e131.
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.

9. Hettle R, Corbett M, Hinde S, et al. The assessment and appraisal of regenerative medicines and cell therapy products: an exploration of methods for review, economic evaluation and appraisal. Health Technol Assess. 2017;21(7):1-204.
10. Ikeda H. T-cell adoptive immunotherapy using tumor-infiltrating T cells and genetically engineered TCR-T cells. Int Immunol. 2016;28(7):349-353.
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. 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 plans are offered through Scott and White Health Plan in the Central Managed Care Service Area (MRSA) and STAR and CHIP plans are offered through SHA LLC dba FirstCare Health Plans (FirstCare) in the Lubbock and West MRSAs.