MEDICAL COVERAGE POLICY	
SERVICE:	Ciltacabtagene autoleucel (Carvykti™)
Policy Number:	**298**
Effective Date:	**12/01/2022**
Last Review:	**10/27/2022**
Next Review Date:	**10/27/2023**

Important note
Unless otherwise indicated, this policy will apply to all lines of business.
Even though this policy may indicate that a particular service or supply may be considered medically necessary and thus covered, this conclusion is not based upon the terms of your particular benefit plan. Each benefit plan contains its own specific provisions for coverage and exclusions. Not all benefits that are determined to be medically necessary will be covered benefits under the terms of your benefit plan. You need to consult the Evidence of Coverage (EOC) or Summary Plan Description (SPD) to determine if there are any exclusions or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and your plan of benefits, the provisions of your benefits plan will govern. However, applicable state mandates will take precedence with respect to fully insured plans and self-funded non-ERISA (e.g., government, school boards, church) plans. Unless otherwise specifically excluded, Federal mandates will apply to all plans. With respect to Medicare-linked plan members, this policy will apply unless there are Medicare policies that provide differing coverage rules, in which case Medicare coverage rules supersede guidelines in this policy. Medicare-linked plan policies will only apply to benefits paid for under Medicare rules, and not to any other health benefit plan benefits. CMS's Coverage Issues Manual can be found on the CMS website. Similarly, for Medicaid-linked plans, the Texas Medicaid Provider Procedures Manual (TMPPM) supersedes coverage guidelines in this policy where applicable.

SERVICE: Ciltacabtagene autoleucel (Carvykti™)

PRIOR AUTHORIZATION: Required.

POLICY:

For Medicaid plans, please confirm coverage as outlined in the Texas Medicaid TMPPM. Texas Mandate HB1584 is applicable for Medicaid plans.

For Medicare plans, please refer to appropriate Medicare NCD (National Coverage Determination).

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.

OVERVIEW:

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.

Important note:
CODES: 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
CPT Not Covered:	
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 C9399 Unclassified drugs or biologicals J9999 Not otherwise classified, antineoplastic drugs
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:	

CMS: NCD 110.24 - Chimeric Antigen Receptor (CAR) T-cell Therapy: Medicare covers autologous treatment for cancer with T-cells expressing at least one chimeric antigen receptor (CAR) when administered at healthcare facilities enrolled in the FDA risk evaluation and mitigation strategies

(REMS) and used for a medically accepted indication as defined at Social Security Act section 1861(t)(2) -i.e., is used for either an FDA-approved indication (according to the FDA-approved label for that product), or for other uses when the product has been FDA-approved and the use is supported in one or more CMS-approved compendia.
Effective date: 08/07/2019. Implementation date: 09/20/2021

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.

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 2022.
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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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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.
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