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/m² intravenously (IV) and fludarabine 30 mg/m² IV daily for 3 days.
   a. Administer ciltacabtagene autoleucel infusion 2 to 4 days after the completion of the lymphodepleting chemotherapy regimen.
10. Member will NOT be treated with more than $1 \times 10^8$ 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 $\geq 70$ 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.

<table>
<thead>
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<th>CPT Codes</th>
<th>Description</th>
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<tr>
<td>0540T</td>
<td>Chimeric antigen receptor T cell (CAR-T) therapy; CAR-T cell administration, autologous</td>
</tr>
<tr>
<td>96409</td>
<td>Chemotherapy administration; intravenous, push technique, single or initial substance/drug</td>
</tr>
<tr>
<td>96413</td>
<td>Chemotherapy administration; intravenous infusion technique; up to 1 hour, single or initial substance/drug</td>
</tr>
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</table>
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

HCPCS Codes:

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<tr>
<td>Q2056</td>
<td>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</td>
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ICD10 codes:

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<td>C90.00</td>
<td>Multiple myeloma not having achieved remission</td>
</tr>
<tr>
<td>C90.01</td>
<td>Multiple myeloma in relapse</td>
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<td>Z51.12</td>
<td>Encounter for antineoplastic immunotherapy</td>
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ICD10 Not covered:

POLICY HISTORY:

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<td>05/26/2022</td>
<td>New policy</td>
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<tr>
<td>Updated</td>
<td>10/09/2023</td>
<td>Updated HCPCS code. Removed Texas Mandate HB1584 language from main policy section as the policy is compliant. Minor formatting update.</td>
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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.
MEDICAL COVERAGE POLICY

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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 MRSA.