Blue Cross Blue Shield Blue Care Network of Michigan

Nonprofit corporations and independent licensees of the Blue Cross and Blue Shield Association

Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

Effective Date: 06/06/2024

Carvykti™ (ciltacabtagene autoleucel)

HCPCS: Q2056

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. FDA approved age
   b. FDA approved indication
   c. Prescribed by an oncologist
   d. Treatment of patients with relapsed or refractory multiple myeloma after at least 1 prior lines of therapy
   e. Patients must have been treated with all of the following:
      i. An immunomodulatory agent
      ii. A proteasome inhibitor
   f. Must have active disease defined by at least one of the following:
      i. Serum M-protein greater or equal to 1.0 g/dL
      ii. Urine M-protein greater or equal to 200 mg/24 h
      iii. Serum free light chain (FLC) assay greater or equal to 10 mg/dL provided the serum FLC ratio is abnormal
   g. Must be refractory to lenalidomide defined as failure to achieve minimal response or progression on or within 60 days of completing lenalidomide therapy
   h. Patients must meet all of the following
      i. ECOG performance status of 0 - 2
      ii. No known central nervous system involvement with myeloma as determined by appropriate testing
      iii. No HIV infection; hepatitis B or C virus infection permitted only if viral load undetectable
      iv. No infection that is uncontrolled or requires IV or long-term oral antimicrobial therapy
      v. Creatinine clearance greater than 30 mL/min
      vi. Alanine aminotransferase less than 5 times upper limit of normal
      vii. Left ventricular ejection fraction greater than 40%
      viii. Platelets greater than 50,000/mm^3
      ix. No second malignancies in addition to myeloma if the second malignancy has required therapy in the last 3 years or is not in complete remission
      x. No myocardial infarction, cardiac angioplasty or stenting, unstable angina, or New York Heart Association Class II or greater congestive heart failure events within 6 months
      xi. No thromboembolic events within 6 months

xii. No pulmonary disease requiring oxygen dependence or pulmonary disease such as idiopathic pulmonary fibrosis, organizing pneumonia (eg, bronchiolitis obliterans), drug-induced pneumonitis, idiopathic pneumonitis, or evidence of active pneumonitis per chest computed tomography (CT) scan at screening

xiii. No clinically significant CNS pathology such as epilepsy, seizure, paresis, aphasia, stroke, severe brain injuries, dementia, Parkinson's disease, cerebellar disease, organic brain syndrome, or psychosis

i. Have not received prior treatment with any CAR-T therapy despite indication or any other genetically-modified T-cell therapy or are being considered for treatment with any other genetically-modified T-cell therapy

j. The requesting physician attests to providing clinical outcome information within the Audaire Health™ provider portal as requested by BCBSM

k. If new diagnoses are FDA approved, coverage will be determined based on the FDA approved indication on a case by case basis until fully evaluated by the BCBSM Pharmacy and Therapeutics Committee

l. Trial and failure, intolerance, or a contraindication to the preferred products as specified in the BCBS/BCN medical utilization management drug list

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limits: Align with FDA recommended dosing
   b. Authorization Period: 3 months with the allowance of only one dose per lifetime
   c. Renewal Criteria: Not applicable as no further authorization will be provided

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- CAR-T therapy is a type of treatment the utilizes the body's own immune system to fight cancer. T-cells are collected from the patient via apheresis and are genetically engineered in the laboratory to produce chimeric antigen receptors on the cell surface, allowing the T-cells to recognize an antigen on target cancer cells. Once the tumor cells are identified, they are attacked and killed by the CAR-T therapy.

- CAR-T therapy has not been studied when given following prior treatment with any CAR-T therapy or following any other genetically-modified T-cell therapy.

- Due to the risk of cytokine release syndrome and neurological toxicities, CAR-T therapies are only allowed to be given at treatment centers certified by their REMS programs. CAR-T REMS programs require certified hospitals and their clinics to have on-site, immediate access to tocilizumab and an understanding of how to manage the risks of the associated CAR-T side effects.

- Carvykti 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 an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody.

- Safety and efficacy for use as second-line therapy in relapsed or refractory multiple myeloma that is lenalidomide-refractory was established in the CARTITUDE-4 trial, an open-label, randomized, phase 3 study of 419 patients who received one to three prior lines of therapy, including a proteasome inhibitor (PI) and immunomodulatory agent (IMiD). The study excluded patients with a creatinine clearance of less than or equal to 40 mL/minute and an alanine

aminotransferase greater than or equal to 3 times upper limit of normal. Patients were also excluded if absolute neutrophil count less than 1,000 cells/mm^3 and platelet count less than 75,000/mm^3. Patients were required to have measurable disease. The primary endpoint was progression free survival (PFS). At a median follow-up of 15.9 months, a 74% (HR = 0.26; 95% CI: 0.18, 0.38; p-value < 0.0001) reduction in the risk of disease progression or death was observed in patients randomized to the Carvykti arm compared to standard of care (SOC) treatments. Among patients in the Carvykti arm, median PFS was not reached and in the SOC arm, median PFS was 11.8 months. PFS at 12 months for patients in the Carvykti arm and SOC arm was 76% (95% CI: 69, 81) and 49% (95% CI: 42, 55), respectively. At the data cut-off, patients randomized to the Carvykti arm achieved an 85% overall response rate (ORR) and 73% achieved a complete response (CR) or better. Among patients in the SOC arm, the ORR was 67% and CR or better was 22%.

- Disease should be measured/staged with PET-CT. Focal uptake in nodal and extranodal sites is considered involvement with lymphoma, including spleen, liver, bone, thyroid, and so on. A measurable node must have a longest diameter (LDi) greater than 1.5 cm. A measurable extranodal lesion should have an LDi greater than 1.0 cm. All other lesions (including nodal, extranodal, and assessable disease) should be followed as nonmeasured disease (eg, cutaneous, GI, bone, spleen, liver, kidneys, pleural or pericardial effusions, ascites).

- While use of Carvykti has not been established in patients with a creatinine clearance of less than 40 mL/minute, other CAR-T therapies have been studied in subjects with a creatinine clearance of 30 mL/minute. The National Institute of Health/National Cancer Institute Common Terminology Criteria of Adverse Events (CTCAE) classify grade 2 chronic kidney disease as a creatinine clearance of 30 – 59 mL/minute. As the classification system uses 30 mL/minute as a cutoff for grade 2 disease and data from other CAR-T therapies support their use in these patients, Carvykti should be able to be tolerated in this population. As there is no data to support administration of CAR-T at levels lower than 30 ml/minute, therapy should not be given in patients not meeting the 30 mL/minute threshold.

- While use of Carvykti has not been established in patients with an alanine aminotransferase of greater than 3 times the upper limit of normal (ULN), other CAR-T therapies have been studied in subjects with an alanine aminotransferase of up to 5 times the ULN and the CTCAE recommendations have set 5 times the ULN as the cutoff for grade 2 adverse reactions. As the classification system uses 5 times the ULN and other CAR-T therapies have data supporting use in this patient population, Carvykti should be tolerated in these patients as well. As there is no data to support administration of CAR-T at levels higher than 5 times the ULN, therapy should not be given to patients not meeting that threshold.

- The CTCAE recommendations set the grade 2 cutoff for left ventricular ejection fraction (LVEF) at 40%. While Carvykti has only been studied in patients with a LVEF greater than or equal to 45%, there is data from other CAR-T therapies to support use in those with a LVEF of 40% of greater. Therefore, Carvykti should be tolerated in these patients as well. There is no data supporting use at LVEF levels less than 40%.

- The Audaire Health™ platform is a provider portal that is used to capture clinical outcome information for patients on select high-cost treatments, such as gene and cellular therapies. If a patient meets medical necessity as defined by this policy and is approved for treatment, the requesting physician must attest to providing clinical outcome information within the Audaire Health™ provider portal at the requested cadence.

References:

1. Carvykti [prescribing information]. Horsham, PA: Janssen Biotech, Inc.; April 2024.
2. 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. Lancet. 2021 Jul 24; 398 (10297): 314 - 24.
3. 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. Lancet. 2021 June 24. Available at: http://dx.doi.org/10.1016/S0140-6736(21)00933-8. Accessed on March 2, 2022.
4. National Comprehensive Cancer Network. Multiple myeloma (Version 3.2024). 2024 March 8. Available at: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed on April 9, 2024.
5. U.S. Department of Health and Human Services. Common terminology criteria for adverse events (Version 5.0). 2017 Nov 27. Available at: https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_8.5x11.pdf. Accessed on July 6, 2022.
6. Clinicaltrials.gov. A study comparing JNJ-68284528, a CAR-T therapy directed against B-cell maturation antigen (BCMA), versus pomalidomide, bortezomib and dexamethasone (PVd) or daratumumab, pomalidomide and dexamethasone (DPd) in participants with relapsed and lenalidomide-refractory multiple myeloma (CARTITUDE-4) (NCT04181827). Available at: https://clinicaltrials.gov/study/NCT04181827. Accessed on December 18, 2023.
7. Janssen. Carvykti (ciltacabtagene autoleucel) reduces risk of disease progression or death by 74 percent in earlier-line multiple myeloma treatment in the landmark phase 3 CARTITUDE-4 study. 2023 June 5. Available at: https://www.janssen.com/carvyktir-ciltacabtagene-autoleucel-reduces-risk-disease-progression-or-death-74-percent-earlier. Accessed on December 18, 2023.

<table>
<tr><th colspan="3">Policy History</th></tr>
<tr><th>#</th><th>Date</th><th>Change Description</th></tr>
<tr><td>1.6</td><td>Effective Date: 06/06/2024</td><td>Updated to include the new indication for use as second-line therapy for relapsed or lenalidomide-refractory multiple myeloma</td></tr>
<tr><td>1.5</td><td>Effective Date: 02/08/2024</td><td>Updated to include preliminary criteria for use as second-line therapy for relapsed or lenalidomide-refractory multiple myeloma</td></tr>
<tr><td>1.4</td><td>Effective Date: 06/08/2023</td><td>Updated to require physicians provide clinical outcomes data using the Audaire Health platform</td></tr>
<tr><td>1.3</td><td>Effective Date: 08/04/2022</td><td>Updated to align criteria across all CAR-T policies</td></tr>
<tr><td>1.2</td><td>Effective Date: 04/14/2022</td><td>New Policy</td></tr>
<tr><td>1.1</td><td>Effective Date: 03/24/2022</td><td>UM medical management system update for BCBSM and BCN
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** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*

Blue Cross Blue Shield/Blue Care Network of Michigan
Medication Authorization Request Form

Blue Cross Blue Shield Blue Care Network of Michigan

Nonprofit corporations and independent licensees of the Blue Cross and Blue Shield Association

This form is to be used by participating physicians to obtain coverage for **drugs covered under the medical benefit**. For commercial members only, please complete this form and submit via fax to 1-877-325-5979. If you have any questions regarding this process, please contact BCBSM Provider Relations and Servicing or the Medical Drug Helpdesk at 1-800-437-3803 for assistance.

PATIENT INFORMATION	PHYSICIAN INFORMATION
Name	**Name**
ID Number	**Specialty**
D.O.B. ☐Male ☐Female	**Address**
Diagnosis	**City /State/Zip**
Drug Name	**Phone/Fax: P**: ( ) - **F**: ( ) -
Dose and Quantity	**NPI**
Directions	**Contact Person**
Date of Service(s)	**Contact Person Phone / Ext.**

STEP 1: DISEASE STATE INFORMATION

1. Is this request for: ☐ Initiation ☐ Continuation *Date patient started therapy:* _____
2. Administered by patient or a medical professional? ☐ patient (self) ☐ health care professional (physician, nurse, etc.)
3. Site of administration? ☐ Provider office/Home infusion ☐ Other: _____
   ☐ Hospital outpatient facility (go to #4) *Reason for Hospital Outpatient administration:* _____
   ☐ Hospital inpatient facility for Car-T therapy only (for example: Kymriah, Yescarta, or Tecartus) (go to #5)
4. Please specify location of administration if hospital outpatient infusion: _____
5. Please specify location of administration if hospital inpatient infusion: _____
6. Please provide the NPI number for the place of administration: _____
7. **Initiation AND Continuation of therapy:**
   a. What is the patient's diagnosis? _____
   b. What other medication has the patient received for their condition? Please list_____
      i. Please describe the response to previous therapies:
      _____
   c. Will the patient be receiving any other treatment for the listed condition while on this medication? Please list:
      _____
   d. Please list any labs values important for diagnosing or monitoring this patient's condition:
      _____
8. **Continuation of therapy:**
   a. Has the patient progressed while on this medication? ☐ yes ☐ no
   b. How has the patient's condition changed while on this medication?
      ☐ Improved: Please describe: _____
      ☐ Stable: please describe: _____
      ☐ Worsened; Please describe: _____
      ☐ Other; Please describe: _____

Chart notes are required for the processing of all requests. Please add any other supporting medical information necessary for our review **(required)**

Coverage will not be provided if the prescribing physician's signature and date are not reflected on this document.

☐ Request for expedited review: I certify that applying the standard review time frame may seriously jeopardize the life or health of the member or the member's ability to regain maximum function

Physician's Name **Physician Signature** **Date**

Step 2: Checklist	☐ Form Completely Filled Out ☐ Provide chart notes	☐ Attach test results
Step 3: Submit	**By Fax: BCBSM Specialty Pharmacy Mailbox 1-877-325-5979**	**By Mail: BCBSM Specialty Pharmacy Program P.O. Box 312320, Detroit, MI 48231-2320**

7/26/2018, 9/18/2018; 1/31/2020; 3/17/2020; 8/9/2021