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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: 02/08/2024

Carvykti™ (ciltacabtagene autoleucl)

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 4 prior lines of therapy
 - e. Patients must have been treated with all of the following:
 - i. An immunomodulatory agent
 - ii. A proteasome inhibitor
 - iii. An anti-CD38 antibody
 - 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. 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/mm³
 - 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

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- 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
 - h. 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
 - i. The requesting physician attests to providing clinical outcome information within the Audaire Health™ provider portal as requested by BCBSM
 - j. 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
 - k. 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 that 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 were established in the CARTITUDE-1 trial, a phase 1b/2, open-label, single-arm, multicenter trial of 97 adult patients with relapsed or refractory multiple myeloma who previously received at least 3 prior lines of therapy including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody. The study excluded patients with an ECOG score of 2 or greater, a creatinine clearance of less than or equal to 40

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mL/minute, alanine aminotransferase greater than or equal to 3 times upper limit of normal, and left ventricular ejection fraction less than 45%. Patients were also excluded if absolute neutrophil count less than 750 cells/mm³ and platelet count less than 50,000/mm³. Patients were required to have measurable disease and could not have active infections or a second malignancy that required therapy within the last 3 years. The primary endpoints included overall response rate (ORR), complete response (CR), and duration of response (DOR). The ORR was 98% (95% CI: 92.7, 99.7) with a stringent complete response rate (sCR) in 83% (95% CI: 68.8, 86.1) of patients. Responses were rapid and durable with a median time to response of 1.0 month (range 0.9 - 5.8; 80.4% ≤ 1.0 month) and median time to complete response or better was 1.8 months (range 0.9 - 12.5; 74.1% ≤ 3.0 months) with responses deepening over time. Median duration of response was not reached (95% CI: 15.9, NE), neither was progression-free survival. The 12-month progression-free rate was 77% (95% CI: 66.0, 84.3) and overall survival rate was 89%.

- 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% or 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.; February 2023.
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

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1b/2 open-label study. Lancet. 2021 June 24. Available at: [http://dx.doi.org/10.1016/S0140-6736\(21\)00933-8](http://dx.doi.org/10.1016/S0140-6736(21)00933-8). Accessed on March 2, 2022.

4. National Comprehensive Cancer Network. Multiple myeloma (Version 2.2024). 2023 Nov 1. Available at: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed on December 18, 2023.
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.

Policy History												
#	Date	Change Description										
1.5	Effective Date: 02/08/2024	Updated to include preliminary criteria for use as second-line therapy for relapsed or lenalidomide-refractory multiple myeloma										
1.4	Effective Date: 06/08/2023	Updated to require physicians provide clinical outcomes data using the Audaire Health platform										
1.3	Effective Date: 08/04/2022	Updated to align criteria across all CAR-T policies										
1.2	Effective Date: 04/14/2022	New Policy										
1.1	Effective Date: 03/24/2022	UM medical management system update for BCBSM and BCN <table border="1" data-bbox="483 1108 1365 1325" style="margin-left: 20px;"> <thead> <tr> <th>Line of Business</th> <th>PA Required in Medical Management System (Yes/No)</th> </tr> </thead> <tbody> <tr> <td>BCBS</td> <td>Yes</td> </tr> <tr> <td>BCN</td> <td>Yes</td> </tr> <tr> <td>MAPPO</td> <td>Yes</td> </tr> <tr> <td>BCNA</td> <td>Yes</td> </tr> </tbody> </table>	Line of Business	PA Required in Medical Management System (Yes/No)	BCBS	Yes	BCN	Yes	MAPPO	Yes	BCNA	Yes
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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>.

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