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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

Breyanzi® (lisocabtagene maraleucel)

HCPCS: Q2054

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 indications
 - b. FDA approved age
 - c. Prescribed by on in consultation with an oncologist
 - d. Treatment of patients with relapsed or refractory Non-Hodgkin's lymphoma of the following subtypes:
 - i. Diffuse large B-cell lymphoma (DLBCL)
 - ii. Primary mediastinal B-cell lymphoma (PMBCL)
 - iii. Follicular lymphoma, grade 3B
 - e. Received ≥ 2 lines of chemotherapy, including rituximab and anthracycline
OR
 - f. Refractory disease or relapse within 12 months of first-line anti-CD20 and anthracycline therapy
OR
 - g. Refractory disease to first-line chemoimmunotherapy or relapse after first-line therapy and are not eligible for hematopoietic stem cell transplantation (HSCT) due to comorbidities or age
 - h. Patients must meet all of the following
 - i. ECOG performance status of 0 - 2
 - ii. Creatinine clearance greater than 30 mL/min
 - iii. Alanine aminotransferase less than 5 times the upper limit of normal
 - iv. Left ventricular ejection fraction greater than 40%
 - v. No known active CNS involvement by primary malignancy (secondary CNS involvement is allowed)
 - vi. No history of another primary malignancy that has not been in remission for at least 2 years prior to consideration of CAR-T therapy
 - vii. No infection that is uncontrolled or requires IV or long-term oral antimicrobial therapy
 - viii. No HIV infection; hepatitis B or C virus infection permitted only if viral load undetectable
 - ix. No presence of graft-vs-host disease (GVHD)
 - 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
 - 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. Only to be administered at certified bone marrow/stem cell transplant centers
 - k. Trial and failure, intolerance, or a contraindication to the preferred products as listed in the BCBSM/BCN utilization management medical drug list
 - l. The requesting physician attests to providing clinical outcome information within the Audaire Health™ provider portal as requested by BCBSM
 - m. 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
- 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.
- Breyanzi is indicated for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified (including DLBCL arising from indolent lymphoma), high-grade B-cell lymphoma, primary mediastinal large B-cell lymphoma, and follicular lymphoma grade 3B. Breyanzi is not indicated for the treatment of patients with primary central nervous system lymphoma.

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- Safety and efficacy as third-line therapy were established in the TRANSCEND trial, an open-label, multicenter, single-arm study of 268 patients with relapsed or refractory large B-cell non-Hodgkin lymphoma. Subjects must have been treated with an anthracycline and rituximab (or other CD20-targeted agent) and have relapsed or refractory disease after at least 2 lines of systemic therapy or after allogeneic HSCT. For patients who received previous CD19-targeted therapy, CD19-positive lymphoma confirmed on a biopsy had to be confirmed since completing the prior CD19-targeted therapy. Patients were excluded from the study if they had an ECOG performance status of greater than 2, a creatinine clearance less than 30 mL/min, alanine aminotransferase greater than 5 times the upper limit of normal, left ventricular ejection fraction less than 40%, active CNS involvement by primary malignancy, history of another primary malignancy that has not been in remission for at least 2 years prior to consideration of CAR-T therapy, had active infection, or the presence of graft-vs-host disease. The primary endpoints were complete response (CR) rate and duration of response (DOR). Seventy-three percent of patients achieved a response (95% CI: 67% - 80%), including 54% who experienced complete response (95% CI: 47% - 61%) and 19% who achieved a partial response (95% CI: 14% - 26%). Median duration of response was 16.7 months in all responders (95% CI: 5.3 – not reached (NR)). For patients who achieved a CR, median duration of response was not reached (95% CI: 16.7 – NR). For patients achieving a PR, median duration of response was 1.4 months (95% CI: 1.1 – 2.2). Of 104 patients treated with Breyanzi who achieved a CR, 65% had remission lasting at least six months and 62% had remission lasting at least nine months.
- Safety and efficacy as second-line therapy were established in the TRANSFORM trial, an randomized, open-label, parallel-group, multicenter study of 184 patients with relapsed or refractory large B-cell non-Hodgkin lymphoma. Subjects must have been treated with an anthracycline and rituximab (or other CD20-targeted agent) and have relapsed or refractory disease after first-line therapy. Patients were excluded from the study if they had an ECOG performance status of greater than 1, a creatinine clearance less than 45 mL/min, alanine aminotransferase greater than 5 times the upper limit of normal, left ventricular ejection fraction less than 40%, active CNS involvement by primary malignancy, history of another primary malignancy that has not been in remission for at least 2 years prior to consideration of CAR-T therapy, or had active infection. The primary endpoint was event free survival (EFS). Breyanzi significantly improved median EFS compared with standard therapy (10.1 months vs. 2.3 months; HR = 0.34; p-value < 0.0001) and also significantly increased median progression free survival (PFS) (14.8 months vs. 5.7 months; HR = 0.4; p-value = 0.0001). Sixty-six percent of patients assigned Breyanzi achieved complete response to therapy compared with 39% of patients assigned standard treatment (p-value < 0.0001).
- 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).
- 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:

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Policy History												
#	Date	Change Description										
1.8	Effective Date: 02/08/2024	Updated to add preliminary criteria for use in relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL)										
1.7	Effective Date: 06/08/2023	Updated to require physicians provide clinical outcomes data using the Audaire Health platform										
1.6	Effective Date: 08/04/2022	Updated to align criteria across all CAR-T policies and include new indication for use as second-line therapy in DLBCL										
1.5	Effective Date: 06/09/2022	Updated to add preliminary criteria for use as second-line therapy in DLBCL										
1.4	Effective Date: 04/14/2022	Updated to remove CD19 requirement as NCCN guidelines state CAR-T can work without being positive for CD19 disease										
1.3	Effective Date: 08/12/2021	New policy - this policy replaces previously approved criteria that was embedded in Chimeric Antigen Receptor-T Cell Class policy which will be retired										
1.2	Effective Date: 03/15/2021	UM medical management system update for BCBS <table border="1" data-bbox="483 680 1365 890"> <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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1.1	Effective Date: 03/08/2021	UM medical management system update for BCN <table border="1" data-bbox="483 963 1365 1184"> <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>No</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	No	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>.