Blue Cross Blue Shield Blue Care Network of Michigan

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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: 08/12/2021

Breyanzi® (lisocabtagene maraleucel)

FDA approval: 02/05/2021
HCPCS: J3590
Benefit: Medical

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. Relapsed following autologous hematopoietic stem cell transplantation (HSCT)
   g. Documentation of CD 19 tumor expression
   h. Patients must not have the following
      i. ECOG performance status of greater than 2
      ii. Creatinine clearance < 30 mL/min
      iii. Alanine aminotransferase > 5 times the upper limit of normal
      iv. Left ventricular ejection fraction < 40%
      v. Active CNS involvement by primary malignancy (secondary CNS involvement is allowed) as determined by appropriate testing. Examples include: MRI and/or CSF analysis (including cytology plus molecular analysis, for example FISH)
      vi. History of another primary malignancy that has not been in remission for at least 2 years prior to consideration of CAR-T therapy
      vii. Active infection including hepatitis B, hepatitis C, HIV, or systemic fungal, bacterial, or viral infection
      viii. Presence of graft-vs-host disease (GVHD)

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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 prescriber needs to submit documentation of response to Breyanzi within 3 months following therapy as a follow-up to the prior approval request
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: 2 months with the allowance of only one dose per lifetime
   c. Renewal Criteria: Not applicable as no further authorization will be provided

***Note: Coverage 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.

Therapeutic considerations:

A. **FDA approved indication / Diagnosis**

**Please refer to most recent prescribing information.*

B. **Background Information**

a. 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.

b. 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.

c. 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.

d. 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.

e. Safety and efficacy 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

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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.

f. 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).

C. **Efficacy**

**Please refer to most recent prescribing information.*

D. **Medication Safety Considerations**

**Please refer to most recent prescribing information.*

E. **Dosing and administration**

**Please refer to most recent prescribing information.*

F. **How supplied**

**Please refer to most recent prescribing information.*

References:

1. Breyanzi [prescribing information]. Bothell, WA: Bristol Myers Squibb; February 2021.
2. National Comprehensive Cancer Network. B-cell lymphomas (Version 4.2021). 2021 May 5. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed on June 18, 2021.
3. Lee DW et al. Current concepts in the diagnosis and management of cytokine release syndrome. Blood. 2014 Jul 10; 124 (2): 188 - 195.
4. Abramson JS, Palomba ML, Gordon LI, et al. Lisocabtagene maraleucel for patients with relapsed or refractory large B-cell lymphomas (TRANSCEND NHL 001): a multicenter seamless design study. Lancet. 2020 Sep 19; 396 (10254): 839 – 52.

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5. Clinicaltrials.gov. A phase 1, multicenter, open-label study of JCAR017, CD19-targeted chimeric antigen receptor (CAR) t-cells, for relapsed and refractory (R/R) b-cell non-hodgkin lymphoma (NHL) (NCT02631044). Available at: https://clinicaltrials.gov/ct2/show/NCT02631044. Accessed on February 8, 2021.
6. Cheson BD, Fisher RI, Barrington SF, et al. Recommendations for initial evaluation, staging, and response assessment of hodgkin and non-hodgkin lymphoma: the lugano classification. J Clin Oncol. 2014 Sep 20; 32 (27): 3059 – 68.

<table>
<tr><th colspan="3">Policy History</th></tr>
<tr><th>#</th><th>Date</th><th>Change Description</th></tr>
<tr><td>1.3</td><td>Effective Date: 08/12/2021</td><td>New policy - this policy replaces previously approved criteria that was embedded in Chimeric Antigen Receptor-T Cell Class policy which will be retired</td></tr>
<tr><td>1.2</td><td>Effective Date: 03/15/2021</td><td>UM medical management system update for BCN
<table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><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></table></td></tr>
<tr><td>1.1</td><td>Effective Date: 03/08/2021</td><td>UM medical management system update for BCN
<table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><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></table></td></tr>
<tr><td>1.0</td><td>Effective Date: 02/11/2021</td><td>UM medical management system update for BCNA and MAPPO
<table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>No</td></tr><tr><td>BCN</td><td>No</td></tr><tr><td>MAPPO</td><td>Yes</td></tr><tr><td>BCNA</td><td>Yes</td></tr></table></td></tr>
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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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