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: 10/03/2024

Epkinly™ (epcoritamab-bysp)

HCPCS: J9321

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 indication
   b. FDA approved age
   c. Treatment of patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) and high grade B-cell lymphoma after at least 2 prior lines of therapy, one of which is an anti-CD20 antibody containing regimen
   d. Treatment of patients with relapsed or refractory follicular lymphoma (FL) after two or more prior lines of systemic therapy one of which is an anti-CD20 antibody containing regimen
   e. Have not received prior treatment with Epkinly or any other bispecific CD20-directed CD3 T-cell engager therapy
   f. Trial and failure, contraindication, or intolerance to the preferred drugs as listed in BCBSM/BCN's utilization management medical drug list

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limits: Align with FDA recommended dosing
   b. Authorization Period: Aligns with FDA recommended or guideline supported treatment duration and provided for at least 60 days and up to 6 months at a time
   c. Renewal Criteria: Treatment may be continued until disease progression or until unacceptable toxicity occurs

***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.

This policy and any information contained herein is the property of Blue Cross Blue Shield of Michigan and its subsidiaries, is strictly confidential, and its use is intended for the P&T committee, its members and BCBSM employees for the purpose of coverage determinations.

Background Information:

- Epkinly is a bispecific CD20-directed CD3 T-cell engager indicated for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, including DLBCL arising from indolent lymphoma, and high-grade B-cell lymphoma after two or more lines of systemic therapy and adult patients with relapsed or refractory follicular lymphoma (FL) after two or more lines of systemic therapy.

- Safety and efficacy were evaluated in the nEPCORE NHL-1 study, an open-label, multi-cohort, multicenter, single-arm trial in 157 patients with relapsed or refractory large B-cell lymphoma (LBCL) and 127 patients with relapsed or refractory FL after two or more lines of systemic therapy, which included at least one therapy containing an anti-CD20 monoclonal antibody. Patients were required to have failed at least two prior lines of therapy one of which was an anti-CD20 antibody containing regimen. Subjects also must have either failed prior autologous hematopoietic stem cell transplantation (HSCT) or be ineligible for autologous stem cell transplantation due to comorbidities or age, have CD20 positive disease, measurable disease, and an ECOG score of 0 – 2. Those who had a prior allogenic stem cell transplant were ineligible for study inclusion. Patients were also excluded from the trial if creatinine clearance was greater than 45 mL/min; alanine aminotransferase was less than 3 times the upper limit of normal; they had known active CNS involvement of lymphoma; there was an infection that was uncontrolled or required IV or long-term oral antimicrobial therapy; or they could not have HIV infection or hepatitis B or C virus infection if the viral load was detectable. Those with myocardial infarction, cardiac angioplasty or stenting, unstable angina, or New York Heart Association Class II or greater congestive heart failure events within 6 months of study entry were not enrolled in the trial. The primary outcomes were overall response rate (ORR) and duration of response (DOR). Overall response rate in patients with relapsed or refractory DLBCL was 68% (95% CI: 45, 86), with 45% achieving a complete response. The median time to response was 1.4 months (range: 1 to 8.4 months). Among responders, the median follow-up for DOR was 9.8 months (range: 0.0 to 17.3 months). In those with FL, the OOR was 82% (95% CI: 74.1, 88.2) with 60% achieving a complete response. The median follow-up for DOR was 14.8 months with over half of the patients remaining responsive to treatment.

- Due to the risk of cytokine release syndrome and immune effector cell-associated neurotoxicity syndrome (ICANS), Epkinly should be administered in an inpatient setting during cycle 1, day 15.

- Epkinly has not been studied when given following prior treatment with Epkinly or following any other bispecific CD20-directed CD3 T-cell engager therapy.

References:

1. Epkinly [prescribing information]. Plainsboro, NJ: Genmab US, Inc.; June 2024.
2. Hutchings M, Mous R, Roost Clausen M, et al. Dose escalation of subcutaneous epcoritamab in patients with relapsed or refractory B-cell non-Hodgkin lymphoma: an open-label, phase 1/2 study. Lancet. 2021 Sept 8; 398 (10306): 1157 – 69.
3. National Comprehensive Cancer Network. B-cell lymphomas (Version 2.2024). 2024 April 30. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed on August 8, 2024.

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<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: 10/03/2024</td><td>Updated to remove the following requirements: failure of prior autologous HSCT or be ineligible for autologous stem cell transplantation due to comorbidities or age, measurable disease, ECOG status, kidney function; liver function, no prior allogenic SCT, no known active CNS involvement of lymphoma, no infection that is uncontrolled or requires IV or long-term oral antimicrobial therapy, no HIV infection; hepatitis B or C virus infection permitted only if viral load undetectable, and 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</td></tr>
<tr><td>1.2</td><td>Effective Date: 08/08/2024</td><td>Updated to include the new indication of relapsed or refractory follicular lymphoma and remove the requirement that the disease is CD20 positive</td></tr>
<tr><td>1.1</td><td>Effective Date: 03/01/2024</td><td>UM medical management system update for BCNA, MAPPO, BCN, and BCBS
<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>1.0</td><td>Effective Date: 08/10/2023</td><td>New Policy</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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