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: 08/10/2023

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. Must have either failed prior autologous hematopoietic stem cell transplantation (HSCT) or be ineligible for autologous stem cell transplantation due to comorbidities or age
   e. Patients must meet all of the following
      i. CD20 positive disease
      ii. Disease must be measurable
      iii. ECOG performance status of 0 - 2
      iv. Creatinine clearance greater than 45 mL/min
      v. Hepatic transaminases less than 2 times the upper limit of normal
      vi. No prior allogenic stem cell transplant
      vii. No known active CNS involvement of lymphoma
      viii. No infection that is uncontrolled or requires IV or long-term oral antimicrobial therapy
      ix. No HIV infection; hepatitis B or C virus infection permitted only if viral load undetectable
      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
   f. Have not received prior treatment with Epkinly or any other bispecific CD20-directed CD3 T-cell engager therapy
   g. 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.

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.

- 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) 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 diffuse large B-cell lymphoma 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).

- 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).

- 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.; May 2023.
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 3.2023). 2023 May 11. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed on May 22, 2023.

<table>
<tr><th colspan="3">Policy History</th></tr>
<tr><th>#</th><th>Date</th><th>Change Description</th></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>
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<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.*