STATE OF IOWA DEPARTMENT OF
Health AND Human
SERVICES

Epkinly (epcoritamab-bysp)
PAM–078

Iowa Medicaid Program:	Prior Authorization	**Effective Date:**	10/01/2023
Revision Number:	1	**Last Rev Date:**	07/19/2024
Reviewed By:	Medicaid Medical Director	**Next Rev Date:**	07/18/2025
Approved By:	Medicaid Clinical Advisory Committee	**Approved Date:**	07/19/2024

Overview

Medication:[1]	epcoritamab-bysp
Brand Name:	Epkinly™
Pharmacologic Category:	Antineoplastic; bispecific CD20-directed CD3 T-cell engager
FDA-Approved Indication(s):	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. ➢ This indication is approved under accelerated approval based on response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).
How Supplied:	Single-dose vial containing either 4 mg/0.8 mL or 48 mg/0.8 mL
Dosage and Administration:	Continue Epkinly™ in 28-day cycles until disease progression or unacceptable toxicity. Administer Epkinly™ subcutaneously according to the dosage schedule in Table 1 to reduce the incidence and severity of cytokine release syndrome (CRS).
Benefit Category:	Medical

28-Day Treatment Cycle	Day of Treatment	Epkinly Dose	
Cycle 1	Day 1	Step-up dose 1	0.16 mg
	Day 8	Step-up dose 2	0.8 mg
	Day 15 *	First full dose	48 mg
	Day 22	48 mg	
Cycles 2 and 3	Days 1, 8, 15, and 22	48 mg	
Cycles 4 to 9	Days 1 and 15	48 mg	
Cycle 10 and beyond	Day 1	48 mg	

* Due to the risk of CRS and ICANS, patients should be hospitalized for 24 hours after administration of the Cycle 1, Day 15 dosage of 48 mg.

WARNING: CYTOKINE RELEASE SYNDROME (CRS) and IMMUNE EFFECTOR CELL-ASSOCIATED NEUROTOXICITY SYNDROME (ICANS)

Cytokine release syndrome (CRS), including serious or life-threatening reactions, can occur in patients receiving Epkinly™. Initiate treatment with the Epkinly™ step-up dosing schedule to reduce the incidence and severity of CRS. Withhold Epkinly™ until CRS resolves or permanently discontinue based on severity.

Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS), including life-threatening and fatal reactions, can occur with Epkinly™. Monitor patients for neurological signs or symptoms of ICANS during treatment. Withhold Epkinly™ until ICANS resolves or permanently discontinue based on severity.

Descriptive Narrative

Diffuse large B-cell lymphoma (DLBCL) is the most common histologic subtype of non-Hodgkin lymphoma (NHL) accounting for approximately 25 percent of NHL cases in the developed world. In the United States, the incidence of DLBCL is approximately 7 cases per 100,000 persons per year. Incidence varies by ethnicity, with White Americans having higher rates than Black, Asian, and American Indian or Alaska Native individuals, in order of decreasing incidence. Like most other NHLs, there is a male predominance with approximately 55 percent of cases occurring in men. Incidence increases with age; the median age at presentation is 64 years for patients as a whole but appears to be younger for Black compared with White Americans.[2]

Guidelines

As new and emerging therapies are rapidly coming to market, oncology treatment recommendations and guidelines are constantly changing. To keep up with these changes, the National Comprehensive Cancer Network (NCCN) publishes guidelines which are developed and updated by 60 individual panels, comprising over 1,660 clinicians and oncology researchers from the 31 NCCN Member Institutions.[3]

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) are a work in progress that may be refined as often as new significant data becomes available. To view the most recent and complete version of the guidelines, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

The information referenced at the time of this policy writing/revision is from:

- NCCN Guidelines® for B-Cell Lymphomas (Version 4.2024 – April 30, 2024)[4]

NCCN Guidelines® recommendation(s) for epcoritamab-bysp (Epkinly®)
(1) Classic Follicular Lymphoma A. Third-line and subsequent therapy [a] i. Epcoritamab-bysp: Category 2A, preferred
(2) Diffuse Large B-Cell Lymphoma (DLBCL) A. Bispecific antibody therapy (only after at least 2 lines of systemic therapy; including patients with disease progression after transplant or CAR T-cell therapy) [a] i. Epcoritamab-bysp: Category 2A, treatment option for third-line therapy
(3) Histologic Transformation of Indolent Lymphomas to DLBCL A. T-cell engager therapy (only after at least 2 lines of systemic therapy; including patients with disease progression after transplant or CAR T-cell therapy) i. Epcoritamab-bysp: Category 2A treatment option
[a] Subsequent systemic therapy options include second-line therapy regimens that were not previously given.

NCCN Categories of Evidence and Consensus (all recommendations are category 2A unless otherwise indicated)	
Category 1	Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A	Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B	Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3	Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

NCCN Categories of Preference (all recommendations are considered appropriate)	
Preferred intervention	Interventions that are based on superior efficacy, safety, and evidence; and, when appropriate, affordability.
Other recommended intervention	Other interventions that may be somewhat less efficacious, more toxic, or based on less mature data; or significantly less affordable for similar outcomes.
Useful in certain circumstances	Other interventions that may be used for select patient populations (defined with recommendation).

Eastern Cooperative Oncology Group (ECOG) Performance Status Scale[5]

Developed by the Eastern Cooperative Oncology Group (ECOG), now part of the ECOG-ACRIN Cancer Research Group, and published in 1982, the ECOG Performance Status Scale describes a patient's level of functioning in terms of their ability to care for themself, daily activity, and physical ability (walking, working, etc.). It is used by doctors and researchers to assess how a patient's disease is progressing, how the disease affects the daily living abilities of the patient and determine appropriate treatment and prognosis.

GRADE	ECOG PERFORMANCE STATUS [Synonyms: WHO/Zubrod score]
0	Fully active, able to carry on all pre-disease performance without restriction.
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work.
2	Ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of waking hours.
3	Capable of only limited self-care; confined to bed or chair more than 50% of waking hours.
4	Completely disabled; cannot carry on any self-care; totally confined to bed or chair.
5	Dead.

Criteria

Prior authorization is required.

Epkinly™ is considered medically necessary when **ALL** of the following are met:

1. Diagnosis of one of the following (a or b):
    a. Diffuse large B-cell lymphoma (DLBCL), not otherwise specified, including DLBCL arising from indolent lymphoma; or
    b. High-grade B-cell lymphoma; **AND**
2. Disease is refractory to or has relapsed after 2 or more lines of systemic therapy; **AND**
3. Epkinly™ is prescribed as a single agent; **AND**
4. Member is 18 years of age or older; **AND**
5. Member has an Eastern Cooperative Oncology Group (ECOG) Performance Status of 0, 1, or 2; **AND**
6. Member does not have central nervous system (CNS) involvement of lymphoma; **AND**
7. Prescribed by, or in consultation with, an oncologist; **AND**
8. Request meets one of the following (a or b):
    a. Regimen is prescribed on a 28-day cycle and does not exceed the following (i, ii, and iii):
        i. Cycle 1: Day 1 (step-up dose 1) of 0.16 mg; Day 8 (step-up dose 2) of 0.8 mg; Day 15 (first full dose) of 48 mg; and Day 22, dose of 48 mg; **AND**
        ii. Cycles 2 and 3: 48 mg on Days 1, 8, 15, and 22 of each cycle; **AND**
        iii. Cycles 4 through 9: 48 mg on Days 1 and 15 of each cycle; or
    b. Regimen is supported by clinical practice guidelines (i.e., must be recommended in NCCN Guidelines®). Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Epkinly™ is considered medically necessary for continuation of therapy when **ALL** of the following are met:

1. Member is currently receiving medication through the Iowa Medicaid benefit or has previously met initial approval criteria; **AND**
2. Documentation of positive clinical response to therapy, as demonstrated by tumor response or lack of disease progression, and an acceptable toxicity profile; **AND**
3. Epkinly™ is prescribed as a single agent; **AND**
4. Prescribed by, or in consultation with, an oncologist; **AND**
5. Request meets one of the following (a or b):
    a. Regimen is prescribed on a 28-day cycle and does not exceed the following (i or ii):
        i. Cycles 4 through 9: 48 mg on Days 1 and 15 of each cycle; or
        ii. Cycle 10 and beyond: 48 mg on Day 1 of each cycle; or
    b. Regimen is supported by clinical practice guidelines (i.e., must be recommended in NCCN Guidelines®). Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Approval Duration and Quantity Limits

	Initial Authorization	Subsequent Authorization(s)
Approval Duration	6 months	12 months per authorization
Quantity Limits (28-day cycle)	Cycle 1: One dose each of 0.16 mg and 0.8 mg, and two 48 mg doses Cycles 2 and 3: four 48 mg doses per cycle Cycles 4 to 9: two 48 mg doses per cycle	Cycles 4 to 9: two 48 mg doses per cycle Cycle 10 and beyond: one 48 mg dose per cycle

Coding and Product Information

The following list(s) of codes and product information are provided for reference purposes only and may not be all inclusive. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment, nor does the exclusion of a code imply that its association to the HCPCS code is inappropriate.

HCPCS	Description
C9155	~~Injection, epcoritamab-bysp, 0.16 mg~~ *(effective 10/1/2023 to 12/31/2023)*
J9321	Injection, epcoritamab-bysp, 0.16 mg *(effective 1/1/2024)*

ICD-10	Description
C83.30 – C83.39	Diffuse large B-cell lymphoma

NDC (Strength)	Labeler	Dosage	Pkg Size	Pkg Qty	Units/Pkg
82705-0002-01 (4 mg/0.8 mL)	Genmab US, Inc. (82705)	0.16 mg	1	EA	25
82705-0010-01 (48 mg/0.8 mL)	Genmab US, Inc. (82705)	0.16 mg	1	EA	300

Compliance

1. Should conflict exist between this policy and applicable statute, the applicable statute shall supersede.
2. Federal and State law, as well as contract language, including definitions and specific contract provisions or exclusions, take precedence over medical policy and must be considered first in determining eligibility for coverage.
3. Medical technology is constantly evolving, and Iowa Medicaid reserves the right to review and update medical policy on an annual or as-needed basis.

Medical necessity guidelines have been developed for determining coverage for member benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. Medical necessity guidelines are developed for selected physician-administered medications found to be safe and proven to be effective in a limited, defined population or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. Criteria are revised and updated annually, or more frequently if new evidence becomes available that suggests needed revisions.

References

[1] Epkinly® prescribing information (05/2023). Genmab US, Inc.: Plainsboro, NJ. Available online at: www.epkinlyhcp.com. Accessed May 24, 2024.

[2] Freedman AS, Aster JC. Epidemiology, clinical manifestations, pathologic features, and diagnosis of diffuse large B cell lymphoma. Rosmarin AG, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed May 28, 2024.

[3] National Comprehensive Cancer Network (NCCN). Development and Update of Guidelines. Available online at www.nccn.org. Accessed October 11, 2023.

[4] Referenced from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for B-Cell Lymphomas (v.4.2024 – April 30, 2024). Accessed June 6, 2024. The NCCN Guidelines® are a work in progress that may be refined as often as new significant data becomes available. To view the most recent and complete version of the guidelines, go online to NCCN.org.

[5] Oken M, Creech R, Tormey D, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol. 1982;5:649-655. PMID 7165009.

Development of utilization management criteria may also involve research into other state Medicaid programs, other payer policies, consultation with experts and review by the Medicaid Clinical Advisory Committee (CAC). These sources may not be referenced individually unless they are specifically published and are otherwise applicable to the criteria at issue.

Criteria Change History

Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]	CAC		
Signature			

Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]	CAC		
Signature			

Change Date	Changed By	Description of Change	Version
07/19/2024	CAC	Criteria implementation.	1
Signature William (Bill) Jagiello, DO			

CAC = Medicaid Clinical Advisory Committee