IOWA Health and Human Services

Epkinly (epcoritamab-bysp)
PAM – 078

Iowa Medicaid Program	Prior Authorization	**Effective Date**	10/01/2023
Revision Number	2	**Last Reviewed**	07/18/2025
Reviewed By	Medicaid Medical Director	**Next Review**	07/17/2026
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):	1. Diffuse Large B-Cell Lymphoma and High-Grade B-Cell Lymphoma • 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 (HGBCL) after two or more lines of systemic therapy. 2. Follicular Lymphoma • Adult patients with relapsed or refractory follicular lymphoma (FL) after two or more lines of systemic therapy. ▶ **NEW** indication (FDA-approved 6/26/2024) Accelerated Approval: These indications are approved under accelerated approval based on response rate and durability of response. Continued approval for these indications 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.
- To reduce the incidence and severity of cytokine release syndrome (CRS), administer Epkinly™ subcutaneously according to the step-up dosage schedule in Table 1 for patients with DLBCL or HGBCL, or Table 2 for patients with FL.
- Due to the risk of CRS and immune effector cell-associated neurotoxicity syndrome (ICANS), monitor all patients for signs and symptoms.
  - Patients with DLBCL or HGBCL should be hospitalized for 24 hours after administration of the Cycle 1, Day 15 dosage of 48 mg.

Table 1: 2-step up Schedule (DLBCL, HGBCL)

Cycle of Treatment*	Day of Treatment	Epkinly™ Dose	
Cycle 1	1	step-up dose 1	0.16 mg
	8	step-up dose 2	0.8 mg
	15	first full dose	48 mg
	22	48 mg	
Cycles 2 & 3	1, 8, 15, 22	48 mg	
Cycles 4-9	1 and 15	48 mg	
Cycle 10 and beyond	1	48 mg	

* Cycle = 28 days

Table 2: 3-step up Schedule (FL)

Cycle of Treatment**	Day of Treatment	Epkinly™ Dose	
Cycle 1	1	step-up dose 1	0.16 mg
	8	step-up dose 2	0.8 mg
	15	step-up dose 3	3 mg
	22	first full dose	48 mg
Cycles 2 & 3	1, 8, 15, 22	48 mg	
Cycles 4-9	1 and 15	48 mg	
Cycle 10 and beyond	1	48 mg	

** Cycle = 28 days

Benefit Category:	Medical

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)

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]

Follicular Lymphoma (FL)

Follicular lymphoma (FL) is the second most common subtype of NHL and is the most common of the clinically indolent NHLs (defined as those lymphomas in which survival of the untreated patient is measured in years). The vast majority of patients treated for FL will have an initial response to therapy, with 40 to 80 percent demonstrating a complete response, depending on the initial regimen used. However, conventional therapy for FL is not curative and most of these patients will ultimately develop progressive disease. In addition, less than 10 percent of patients treated with initial chemoimmunotherapy will not respond to treatment (i.e., refractory disease).[3]

In the United States as a whole, the estimated incidence of FL is 3.18 cases per 100,000 people. The incidence is stable over time, but varies, with the incidence in White populations being more than twice that in African and Asian populations. The incidence increases with age; FL most frequently presents in middle-aged individuals and the elderly; the median age at diagnosis is 65 years. Rarely, FL arises in children or adolescents.[4]

Guidelines

The National Comprehensive Cancer Network (NCCN) publishes guidelines for the prevention, diagnosis, and management of malignancies across the continuum of care. The NCCN Guidelines® are a comprehensive set of guidelines detailing the sequential management decisions and interventions that currently apply to 97 percent of cancers affecting patients in the United States. The guidelines are developed and updated by 61 individual panels, comprising over 1,700 clinicians and oncology researchers from the 33 NCCN Member Institutions.

Guidelines are reviewed and updated on a continual basis to ensure that the recommendations take into account the most current evidence. 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.[5,6]

The information referenced at the time of this policy writing/revision is from the NCCN Guidelines® for (note version number and effective date):[7]

- B-Cell Lymphomas (v.2.2025 – February 10, 2025)

Recommendation(s) – Classic Follicular Lymphoma
(1) Third-Line and Subsequent Therapy (subsequent systemic therapy options include second-line therapy regimens that were not previously given) a. Bispecific antibody therapy [a] i. Epcoritamab-bysp: Category 2A, Preferred Regimen

Recommendation(s) – Diffuse Large B-Cell Lymphoma (DLBCL)
(1) Second-Line Therapy (relapsed disease < 12 months or primary refractory disease) a. Non-Candidates for CAR T-Cell Therapy i. Epcoritamab-bysp + GemOx (gemcitabine, oxaliplatin)[a]: Category 2A, Preferred Regimen (2) Second-Line Therapy (relapsed disease > 12 months) a. No Intention to Proceed to Transplant i. Epcoritamab-bysp + GemOx [a]: Category 2A, Preferred Regimen (3) Third-Line and Subsequent Therapy (subsequent systemic therapy options include second-line therapy regimens that were not previously given) a. Bispecific antibody therapy (only after at least two lines of systemic therapy; including patients with disease progression after transplant or CAR T-cell therapy) i. Epcoritamab-bysp [a]: Category 2A, Preferred Regimen

Recommendation(s) – Histologic Transformation of Indolent Lymphomas to DLBCL
(1) Systemic Therapy Regimens – T-cell Engager Therapy a. Bispecific antibody therapy (only after at least two lines of systemic therapy; including patients with disease progression after transplant or CAR T-cell therapy) i. Epcoritamab-bysp [a]: Category 2A Treatment Option

[a] In the setting of CD20-negative lymphomas, the activity of CD3 x CD20 bispecific antibody therapy is unclear. Re-biopsy to confirm CD20 positivity is recommended prior to initiating CD3 x CD20 bispecific antibody therapy.

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 [8]

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 themselves, 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 to 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 housework, 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.

Diffuse Large B-Cell Lymphoma (DLBCL)

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 (0.16 mg); Day 8 – step-up dose 2 (0.8 mg); Day 15 – first full dose (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.

Follicular Lymphoma (FL)

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

1. Diagnosis of follicular 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 (0.16 mg); Day 8 – step-up dose 2 (0.8 mg); Day 15 – step-up dose 3 (3 mg); and Day 22 – first full dose (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

- 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

	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 2 doses of 48 mg Cycles 2 and 3: four 48 mg doses per cycle Cycles 4–9: two 48 mg doses per cycle	Cycles 4–9: two 48 mg doses per cycle Cycle 10 and beyond: one 48 mg dose per cycle

- 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

	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, 0.8 mg, 3 mg, and 48 mg Cycles 2 and 3: four 48 mg doses per cycle Cycles 4–9: two 48 mg doses per cycle	Cycles 4–9: 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
C82.00 – C82.99	Follicular lymphoma
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 the 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 (08/2024). Genmab US, Inc.: Plainsboro, NJ. Available online: www.epkinlyhcp.com. Accessed June 9, 2025.

[2] Aster JC, Herrera AF. Diffuse large B cell lymphoma and other large B cell lymphomas: Presentation, diagnosis, and classification. Rosmarin AG, ed. UpToDate. Waltham, MA: UpToDate, Inc. www.uptodate.com. Accessed June 9, 2025.

[3] Freedman AS, Friedberg JW. Treatment of relapsed or refractory follicular lymphoma. Connor RF, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed March 5, 2025.

[4] Freedman AS, Aster JC. Clinical manifestations, pathologic features, diagnosis, and prognosis of follicular lymphoma. Connor RF, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed March 5, 2025.

[5] National Comprehensive Cancer Network (NCCN). Guidelines Process: About Clinical Practice Guidelines. Available online at www.nccn.org. Accessed July 29, 2024.

[6] National Comprehensive Cancer Network (NCCN). Guidelines Process: Development and Update of Guidelines. Available online at www.nccn.org. Accessed July 29, 2024.

[7] NCCN Clinical Practice Guidelines in Oncology. 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, go online to NCCN.org. NCCN Guidelines® referenced (note version number and effective date):

- B-Cell Lymphomas (v.2.2025 – February 10, 2025)

[8] 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
07/18/2025	CAC	Annual review. Updated Overview table, Descriptive Narrative, and Criteria to include new indication for Follicular Lymphoma (FDA-approved 6/26/2024). Reviewed and updated NCCN Guidelines.	2
Signature William (Bill) Jagiello, DO			
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