

Medical Drug Clinical Criteria

Subject: Epkinly (epcoritamab-bysp)

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Overview

This document addresses the use of Epkinly (epcoritamab-bysp), a T-cell-engaging bispecific antibody is FDA indicated for the treatment of adults 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 (HGBL), after two or more lines of systemic therapies. Epkinly is also FDA indicated in the treatment of adults with relapsed or refractory follicular lymphoma after two or more lines of systemic therapy.

The National Comprehensive Cancer Network® (NCCN) provides recommendations with a category 2A level of evidence for the use of Epkinly in these additional B-cell lymphomas: Post-transplant lymphoproliferative disorders and HIV-related B-Cell Lymphomas.

Epkinly is administered by a subcutaneous injection once every 28 days after initial step-up dosing cycles. Two dosages are available for the step-up dosing 4 mg/0.8 mL vial and a maintenance dose vial of 48 mg/0.8 mL.

Epkinly has a boxed warning for serious or life-threatening cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS).

Definitions and Measures

ECOG or Eastern Cooperative Oncology Group Performance Status: A scale and criteria used by doctors and researchers to assess how an individual's disease is progressing, assess how the disease affects the daily living abilities of the individual, and determine appropriate treatment and prognosis. This scale may also be referred to as the WHO (World Health Organization) or Zubrod score which is based on the following scale:

- 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, for example, 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

Line of Therapy:

- **First-line therapy:** The first or primary treatment for the diagnosis, which may include surgery, chemotherapy, radiation therapy or a combination of these therapies.
- **Second-line therapy:** Treatment given when initial treatment (first-line therapy) is not effective or there is disease progression.
- **Third-line therapy:** Treatment given when both initial (first-line therapy) and subsequent treatment (second-line therapy) are not effective or there is disease progression.

Refractory Disease: Illness or disease that does not respond to treatment.

Relapse or recurrence: After a period of improvement, during which time a disease (for example, cancer) could not be detected, the return of signs and symptoms of illness or disease. For cancer, it may come back to the same place as the original (primary) tumor or to another place in the body.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Epkinly (epcoritamab-bysp)

Requests for Epkinly (epcoritamab-bysp) may be approved if the following criteria are met:

- I. Individual has a diagnosis of one of the following B-Cell Lymphomas:
 - A. CD20+ relapsed or refractory diffuse large B-cell lymphoma (DLBCL), including DLBCL arising from indolent lymphoma; **OR**
 - B. High-grade B-cell lymphoma (HGBL); **OR**
 - C. Post-transplant lymphoproliferative disorders (NCCN 2A); **OR**
 - D. HIV-related B-Cell Lymphomas (NCCN 2A); **OR**
 - E. Classic Follicular lymphoma (Label, NCCN 2A);

AND

- II. Individual has received two or more prior lines of therapy, including at least one anti-CD20 monoclonal antibody; **AND**

III. Individual is using in one of the following ways:

- A. Individual is using Epkinly as a single agent for any of the B-Cell Lymphomas; **OR**
- B. Individual is using Epkinly in combination with gemcitabine and oxaliplatin for DLBCL, High-Grade B-cell lymphoma, HIV-Related B-cell Lymphoma, or PTLD;

III. Individual is using Epkinly as a single agent; **AND**

AND

- IV. Individual has an Eastern Cooperative Oncology Group (ECOG) performance status of 0-2.

Requests for Epkinly (epcoritamab-bysp) may not be approved for the following;

- I. Individual has central nervous system involvement of lymphoma; **OR**
- II. Individual has an ongoing active infection; **OR**
- III. Individual with known impaired T-cell immunity; **OR**
- IV. When the above criteria are not met and for all other indications.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J9321 Injection, epcoritamab-bysp, 0.16 mg [Epkinly]

ICD-10 Diagnosis

B20 Human immunodeficiency virus [HIV] disease
C82.00-C82.99 Follicular lymphoma
C83.30-C83.389 Diffuse large B-cell lymphoma

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C83.398	Diffuse large B-cell lymphoma of other extranodal and solid organ sites
C83.80-C83.89	Other non-follicular lymphoma
C85.10-C85.19	Unspecified B-cell lymphoma
C85.20-C85.29	Mediastinal (thymic) large B-cell lymphoma
D47.Z1	Post-transplant lymphoproliferative disorder (PTLD)

Document History

Revised: 08/15/2025

Document History:

- 08/15/2025 – Annual Review: Clarify NCCN nomenclature for follicular lymphoma (FL) to classic FL. Add NCCN recommendation for combination use with Gem/Ox and Epkinly in DLBCL, High-Grade, HIV-related, and PTLD B-cell lymphomas. Coding Reviewed: Removed ICD-10-CM C83.39. Added ICD-10-CM B20, C83.398, C83.80-C83.89, C85.10-C85.19, C85.20-C85.29, D47.Z1.
- 08/16/2024 – Annual Review: Add 2A recommendations for additional B-cell lymphomas. Add FDA approval for use in relapsed/refractory follicular lymphoma. Coding Reviewed: Add ICD-10-CM C82.00-C82.99.
- 06/12/2023 – Select Review: New criteria document for Epkinly PA. Coding Reviewed: Added HCPCS J3490, J3590, J9999, C9399. All diagnoses pend. Effective 10/1/2023 Added HCPCS C9155. Removed HCPCS C9399. Effective 1/1/2024 Added HCPCS J9321. Added ICD-10-CM C83.30-C83.39. Removed J3490, J3590, J9999, C9155.

References

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2. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
3. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc. Updated periodically.
4. NCCN Clinical Practice Guidelines in Oncology™. © 2025 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: <http://www.nccn.org/index.asp>. Accessed on July 2, 2025.
 - a. B-cell lymphomas. V2.2025. Revised February 10, 2025.

Federal and state laws or requirements, contract language, and Plan utilization management programs or policies may take precedence over the application of this clinical criteria.

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