BlueCross BlueShield
Federal Employee Program
Blue Cross Blue Shield Association
750 9th St NW, Suite 900
Washington, D.C. 20001
1-800-624-5060
Fax 1-877-378-4727

5.21.206

Section:	Prescription Drugs	**Effective Date:**	April 1, 2025
Subsection:	Antineoplastic Agents	**Original Policy Date:**	June 16, 2023
Subject:	Epkinly	**Page:**	1 of 4

Last Review Date: March 7, 2025

Epkinly

Description

Epkinly (epcoritamab-bysp)

Background
Epkinly (epcoritamab-bysp) is a T-cell engaging bispecific antibody that binds to the CD3 receptor expressed on the surface of T-cells and CD20 expressed on the surface of lymphoma cells and healthy B-lineage cells. In vitro, Epkinly activated T-cells, caused the release of proinflammatory cytokines, and induced lysis of B-cells (1).

Regulatory Status
FDA-approved indications: Epkinly is a bispecific CD20-directed CD3 T-cell engager indicated for the treatment of (1):

- 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.
- adult patients with relapsed or refractory follicular lymphoma (FL) after two or more lines of systemic therapy.

Epkinly carries a boxed warning regarding cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS). Treatment should be initiated with a step-up dosing schedule to reduce the risk of CRS. Epkinly should be withheld until CRS resolves or permanently discontinue based on severity. Patients should also be monitored for neurological signs or symptoms of ICANS during treatment (1).

Epkinly also has warnings regarding infections and cytopenias. Complete blood cell counts should be monitored throughout treatment. Prophylactic granulocyte colony-stimulating factor should be administered as applicable (1).

Epkinly may cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential to use effective contraception during treatment with Epkinly and for 4 months after the last dose (1).

The safety and effectiveness of Epkinly in pediatric patients less than 18 years of age have not been established (1).

Related policies
Columvi

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Epkinly may be considered **medically necessary** if the conditions indicated below are met.

Epkinly may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Diffuse large B-cell lymphoma (DLBCL)
2. Diffuse large B-cell lymphoma (DLBCL) arising from indolent lymphoma
3. High-grade B-cell lymphoma
4. Follicular lymphoma

AND ALL of the following:

1. Patient has received two or more lines of systemic therapies
2. Prescriber agrees to monitor for signs and symptoms of cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome

(ICANS)
3. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Epkinly and for 4 months after the last dose

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Diffuse large B-cell lymphoma (DLBCL)
2. Diffuse large B-cell lymphoma (DLBCL) arising from indolent lymphoma
3. High-grade B-cell lymphoma
4. Follicular lymphoma

AND ALL of the following:
1. **NO** disease progression or unacceptable toxicity
2. Prescriber agrees to monitor for signs and symptoms of cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS)
3. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Epkinly and for 4 months after the last dose

Policy Guidelines

Pre - PA Allowance
None

Prior - Approval Limits

Duration 12 months

Prior – Approval *Renewal* Limits
Same as above

Rationale

Summary
Epkinly is indicated for the treatment of diffuse large B-cell lymphoma (DLBCL), not otherwise specified, including DLBCL arising from indolent lymphoma, and high-grade B-cell lymphoma. It is also indicated to treat follicular lymphoma. Epkinly carries a boxed warning regarding cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS). The safety and effectiveness of Epkinly in pediatric patients less than 18 years of age have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Epkinly while maintaining optimal therapeutic outcomes.

References
1. Epkinly [package insert]. Plainsboro, NJ: Genmab US, Inc.; August 2024.
2. NCCN Drugs & Biologics Compendium® Epcoritamab-bysp 2025. National Comprehensive Cancer Network, Inc. Accessed on January 15, 2025.

Policy History

Date	Action
June 2023	Addition to PA
September 2023	Annual review and reference update
December 2023	Annual review and reference update
March 2024	Annual review and reference update
July 2024	Per PI update, added indication of follicular lymphoma
September 2024	Annual review and reference update
March 2025	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 7, 2025 and is effective on April 1, 2025.