UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Oncology (Injectable – Bispecific – CD20-Directed) – Epkinly Utilization Management Medical Policy
- Epkinly™ (epcoritamab-bysp subcutaneous injection – Genmab)

REVIEW DATE: 06/04/2025

OVERVIEW

Epkinly, a bispecific CD20-directed CD3 T-cell engager, is indicated for the treatment of:
- Relapsed or refractory **diffuse large B-cell lymphoma** (DLBCL), not otherwise specified, including DLBCL arising from indolent lymphoma, and high-grade B-cell lymphoma, in adults after two or more lines of systemic therapy.[1]
- Relapsed or refractory follicular lymphoma (FL) in adults after two or more lines of systemic therapy.[1]

Dosing Information

Epkinly is administered by subcutaneous injection.[1] Table 1 and 2 summarize the dosing schedule for Epkinly.

Table 1. Epkinly Dosing Schedule for DLBCL and High-grade B-cell Lymphoma.[1]

Treatment Cycle	Treatment Day	Dose
Cycle 1	Day 1	0.16 mg
	Day 8	0.8 mg
	Day 15	48 mg
	Day 22	48 mg
Cycle 2 and 3	Days 1, 8, 15, 22	48 mg
Cycle 4 to 9	Days 1 and 15	48 mg
Cycle 10+	Day 1	48 mg

Table 2. Epkinly Dosing Schedule for Follicular Lymphoma[1]

Treatment Cycle	Treatment Day	Dose
Cycle 1	Day 1	0.16 mg
	Day 8	0.8 mg
	Day 15	3 mg
	Day 22	48 mg
Cycle 2 and 3	Days 1, 8, 15, 22	48 mg
Cycle 4 to 9	Days 1 and 15	48 mg
Cycle 10+	Day 1	48 mg

Guidelines

Epkinly has been addressed by National Comprehensive Cancer Network. The **B-cell lymphoma** clinical practice guidelines (version 2.2025 – February 10, 2025) recommend Epkinly for the second-line and subsequent treatment of classic follicular lymphoma, DLBCL, histologic transformation of indolent lymphomas to DLBCL, high-grade B-cell lymphomas, human immunodeficiency virus (HIV)-related B-cell lymphomas, and post-transplant lymphoproliferative disorders.[2,3]

Safety

Epkinly has Boxed Warnings for cytokine release syndrome and immune effector cell-associated neurotoxicity syndrome.[1]

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Epkinly. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Epkinly as well as the monitoring required for adverse events and long-term efficacy, approval requires Epkinly to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Epkinly is recommended in those who meet the following criteria:

FDA-Approved Indication

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1. Diffuse Large B-Cell Lymphoma. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
Note: Diffuse large B-cell lymphoma (DLBCL) includes DLBCL not otherwise specified, DLBCL arising from indolent lymphoma, and high-grade B-cell lymphoma.

A) Patient is ≥ 18 years of age; AND

B) Patient has received one or more lines of systemic therapy; AND
Note: Examples of systemic therapy include RCHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone) and DHA (dexamethasone, cytarabine) + platinum (carboplatin, cisplatin, or oxaliplatin) ± rituximab.

C) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimen (A and B):

A) The dose is up to 48 mg administered by subcutaneous injection; AND

B) The agent is given in 28-day cycles that meet the following (i, ii, and iii):

i. Cycles 1, 2, and 3: Maximum of 4 injections; AND

ii. Cycles 4 to 9: Maximum of 2 injections; AND

iii. Cycles 10 and beyond: maximum of 1 injection.

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2. Classic Follicular Lymphoma. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):

A) Patient is ≥ 18 years of age; AND

B) Patient has received two or more lines of systemic therapy; AND
Note: Examples of systemic therapy include CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) plus rituximab or Gazyva (Obinutuzumab intravenous infusion) and CVP (cyclophosphamide, vincristine, prednisone) plus rituximab or Gazyva.

C) The medication is given as a single agent; AND

D) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimen (A and B):

A) The dose is up to 48 mg administered by subcutaneous injection; AND

B) The agent is given in 28-day cycles that meet the following (i, ii, and iii):
- **i.** Cycles 1, 2, and 3: Maximum of 4 injections; AND
- **ii.** Cycles 4 to 9: Maximum of 2 injections; AND
- **iii.** Cycles 10 and beyond: maximum of 1 injection.

Other Uses with Supportive Evidence

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3. Human Immunodeficiency Virus (HIV)-Related B-Cell Lymphomas. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
Note: HIV-related B-cell lymphomas includes HIV-related diffuse large B-cell lymphoma (DLBCL), primary effusion lymphoma, and human herpes virus-8 (HHV8) positive DLBCL.

A) Patient is ≥ 18 years of age; AND

B) Patient has received one or more lines of systemic therapy; AND
Note: Examples of systemic therapy include RCHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone) and R-EPOCH (rituximab, etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin).

C) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimen (A and B):

A) The dose is up to 48 mg administered by subcutaneous injection; AND

B) The agent is given in 28-day cycles that meet the following (i, ii, and iii):
- **i.** Cycles 1, 2, and 3: Maximum of 4 injections; AND
- **ii.** Cycles 4 to 9: Maximum of 2 injections; AND
- **iii.** Cycles 10 and beyond: maximum of 1 injection.

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4. Post-Transplant Lymphoproliferative Disorders. Approve for 1 year if the patient meets ALL of the following (A, B, and C):

A) Patient is ≥ 18 years of age; AND

B) Patient has received one or more lines of systemic therapy; AND
Note: Examples of systemic therapy include RCHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone) and RCEPP (rituximab, cyclophosphamide, etoposide, prednisone, procarbazine).

C) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimen (A and B):

A) The dose is up to 48 mg administered by subcutaneous injection; AND

B) The agent is given in 28-day cycles that meet the following (i, ii, and iii):
- **i.** Cycles 1, 2, and 3: Maximum of 4 injections; AND
- **ii.** Cycles 4 to 9: Maximum of 2 injections; AND
- **iii.** Cycles 10 and beyond: maximum of 1 injection.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Epkinly is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Epkinly subcutaneous injection [prescribing information]. Plainsboro, NJ: Genmab; June 2024.
2. The NCCN Drugs and Biologics Compendium. © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 28, 2025. Search term: epcoritamab.
3. The NCCN B-Cell Lymphomas Clinical Practice Guidelines in Oncology (version 2.2025 – February 10, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 28, 2025.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	06/05/2023
Annual Revision	**Classic Follicular Lymphoma:** Added new condition of approval.	06/12/2024
Update	04/08/2025: The policy name was changed from "Oncology (Injectable) – Epkinly UM Medical Policy" to "Oncology (Injectable – Bispecific – CD20-Directed) – Epkinly UM Medical Policy".	N/A
Annual Revision	**Diffuse Large B-Cell Lymphoma, Human Immunodeficiency Virus (HIV)-Related B-Cell Lymphomas, and Post-Transplant Lymphoproliferative Disorders :** Removed the requirement that the medication is used as a single agent. For the requirement that patient has received two or more lines of systemic therapy, this was changed to one or more lines of systemic therapy. **Classic Follicular Lymphoma:** Moved Classic Follicular Lymphoma from "Other Uses with Supportive Evidence" to "FDA-Approved Indication".	06/04/2025