Clinical Policy: Epcoritamab-bysp (Epkinly)

Reference Number: PA.CP.PHAR.634
Effective Date: 08/2023
Last Review Date: 07/2023

Description
Epcoritamab-bysp (Epkinly™) is a bispecific CD20-directed CD3 T-cell engager.

FDA Approved Indication(s)
Epkinly is 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).

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of PA Health & Wellness® that Epkinly is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Diffuse Large B-Cell Lymphoma (must meet all)**:**

1. Diagnosis of DLBCL (including DLBCL not otherwise specified, DLBCL arising from indolent lymphoma, high-grade B-cell lymphoma, HIV-related DLBCL, primary effusion lymphoma, HHV8-positive DLBCL not otherwise specified, and monomorphic post-transplant lymphoproliferative disorders);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Member has received ≥ 2 lines of systemic therapy (*see Appendix B*);
5. Member had partial response, no response, progressive, relapsed, or refractory disease following prior systemic therapy;
6. If member has histologic transformation of indolent lymphoma to DLBCL, both of the following (a and b):
   a. Member does not intend to proceed to transplant;
   b. Member has received systemic therapy that included an anthracycline-based regimen (*see Appendix B*);
7. Prescribed as a single agent;
8. Request meets one of the following (a or b):
   a. Both of the following (i and ii):
      i. Cycle 1 step-up doses: Dose does not exceed all the following (1, 2, and 3):
         1) 0.16 mg on day 1;
         2) 0.8 mg on day 8;

3) Two 4 mg/0.8 mL vials;

ii. 48 mg per dose (one 48 mg vial; see *Section V* below for details on dosing schedule by cycle);

b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

A. Diffuse Large B-Cell Lymphoma (must meet all)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):
   a. New dose does not exceed 48 mg per dose (one 48 mg vial; see *Section V* below for details on dosing schedule by cycle);
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

DLBCL: diffuse large B-cell lymphoma FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Examples of First-Line Treatment Regimens		
RCHOP (Rituxan® (rituximab), cyclophosphamide, doxorubicin, vincristine, prednisone)	Varies	Varies
RCEPP (Rituxan® (rituximab), cyclophosphamide, etoposide, prednisone, procarbazine)	Varies	Varies
RCDOP (Rituxan® (rituximab), cyclophosphamide, liposomal doxorubicin, vincristine, prednisone)	Varies	Varies
DA-EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicine) + Rituxan® (rituximab)	Varies	Varies
RCEOP (Rituxan® (rituximab), cyclophosphamide, etoposide, vincristine, prednisone)	Varies	Varies
RGCVP (Rituxan®, gemcitabine, cyclophosphamide, vincristine, prednisone)	Varies	Varies
Pola-R-CHP (Polivy™ (polatuzumab vedotin-piiq), rituximab, cyclophosphamide, doxorubicin, prednisone)	Varies	Varies
Examples of Second-Line Treatment Regimens		
Bendeka® (bendamustine) ± Rituxan® (rituximab)	Varies	Varies
CEPP (cyclophosphamide, etoposide, prednisone, procarbazine) ± Rituxan® (rituximab)	Varies	Varies
CEOP (cyclophosphamide, etoposide, vincristine, prednisone) ± Rituxan® (rituximab)	Varies	Varies
DA-EPOCH ± Rituxan® (rituximab)	Varies	Varies
GDP (gemcitabine, dexamethasone, cisplatin) ± Rituxan® (rituximab)	Varies	Varies
gemcitabine, dexamethasone, carboplatin ± Rituxan® (rituximab)	Varies	Varies
GemOx (gemcitabine, oxaliplatin) ± Rituxan® (rituximab)	Varies	Varies
gemcitabine, vinorelbine ± Rituxan® (rituximab)	Varies	Varies
lenalidomide ± Rituxan® (rituximab)	Varies	Varies
Rituxan® (rituximab)	Varies	Varies
DHAP (dexamethasone, cisplatin, cytarabine) ± Rituxan® (rituximab)	Varies	Varies
DHAX (dexamethasone, cytarabine, oxaliplatin) ± Rituxan® (rituximab)	Varies	Varies
ESHAP (etoposide, methylprednisolone, cytarabine, cisplatin) ± Rituxan® (rituximab)	Varies	Varies
ICE (ifosfamide, carboplatin, etoposide) ± Rituxan® (rituximab)	Varies	Varies
MINE (mesna, ifosfamide, mitoxantrone, etoposide) ± Rituxan® (rituximab)	Varies	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): none reported
- Boxed warning(s): cytokine release syndrome and immune effector cell-associated neurotoxicity syndrome

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose

DLBCL	Administer in 28-day cycles until disease progression or unacceptable toxicity:
	• Cycle 1:
	  o Day 1: step-up dose 1 – 0.16 mg SC
	  o Day 8: step-up dose 2 – 0.8 mg SC
	  o Day 15: first full dose – 48 mg SC
	  o Day 22: 48 mg SC
	• Cycle 2 and 3; days 1, 8, 15, 22: 48 mg SC
	• Cycles 4 to 9; days 1 and 15: 48 mg SC
	• Cycle 10 and beyond; day 1: 48 mg SC
		See regimen

VI. Product Availability

Single-dose vials for injection: 4 mg/0.8 mL, 48 mg/0.8 mL

VII. References

1. Epkinly Prescribing Information. Plainsboro, NJ: Genmab US, Inc.; May 2023. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/761324s000lbl.pdf. Accessed June 1, 2023.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed June 5, 2023.
3. National Comprehensive Cancer Network. B-Cell Lymphomas Version 4.2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed June 5, 2023.
4. Thieblemont C, Phillips T, Ghesquieres H, et al. Epcoritamab, a novel, subcutaneous CD3xCD20 bispecific T-cell-engaging antibody, in relapsed or refractory large B-cell lymphoma: Dose expansion in a phase I/II trial. J Clin Oncol. 2023 Apr 20; 41(12): 2238-2247.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9999	Not otherwise classified, antineoplastic drugs
C9399	Unclassified drugs or biologicals

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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