Clinical Policy: Epcoritamab-bysp (Epkinly)

Reference Number: LA.PHAR.634
Effective Date: 12.21.23
Last Review Date: 08.20.24 ~~08.08.23~~ Coding Implications
Line of Business: Medicaid Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Please note: This policy is for medical benefit*

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:

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

These indications are approved under accelerated approval based on response rate and durability of response. Continued approval for ~~this indication~~these indications 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~~/enrollee~~ has met all approval criteria.

It is the policy of Louisiana Healthcare Connections that Epkinly is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of one of the following (a or b):
   ~~1.~~a. 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);
   b. Classic FL (grades 1, 2 and 3A);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
~~4. Request meets one of the following (a or b):~~
~~5.~~4. Member~~/enrollee~~ has received ≥ 2 lines of systemic therapy (*see Appendix B*);

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6.5. Member~~/enrollee~~ had partial response, no response, progressive, relapsed, or refractory disease following prior systemic therapy;
7.6. If member~~/enrollee~~ has histologic transformation of indolent lymphoma to DLBCL, both of the following (a and b):
   a. Member~~/enrollee~~ does not intend to proceed to transplant;
   b. Member~~/enrollee~~ has received systemic therapy that included an anthracycline-based regimen (*see Appendix B*);
8.7. Prescribed as a single agent;
9.8. 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, 3, and ~~3~~4):
         1) 0.16 mg on day 1;
         2) 0.8 mg on day 8;
         3) ~~Two~~For FL: 3 mg on day 15;
         ~~3)~~4) Three 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*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid – 6 months

~~**B.A. Other diagnoses/indications (must meet 1 or 2):**~~
~~If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is~~

B. Other diagnoses/indications (must meet 1 or 2):
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to ~~not yet reflected in this policy, refer to~~ ~~LA~~LA.PMN.255 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: LA.PMN.53 for Medicaid.

II. Continued Therapy

A. ~~Diffuse Large~~ B-Cell ~~Lymphoma~~Lymphomas (must meet all)**:**
1. Currently receiving medication via Louisiana Healthcare Connections benefit, or documentation supports that member~~/enrollee~~ is currently receiving Epkinly for a covered indication and has received this medication for at least 30 days;
2. Member~~/enrollee~~ is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):*

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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*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid – 12 months

~~**B.A. Other diagnoses/indications (must meet 1 or 2):**~~
~~If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to~~

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: LA.PMN.53 for Medicaid.

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 policy – LA.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
DLBCL: diffuse large B-cell lymphoma
FDA: Food and Drug Administration
FL: follicular lymphoma

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
DLBCL: 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

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Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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
DLBCL: 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
FL: Examples of Second-Line Treatment Regimens		
Examples of first-line, second-line and subsequent therapies: • bendamustine + obinutuzumab or rituximab • CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) + obinutuzumab or rituximab • CVP (cyclophosphamide, vincristine, prednisone) + obinutuzumab or rituximab	Varies	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
• Lenalidomide + rituximab *Single-agent examples*: rituximab; Leukeran® (chlorambucil) ± rituximab; cyclophosphamide ± rituximab; Revlimid® (lenalidomide) ± rituximab		

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
FL	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: step-up dose 3 – 3 mg SC o Day 22: first full dose – 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~~June 2024. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/~~2023/761324s000lbl~~2024/761324s003lbl.pdf. Accessed ~~June 1, 2023~~July 3, 2024.

2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed ~~June 5, 2023~~July 3, 2024.
3. National Comprehensive Cancer Network. B-Cell Lymphomas Version ~~4.2023~~2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed ~~June 5, 2023~~July 3, 2024.
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.
5. Linton KM, Vitolo U, Jurczak W, et al. Epcoritamab monotherapy in patients with relapsed or refractory follicular lymphoma (EPCORE NHL-1): a phase 2 cohort of a single-arm, multicentre study. Lancet Haematol. 2024 Jun 13: S2352-3026(24)00166-2.
6. Linton K, Jurczak W, Lugtenburg P, et al. Epcoritamab SC monotherapy leads to deep and durable responses in patients with relapsed or refractory follicular lymphoma: First data disclosure from the Epcore NHL-1 follicular lymphoma dose-expansion cohort [abstract]. Blood 2023;142: Abstract 1655.

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~~J9321	~~Not otherwise classified, antineoplastic drugs~~Injection, epcoritamab-bysp, 0.16 mg
~~C9399~~	~~Unclassified drugs or biologicals~~

Reviews, Revisions, and Approvals	Date	LDH Approval Date
Converted corporate to local policy.	08.08.23	10.24.23
Annual review: added HCPCS code [J9321]; added NCCN Compendium supported off-label use for classic follicular lymphoma; references reviewed and updated; updated FDA approved indications to include follicular lymphoma per updated prescribing information.	08.20.24	

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. Louisiana Healthcare Connections makes no representations and accepts no liability with respect to the content of any external information

used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Louisiana Healthcare Connections administrative policies and procedures.

This clinical policy is effective as of the date determined by Louisiana Healthcare Connections. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. Louisiana Healthcare Connections retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members~~/enrollees~~. This clinical policy is not intended to recommend treatment for members~~/enrollees~~. Members~~/enrollees~~ should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom Louisiana Healthcare Connections has no control or right of control. Providers are not agents or employees of Louisiana Healthcare Connections.

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