Clinical Policy: Loncastuximab Tesirine-lpyl (Zynlonta)

Reference Number: LA.PHAR.539
Effective Date: 09.29.23
Last Review Date: ~~02.01.24~~ 09.16.24 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****

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Description
Loncastuximab tesirine-lpyl (Zynlonta®) is a CD19-directed antibody and alkylating agent conjugate.

FDA Approved Indication(s)
Zynlonta is indicated for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, DLBCL arising from low-grade lymphoma, and high-grade B-cell lymphoma.

This indication is approved under accelerated approval based on overall response rate. 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 Louisiana Healthcare Connections® that Zynlonta is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of large B-cell lymphoma (including DLBCL not otherwise specified, DLBCL arising from low-grade lymphoma, high-grade B-cell lymphoma, ~~AIDS~~HIV-related DLBCL, primary effusion lymphoma, ~~and~~ HHV8-positive DLBCL not otherwise specified, post-transplant lymphoproliferative disorders (PTLD), and histologic transformation of indolent lymphomas related to DLBCL);
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):
   a. Disease is refractory or member has relapsed after ≥ 2 lines of systemic therapy (*see Appendix B*);
   b. Member is not a candidate for transplant and request is for second-line therapy for partial response, no response, or progressive disease following

chemoimmunotherapy in patients with histologic transformation to DLBCL (off-label);
5. Prescribed as a single agent;
6. Request meets one of the following (a or b):*
   a. Dose does not exceed 0.15 mg/kg IV every 3 weeks for 2 cycles, then 0.075 mg/kg every 3 weeks for subsequent cycles;
   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: 6 months

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
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. Large B-Cell Lymphoma (must meet all)**:**
1. Currently receiving medication via Louisiana Healthcare Connections benefit, or documentation supports that member is currently receiving Zynlonta for a covered indication and has received this medication for at least 30 days;
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 0.075 mg/kg every 3 weeks;
   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: 12 months

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
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 policies – 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

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
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
DHA (dexamethasone, cytarabine) + platinum (carboplatin, cisplatin, or oxaliplatin) ± Rituxan® (rituximab)		
DA-EPOCH ± Rituxan® (rituximab)	Varies	Varies
GDP (gemcitabine, dexamethasone, cisplatin) ± Rituxan® (rituximab)	Varies	Varies
gemcitabine, dexamethasone, carboplatin ± Rituxan® (rituximab)	Varies	Varies

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Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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
Polivy® (polatuzumab vedotin) ± bendamustine ± Rituxan® (rituximab)	Varies	Varies
Monjuvi® (tafasitamab-cxix) + lenalidomide	Varies	Varies
Yescarta® (axicabtagene ciloleucel)	Varies	Varies
Breyanzi® (lisocabtagene maraluecel)	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.

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Appendix C: Contraindications/Boxed Warnings
None reported

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Large B-cell lymphoma	0.15 mg/kg IV every 3 weeks for 2 cycles, then 0.075 mg/kg every 3 weeks for subsequent cycles	See regimen

VI. Product Availability

Lyophilized powder for reconstitution in a single-dose vial: 10 mg

VII. References

1. Zynlonta Prescribing Information. Murray Hill, NJ: ADC Therapeutics America; ~~September 2021.~~October 2022. Available at: www.zynlonta.com. Accessed ~~April 7,2023~~May 6, 2024.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed ~~May 19, 2023~~April 26, 2024.

3. National Comprehensive Cancer Network. B-Cell Lymphomas Version ~~3.2023~~2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed May ~~19, 2023~~6, 2024.

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
J9359	Injection, loncastuximab tesirine-lpyl, 0.075 mg

Reviews, Revisions, and Approvals	Date	LDH Approval Date
Policy created	05.01.23	09.28.23
Added Zynlonta prescribed as a single agent per NCCN; references reviewed and updated.	02.01.24	05.10.24
Annual review: revised language from "AIDS-related DLBCL" to "HIV-related DLBCL" to align with NCCN; added post-transplant lymphoproliferative disorders (PTLD) and histologic transformation of indolent lymphomas related to DLBCL as additional examples of large B-cell lymphoma; updated appendix B; references reviewed and updated.	09.16.24	

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. LHCC 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 LHCC administrative policies and procedures.

This clinical policy is effective as of the date determined by LHCC. 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. LHCC 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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