Clinical Policy: Loncastuximab Tesirine-lpyl (Zynlonta)

Reference Number: PA.CP.PHAR.539
Effective Date: 10/2021
Last Review Date: 07/2025

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 PA Health & Wellness® that Zynlonta is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of B-cell lymphoma (including DLBCL not otherwise specified, DLBCL arising from low-grade lymphoma, high-grade B-cell lymphoma, HIV-related DLBCL, primary effusion lymphoma, HHV8-positive DLBCL not otherwise specified, post-transplant lymphoproliferative disorders (PTLD), and histologic transformation of indolent lymphomas to DLBCL, classic follicular lymphoma);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Request meets one of the following (a, b or c):
   a. Disease is partial response, no response, progressive, 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 being used as additional therapy for partial response, no response, or progressive or relapsed disease following chemoimmunotherapy in patients with histologic transformation to DLBCL (off-label);
   c. Other category 1, 2A, or 2B NCCN-recommended uses not listed;
5. Prescribed as a single agent, except histologic transformation of indolent lymphomas to DLBCL or classic follicular lymphoma;
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*).

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. 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.PHARM.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 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*).

Approval duration: 6 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.PHARM.01) applies.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. 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

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 and may require prior authorization.

Commented [ST1]: Zynlonta is also recommended by NCCN (Category 2B) for classic follicular lymphoma as a third-line or subsequent therapy in combination with rituximab for partial response, no response, relapsed, or progressive disease in patients with indications for treatment.

How would requests for treatment of classic follicular lymphoma be reviewed?

Commented [SK2R1]: It would be reviewed with PA.CP.PMN.53, I did add criteria above

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		
CEOP (cyclophosphamide, etoposide, vincristine, prednisone) ± Rituxan® (rituximab)	Varies	Varies
DA-EPOCH ± Rituxan® (rituximab)	Varies	Varies
DHA (dexamethasone, cytarabine) + platinum (carboplatin, cisplatin, or oxaliplatin) ± 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
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.

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; October 2022. Available at: www.zynlonta.com. Accessed April 24, 2025.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed May 16, 2025.
3. National Comprehensive Cancer Network. B-Cell Lymphomas Version 2.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed May 16, 2025.

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
Policy created	10/2021
3Q 2022 annual review: per NCCN compendium, added use in AIDS-related DLBCL, primary effusion lymphoma, and HHV8-positive DLBCL not otherwise specified; added additional off-label use in member that 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; updated HCPCS code; references reviewed and updated.	07/2022
3Q 2023 annual review: added Zynlonta prescribed as a single agent per NCCN; references reviewed and updated.	07/2023
3Q 2024 annual review: updated wording of large B-cell lymphoma diagnosis; updated appendix B; references reviewed and updated.	07/2024
3Q 2025 annual review: no significant changes; references reviewed and updated.	07/2025