

**Clinical Policy: Loncastuximab Tesirine-Ipyl (Zynlonta)**

Reference Number: CP.PHAR.539

Effective Date: 09.01.21

Last Review Date: 08.22

Line of Business: Commercial, HIM, Medicaid

[Coding Implications](#)[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

**Description**

Loncastuximab tesirine-Ipyl (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 health plans affiliated with Centene Corporation<sup>®</sup> 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-related DLBCL, primary effusion lymphoma, and HHV8-positive DLBCL not otherwise specified);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age  $\geq$  18 years;
4. Request meets one of the following (a or b):
  - a. Disease is refractory or member has relapsed after  $\geq$  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. 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:**

**Medicaid/HIM** – 6 months

**Commercial** – 6 months or to the member’s renewal date, whichever is longer

**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 one of the following policies (a or b):
  - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
  - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 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: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

**II. Continued Therapy**

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

1. Currently receiving medication via Centene 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:**

**Medicaid/HIM** – 12 months

**Commercial** – 6 months or to the member’s renewal date, whichever is longer

**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 one of the following policies (a or b):

- a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
  - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 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: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.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 – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.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.*

<b>Drug Name</b>	<b>Dosing Regimen</b>	<b>Dose Limit/ Maximum Dose</b>
<b>Examples of First-Line Treatment Regimens</b>		
RCHOP (Rituxan <sup>®</sup> (rituximab), cyclophosphamide, doxorubicin, vincristine, prednisone)	Varies	Varies
RCEPP (Rituxan <sup>®</sup> (rituximab), cyclophosphamide, etoposide, prednisone, procarbazine)	Varies	Varies
RCDOP (Rituxan <sup>®</sup> (rituximab), cyclophosphamide, liposomal doxorubicin, vincristine, prednisone)	Varies	Varies
DA-EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicine) + Rituxan <sup>®</sup> (rituximab)	Varies	Varies
RCEOP (Rituxan <sup>®</sup> (rituximab), cyclophosphamide, etoposide, vincristine, prednisone)	Varies	Varies
RGCVP (Rituxan <sup>®</sup> , gemcitabine, cyclophosphamide, vincristine, prednisone)	Varies	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
<b>Examples of Second-Line Treatment Regimens</b>		
Bendeka <sup>®</sup> (bendamustine) ± Rituxan <sup>®</sup> (rituximab)	Varies	Varies
CEPP (cyclophosphamide, etoposide, prednisone, procarbazine) ± Rituxan <sup>®</sup> (rituximab)	Varies	Varies
CEOP (cyclophosphamide, etoposide, vincristine, prednisone) ± Rituxan <sup>®</sup> (rituximab)	Varies	Varies
DA-EPOCH ± Rituxan <sup>®</sup> (rituximab)	Varies	Varies
GDP (gemcitabine, dexamethasone, cisplatin) ± Rituxan <sup>®</sup> (rituximab)	Varies	Varies
gemcitabine, dexamethasone, carboplatin ± Rituxan <sup>®</sup> (rituximab)	Varies	Varies
GemOx (gemcitabine, oxaliplatin) ± Rituxan <sup>®</sup> (rituximab)	Varies	Varies
gemcitabine, vinorelbine ± Rituxan <sup>®</sup> (rituximab)	Varies	Varies
lenalidomide ± Rituxan <sup>®</sup> (rituximab)	Varies	Varies
Rituxan <sup>®</sup> (rituximab)	Varies	Varies
DHAP (dexamethasone, cisplatin, cytarabine) ± Rituxan <sup>®</sup> (rituximab)	Varies	Varies
DHAX (dexamethasone, cytarabine, oxaliplatin) ± Rituxan <sup>®</sup> (rituximab)	Varies	Varies
ESHAP (etoposide, methylprednisolone, cytarabine, cisplatin) ± Rituxan <sup>®</sup> (rituximab)	Varies	Varies
ICE (ifosfamide, carboplatin, etoposide) ± Rituxan <sup>®</sup> (rituximab)	Varies	Varies
MINE (mesna, ifosfamide, mitoxantrone, etoposide) ± Rituxan <sup>®</sup> (rituximab)	Varies	Varies

*Therapeutic alternatives are listed as Brand name<sup>®</sup> (generic) when the drug is available by brand name only and generic (Brand name<sup>®</sup>) 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; September 2021. Available at: [www.zynlonta.com](http://www.zynlonta.com). Accessed May 3, 2022.

- National Comprehensive Cancer Network. B-Cell Lymphomas Version 3.2022. Available at: [https://www.nccn.org/professionals/physician\\_gls/pdf/b-cell.pdf](https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf). Accessed May 3, 2022.

**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	P&T Approval Date
Policy created	05.03.21	08.21
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; clarified Commercial approval duration is the longer of 6 months or member’s renewal date; updated HCPCS code; references reviewed and updated.	05.03.22	08.22
Template changes applied to other diagnoses/indications.	10.05.22	

**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. The Health Plan 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. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

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 Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. 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. The Health Plan 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.

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

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**Note:**

**For Medicaid members**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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