Clinical Policy Title:	loncastuximab tesirine-lpyl
Policy Number:	RxA.687
Drug(s) Applied:	Zynlonta™
Original Policy Date:	05/18/2021
Last Review Date:	06/10/2021
Line of Business Policy Applies to:	All lines of business

Background

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

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
loncastuximab tesirine-lpyl (Zynlonta™)	Large B-cell Lymphoma	Intravenous infusion over 30 minutes on Day 1 of each cycle (every 3 weeks). The recommended dosage is: • 0.15 mg/kg every 3 weeks for 2 cycles. • 0.075 mg/kg every 3 weeks for subsequent cycles	0.15 mg/kg IV every 3 weeks; use adjusted body weight for patients with body mass index (BMI) of 35 kg/m^2 or more

Dosage Forms

- Injection: 10 mg of loncastuximab tesirine-lpyl as a lyophilized powder in a single-dose vial for reconstitution and further dilution.

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

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

1. Diagnosis of relapsed or refractory large B-cell lymphoma, including DLBCL not otherwise specified, DLBCL arising from low grade lymphoma, and high-grade B-cell lymphoma;
2. Prescribed by or in consultation with an oncologist or hematologist;

3. Age of 18 years or older;
4. Member has received two or more lines of systemic therapy prior to initiate Zynlonta™;
   **Please refer to clinical guidelines, such as NCCN, for first-line and second-line therapies.*
5. Member has an Eastern Cooperative Oncology Group (ECOG) performance status of 0-1;
6. Dose does not exceed 0.15 mg/kg IV every 3 weeks.
   **Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval Duration
Commercial: 6 months
Medicaid: 6 months

B. B-Cell lymphoma (off-label) (must meet all):

1. Diagnosis of one of the following B-cell lymphoma subtypes (a-e):
   a. Follicular lymphoma (grade 1-2);
   b. Marginal zone lymphoma (i, ii or iii):
      i. Splenic marginal zone lymphoma;
      ii. Gastric MALT lymphoma;
      iii. Nongastric MALT lymphoma (Noncutaneous);
   c. Histologic transformation of marginal zone lymphoma to diffuse large B-cell lymphoma;
   d. High-Grade B-Cell Lymphomas with Translocations of MYC and BCL2 and/or BCL6 (Double/Triple Hit Lymphoma);
2. If the request is for one of the following (a or b);
   a. Follicular lymphoma or Marginal zone lymphoma subtypes: member has prior therapies including ≥ 2 lines of chemoimmunotherapy for indolent or transformed disease (patients has received at least one anthracycline or anthracenedione-based regimen, unless contraindicated);
   b. Histologic transformation of marginal zone lymphoma to diffuse large B-cell lymphoma or high-grade B-Cell lymphomas with translocations of MYC and BCL2 and/or BCL6 (double/triple hit lymphoma): disease is refractory or member has relapsed after ≥ 2 lines of systemic therapy;
3. Prescribed by or in consultation with an oncologist or hematologist;
4. Age 18 years of age or older;
5. Dose is within FDA maximum limit for any FDA-approved indication or 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
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

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

1. Member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to the therapy;
3. Dose does not exceed 0.15 mg/kg IV every 3 weeks.

Approval Duration
Commercial: 6 months

Medicaid: 6 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key

DLBCL: diffuse large B-cell lymphoma
BMI: Body Mass Index
ECOG: Eastern Cooperative Oncology Group
FDA: Food and Drug Administration
NCCN: National Comprehensive Cancer Network

APPENDIX B: Therapeutic Alternatives

Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements

Drug Name	Dosing Regimen	Dose Limit/ Maximum dose
Polivy™ (polatuzumab vedotin-piiq)	1.8 mg/kg as an intravenous infusion over 90 minutes every 21 days for 6 cycles in combination with bendamustine and a rituximab product. Subsequent infusions may be administered over 30 minutes if the previous infusion is tolerated.	1.8 mg/kg IV every 21 days.
Xpovio® (selinexor)	60 mg taken orally on Days 1 and 3 of each week	60 mg PO twice weekly on days 1 and 3
Kymriah® (tisagenlecleucel)	0.6 to 6 x 10^8 CAR-positive viable T cells (non-weight based) intravenously	6.0 x 10^8 CAR-positive viable T cells
Yescarta® (axicabtagene ciloleucel)	Target dose: 2 × 10^6 CAR-positive viable T cells per kg body weight	2 × 10^8 CAR-positive viable T cells
Breyanzi® (lisocabtagene maraleucel)	50 X 106 CAR-positive viable T-cells to 110 X 106 CAR-positive viable T-cells as a single IV dose; administer at 2 to 7 days after the completion of lymphocyte depletion therapy.	110 X 10^6 CAR-positive viable T-cells as a single IV dose.

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

- Boxed Warning(s):
  - None

APPENDIX D: General Information

- ECOG Performance Status
  - Grade 0: Fully active, able to carry on all pre-disease performance without restriction.
  - Grade 1: Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work.
  - Grade 2: Ambulatory and capable of all selfcare but unable to carry out any work activities; up and

about more than 50% of waking hours.
- Grade 3: Capable of only limited selfcare; confined to bed or chair more than 50% of waking hours.
- Grade 4: Completely disabled; cannot carry on any selfcare; totally confined to bed or chair.
- Grade 5: Dead.

References

1. Zynlonta prescribing information. Murray Hill, NJ, ADC Therapeutics; April 2021. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/761196s000lbl.pdf . Accessed May 18, 2021.
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Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	05/18/2021	06/10/2021