

Zynlonta (loncastuximab
tesirine-lpyl)

New Product Slideshow

MPR

Introduction

- **Brand name:** Zynlonta
- **Generic name:** Loncastuximab tesirine-lpyl
- **Pharmacologic class:** CD19-directed antibody + alkylating agent conjugate
- **Strength and Formulation:** 10mg; per vial; lyophilized powder for intravenous (IV) infusion after reconstitution and dilution; preservative-free
- **Manufacturer:** ADC Therapeutics
- **How supplied:** Single-dose vial—1
- **Legal Classification:** Rx

Indication

- Treatment of adults with **relapsed or refractory large B-cell lymphoma** after 2 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.
 - Approved under accelerated approval based on overall response rate.
 - Continued approval may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

Dosage and Administration

- Recommended premedication: dexamethasone 4mg (oral or IV) for 3 days beginning the day prior to treatment (or at least 2hrs prior to treatment).
- Administer Zynlonta by IV infusion over 30 minutes on day 1 of each cycle (every 3 weeks).
 - 0.15mg/kg every 3 weeks for 2 cycles, then 0.075mg/kg every 3 weeks for subsequent cycles.
- For BMI $\geq 35\text{kg/m}^2$, calculate dose based on adjusted body weight (ABW): $\text{ABW in kg} = 35\text{kg/m}^2 \times (\text{height in meters})^2$.
- Monitor infusion site for possible subcutaneous infiltration during administration.

Dosage Delays/Modifications for Adverse Reactions

Neutropenia

- **Absolute neutrophil count $<1 \times 10^9/L$**
 - Withhold Zynlonta until neutrophil counts return to $\geq 1 \times 10^9/L$.

Thrombocytopenia

- **Platelet count $<50,000/mcL$**
 - Withhold Zynlonta until platelet count returns to $\geq 50,000/mcL$.

Dosage Delays/Modifications for Adverse Reactions

Edema or Effusion

- **Grade 2 or higher**

- Withhold Zynlonta until toxicity resolves to grade 1 or less.

Other Adverse Reactions

- **Grade 3 or higher**

- Withhold Zynlonta until toxicity resolves to grade 1 or less.

Dosage Delays/Modifications for Adverse Reactions

- If dosing is delayed by >3 weeks due to toxicity, reduce subsequent doses by 50%.
- If toxicity reoccurs after dose reduction, consider discontinuation.
- If toxicity requires dose reduction after the 2nd dose of 0.15mg/kg (Cycle 2), the patient should receive the dose of 0.075mg/kg for Cycle 3.

Considerations for Specific Populations

- **Pregnancy:** Can cause embryo-fetal harm; exclude status prior to initiation.
- **Nursing mothers:** Not recommended during treatment and for 3 months after last dose.
- **Pediatrics:** Not established.
- **Geriatrics:** No overall differences in safety or effectiveness observed from younger patients.
- **Renal impairment:** Severe renal impairment and end-stage renal disease with or without hemodialysis: not studied.
- **Hepatic impairment:** Mild hepatic impairment (total bilirubin \leq upper limit of normal [ULN] and AST $>$ ULN or total bilirubin $>1-1.5$ x ULN and any AST): monitor. Moderate or severe hepatic impairment (total bilirubin >1.5 x ULN and any AST): not studied.

Warnings and Precautions

- Monitor for new or worsening edema or effusions (see Dosage Delays/Modifications).
- Consider diagnostic imaging if symptoms of pleural or pericardial effusion (eg, dyspnea, chest pain, and/or ascites) develop.
- Risk of severe myelosuppression; monitor CBCs during therapy (see Dosage Delays/Modifications).
 - Consider prophylactic granulocyte colony-stimulating factor administration as applicable.

Warnings and Precautions

- Monitor for infections; withhold if grade 3 or 4 infection occurs until resolved.
- Monitor for new or worsening cutaneous reactions (including photosensitivity); withhold if grade 3 reaction occurs until resolved.
- Advise patients to minimize or avoid exposure to direct natural or artificial sunlight including exposure through glass windows.
 - Consider dermatologic consultation if skin reaction or rash develops.

Warnings and Precautions

- Embryo-fetal toxicity.
- Advise females of reproductive potential to use effective contraception during and for 9 months after last dose.
- Advise males with female partners of reproductive potential to use effective contraception during and for 6 months after last dose.

Adverse Reactions

- **Most common ($\geq 20\%$):** Thrombocytopenia, increased gamma-glutamyltransferase, neutropenia, anemia, hyperglycemia, transaminase elevation, fatigue, hypoalbuminemia, rash, edema, nausea, musculoskeletal pain.
- **Others:** Febrile neutropenia, pneumonia, pleural effusion, sepsis, hyperpigmentation.

Mechanism of Action

- **Loncastuximab tesirine-lpyl** is an antibody-drug conjugate composed of a monoclonal IgG1 kappa antibody component that binds to human CD19, a transmembrane protein expressed on the surface of cells of B-lineage origin.
- Upon binding to CD19, loncastuximab tesirine-lpyl is internalized followed by the release of SG3199, a pyrrolobenzodiazepine dimer cytotoxic alkylating agent.
- The released SG3199 binds to the DNA minor groove and forms highly cytotoxic DNA interstrand crosslinks, subsequently inducing cell death.

Clinical Trials

- Approval was based on data from the open-label, single-arm LOTIS-2 trial (ClinicalTrials.gov: NCT03589469), which evaluated the efficacy and safety of loncastuximab tesirine-lpyl in 145 adult patients with relapsed or refractory DLBCL after at least 2 prior systemic regimens.
- Patients received loncastuximab tesirine-lpyl 0.15mg/kg every 3 weeks for 2 cycles, then 0.075mg/kg every 3 weeks for subsequent cycles until progressive disease or unacceptable toxicity.

Clinical Trials

■ Patient demographics

- Median age: 66 years (range, 23-94).
- 94% with ECOG performance status of 0 to 1.
- 59% Male; 90% White; 3% Black; 2% Asian.
- 88% with DLBCL not otherwise specified, including 20% with DLBCL arising from low grade lymphoma; 8% with high-grade B-cell lymphoma.
- Median number of prior therapies: 3 (range, 2-7); 63% with refractory disease; 17% with prior stem cell transplant; 9% with prior CAR T-cell therapy.

Clinical Trials

- Median follow-up time was 7.3 months (range, 0.3-20.2).
- Overall response rate (ORR) was 48.3% (95% CI, 39.9-56.7).
 - 24.1% (95% CI, 17.4-31.9) achieved complete response.
 - 24.1% (95% CI, 17.4-31.9) achieved partial response.
- Median duration of response was 10.3 months (95% CI, 6.9-not estimable) among responders.
- Median time to response was 1.3 months (range, 1.1-8.1).

New Product Monograph

- For more information view the product monograph available at:

<https://www.empr.com/drug/zynlonta/>