NOW APPROVED!

Dosage & Administration Guide

Zynlonta™

loncastuximab tesirine-lpyl

for injection, for intravenous use

INDICATION AND USAGE

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).

SELECT IMPORTANT SAFETY INFORMATION

ZYNLONTA can cause serious adverse reactions including: effusion and edema, myelosuppression, fatal and serious infections, cutaneous reactions, and embryo-fetal toxicity.

Please see additional Important Safety Information on pages 10-11, and accompanying full Prescribing Information, including Patient Information.

Learn more at www.zynlontahcp.com

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How Supplied

ZYNLONTA for injection is a sterile, preservative-free, white to off-white lyophilized powder, which has a cake-like appearance, supplied in a single-dose vial for reconstitution and further dilution. Each carton (NDC 79952-110-01) contains one 10 mg single-dose vial.

Storage and Handling

Store refrigerated at 2°C to 8°C (36°F to 46°F) in original carton to protect from light. Do not use beyond the expiration date shown on the carton. Do not freeze. Do not shake.

Special Handling

ZYNLONTA is a hazardous drug. Follow applicable special handling and disposal procedures.

Any unused drug product or waste material should be disposed in accordance with local requirements. Please refer to OSHA hazardous drug guidelines at http://www.osha.gov/SLTC/hazardousdrugs/index.html

What's Needed

ZYNLONTA must be administered using a dedicated infusion line equipped with a sterile, non-pyrogenic, low-protein binding in-line or add-on filter (0.2- or 0.22-micron pore size) and catheter.

Extravasation of ZYNLONTA has been associated with irritation, swelling, pain, and/or tissue damage, which may be severe. Monitor the infusion site for possible subcutaneous infiltration during drug administration.

Do not mix ZYNLONTA with or administer as an infusion with other drugs.

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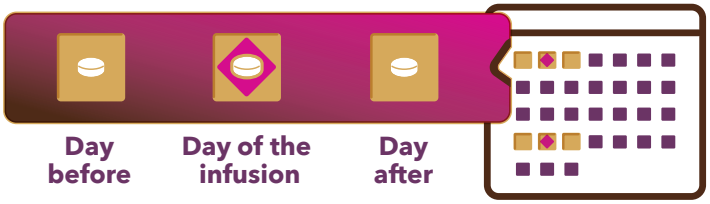
Recommended Dose

0.15 mg/kg every 3 weeks for first 2 cycles ◆ 0.075 mg/kg every 3 weeks for subsequent cycles

Administration

Premedication



Dexamethasone 4 mg (oral or IV) twice daily for 3 days, beginning the day before infusion (unless contraindicated).

If dexamethasone administration does not begin the day before ZYNLONTA, dexamethasone should begin at least 2 hours prior to administration of ZYNLONTA.

Use in Specific Populations

In LOTIS-2, 55% of patients were ≥65 years of age, while 14% were 75 and older. No overall differences in safety or effectiveness were observed between older (>65 years) and younger patients.

No dose adjustment is recommended for patients with mild hepatic impairment (total bilirubin ≤ ULN and AST > ULN, or total bilirubin >1-1.5 × ULN and any AST). Monitor patients with mild hepatic impairment for potential increased incidence of ARs; for grade 3 or higher toxicity ZYNLONTA should be held until toxicity resolves to ≤ grade 1.

ZYNLONTA has not been studied in patients with moderate or severe hepatic impairment (total bilirubin > 1.5 × ULN and any AST).

No clinically significant differences in the pharmacokinetics of ZYNLONTA were observed based on age (20-94 years), sex, race (White vs Black), body weight (42.1 to 160.5 kg), or ECOG status (0-2).

No clinically significant differences in the pharmacokinetics of ZYNLONTA were observed based on mild to moderate renal impairment (CLcr 30 to <90 mL/min). The effect of severe renal impairment (CLcr 15-29 mL/min) and end-stage renal disease is unknown.

Please see Indication and Important Safety Information on pages 10-11, and accompanying full Prescribing Information, including Patient Information.

Dosage Delays and Modifications

Toxicity	Severity[a]	Dose Delay
Hematologic Adverse Reactions		
Neutropenia	Absolute neutrophil count <1 x 10^9/L	Hold until neutrophil counts return to ≥1 × 10^9/L
Thrombocytopenia	Platelet count <50,000 mcL	Hold until platelet count returns to ≥50,000/mcL
Nonhematologic Adverse Reactions		
Edema or effusion	Grade ≥2[a]	Hold until toxicity resolves to ≤ grade 1
Other adverse reactions	Grade ≥3[a]	Hold until toxicity resolves to ≤ grade 1

[a] National Cancer Institute Common Terminology Criteria for Events version 4.0.

If dosing is delayed by more than 3 weeks due to toxicity related to ZYNLONTA, reduce subsequent doses by 50%. If toxicity reoccurs following dose reduction, consider discontinuation.

Note: If toxicity requires dose reduction following the second dose of 0.15 mg/kg (Cycle 2), the patient should receive the dose of 0.075 mg/kg for Cycle 3.

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Preparation

Dose calculation


Calculate

Calculate the dose (mg/kg) and number of vials of ZYNLONTA needed to prepare the infusion solution based on patient weight and prescribed dose. For patients with a body mass index ≥35 kg/m^2, calculate the dose based on an adjusted body weight as follows: 35 kg/m^2×(height in meters)

More than one vial may be needed

Convert the calculated dose (mg) to volume using 5 mg/mL

Reconstitution


Reconstitute

Use appropriate aseptic technique. Use a sterile syringe to slowly inject 2.2 mL of Sterile Water for Injection, USP, with the stream directed toward the inside wall of the 10 mg vial to obtain a final concentration of 5 mg/mL


Swirl

Swirl the vial gently until the powder is completely dissolved.
Do not shake. Do not expose to direct sunlight


Inspect

Visually inspect the solution for particulate matter and discoloration prior to administration. The solution should appear clear to slightly opalescent, colorless to slightly yellow. Do not use if the solution is discolored, cloudy, or contains visible particulates


Store

Use the solution from the vial(s) immediately or store refrigerated at 2°C to 8°C (36°F to 46°F) or room temperature 20°C to 25°C (68°F to 77°F) for up to 4 hours. Do not freeze

Discard unused portion, following special handling and disposal procedures in accordance with local requirements as this product is hazardous

Dilution

Add the calculated dose volume directly into a 50 mL 5% Dextrose Injection, USP, intravenous (IV) infusion bag. **Do not use Sodium Chloride for Injection, USP**

Gently mix by slowly inverting the IV bag. Do not shake

If not used immediately, store the diluted ZYNLONTA solution in the IV bag refrigerated at 2°C to 8°C (36°F to 46°F) for up to 24 hours or at room temperature, 20°C to 25°C (68°F to 77°F), for up to 8 hours. Discard diluted infusion bag if storage time exceeds these limits. Do not freeze

Discard unused portion, following special handling and disposal procedures in accordance with local requirements as this product is hazardous

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Treatment Checklists

Prior to Treatment

- ◇ This document has been reviewed in its entirety
- ◇ The Prescribing Information has been reviewed
  - Dose modifications for treatment-related toxicity *(see section 2.3 of Prescribing Information)*
  - Warnings and precautions *(see section 5 of Prescribing Information)*
- ◇ The patient's infusion schedule has been confirmed
- ◇ The patient's laboratory results have been reviewed per institution's routine monitoring protocol
- ◇ For a female patient with reproductive potential, her pregnancy status has been verified *(see section 8.1 of Prescribing Information)*
- ◇ For a female patient with reproductive potential, she has been advised to use effective contraception during treatment with ZYNLONTA and for 9 months following the last ZYNLONTA dose *(see section 8.3 of Prescribing Information)*
- ◇ For male patients with female partners of reproductive potential, he has been advised to use effective contraception during treatment with ZYNLONTA and for 6 months following the last ZYNLONTA dose
- ◇ Patient has been advised not to breastfeed during treatment and for 3 months after her last dose of ZYNLONTA
- ◇ Patient has been advised to minimize or avoid exposure to direct natural or artificial sunlight during treatment, including exposure through windows. Patients should be instructed to protect skin from exposure to sunlight by wearing sun-protective clothing and/or the use of sunscreen products

Please see Indication and Important Safety Information on pages 10-11, and accompanying full Prescribing Information, including Patient Information.

Treatment Checklists *(continued)*

Administering an Infusion

- ◇ The patient's weight has been confirmed to calculate dosage *(see section 2.4 of Prescribing Information)*
- ◇ Premedication with dexamethasone has been administered
  - Confirm that the patient has taken dexamethasone the day before (if not contraindicated). If the patient has not, dexamethasone should begin at least 2 hours prior to administration of ZYNLONTA
- ◇ After mixing ZYNLONTA, it appears clear to slightly opalescent, colorless to slightly yellow and contains no particulates
- ◇ ZYNLONTA is being administered through a 0.2- or 0.22-micron in-line or add-on filter
- ◇ ZYNLONTA is being infused over 30 minutes

Throughout Treatment

- ◇ The patient is being monitored for effusion and edema *(see section 5.1 of Prescribing Information)*
- ◇ The patient's complete blood counts are being monitored *(see section 5.2 of Prescribing Information)*
- ◇ The patient is being monitored for signs and symptoms of infections *(see section 5.3 of Prescribing Information)*
- ◇ The patient is being monitored for signs and symptoms of new or worsening skin reactions *(see section 5.4 of Prescribing Information)*

Please see Indication and Important Safety Information on pages 10-11, and accompanying full Prescribing Information, including Patient Information.

Treatment Checklists *(continued)*

Patient Counseling/Monitoring

- **Effusion and Edema:** Advise patients to contact their healthcare provider if they experience swelling, weight gain, shortness of breath, or difficult, labored breathing
  - Grade 3 edema occurred in 3% of patients treated with ZYNLONTA (primarily peripheral edema or ascites) and pleural effusion (3%). Grade 3 or 4 pleural effusion occurred in 1%
  - ZYNLONTA should be withheld until the toxicity resolves
  - Consider diagnostic imaging in patients who develop symptoms of pleural effusion or pericardial effusion, such as new or worsened dyspnea, chest pain and/or ascites such as swelling in the abdomen and bloating
- **Myelosuppression:** Advise patients to immediately contact their healthcare provider for a fever of 100.4°F (38°C) or greater or signs or symptoms of bruising or bleeding. Advise patients of the need for periodic monitoring of blood counts
  - Grade 3 or 4 neutropenia occurred in 32% of patients, thrombocytopenia in 20%, and anemia in 12% of patients treated with ZYNLONTA. Grade 4 neutropenia occurred in 21%, and thrombocytopenia in 7%. Febrile neutropenia occurred in 3%
  - Monitor complete blood counts throughout treatment. Cytopenias may require interruption, dose reduction, or discontinuation of ZYNLONTA. Consider prophylactic granulocyte colonystimulating factor administration as applicable

Please see Indication and Important Safety Information on pages 10-11, and accompanying full Prescribing Information, including Patient Information.

Treatment Checklists *(continued)*

Patient Counseling/Monitoring *(continued)*

- **Infections:** Advise patients to contact their healthcare provider if evidence of potential infection such as fever, chills, weakness, and/or difficulty breathing develops
  - Grade 3 or higher infections were seen in 10% of patients, with fatal infections occurring in 2% of patients treated with ZYNLONTA
  - Monitor for any new or worsening signs or symptoms consistent with infection
  - For grade 3 or 4 infection, withhold ZYNLONTA until infection has resolved
- **Cutaneous Reactions:** Advise patients to minimize or avoid exposure to direct natural or artificial sunlight, including sunlight exposure through glass windows. Patients should be instructed to protect skin from exposure to sunlight by wearing sun-protective clothing and/or the use of sunscreen products
  - Grade 3 cutaneous reactions were seen in 4% of patients and included photosensitivity reaction, rash (including exfoliative and maculo-papular), and erythema
  - If a skin reaction or rash develops, dermatologic consultation should be considered

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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).

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Effusion and Edema

Serious effusion and edema occurred in patients treated with ZYNLONTA. Grade 3 edema occurred in 3% (primarily peripheral edema or ascites) and Grade 3 pleural effusion occurred in 3% and Grade 3 or 4 pericardial effusion occurred in 1%.

Monitor patients for new or worsening edema or effusions. Withhold ZYNLONTA for Grade 2 or greater edema or effusion until the toxicity resolves. Consider diagnostic imaging in patients who develop symptoms of pleural effusion or pericardial effusion, such as new or worsened dyspnea, chest pain, and/or ascites such as swelling in the abdomen and bloating. Institute appropriate medical management for edema or effusions.

Myelosuppression

Treatment with ZYNLONTA can cause serious or severe myelosuppression, including neutropenia, thrombocytopenia, and anemia. Grade 3 or 4 neutropenia occurred in 32%, thrombocytopenia in 20%, and anemia in 12% of patients. Grade 4 neutropenia occurred in 21% and thrombocytopenia in 7% of patients. Febrile neutropenia occurred in 3%.

Monitor complete blood counts throughout treatment. Cytopenias may require interruption, dose reduction, or discontinuation of ZYNLONTA. Consider prophylactic granulocyte colony-stimulating factor administration as applicable.

Infections

Fatal and serious infections, including opportunistic infections, occurred in patients treated with ZYNLONTA. Grade 3 or higher infections occurred in 10% of patients, with fatal infections occurring in 2%. The most frequent Grade ≥3 infections included sepsis and pneumonia.

Monitor for any new or worsening signs or symptoms consistent with infection. For Grade 3 or 4 infection, withhold ZYNLONTA until infection has resolved.

Please see accompanying full Prescribing Information, including Patient Information.

Cutaneous Reactions

Serious cutaneous reactions occurred in patients treated with ZYNLONTA. Grade 3 cutaneous reactions occurred in 4% and included photosensitivity reaction, rash (including exfoliative and maculo-papular), and erythema.

Monitor patients for new or worsening cutaneous reactions, including photosensitivity reactions. Withhold ZYNLONTA for severe (Grade 3) cutaneous reactions until resolution. Advise patients to minimize or avoid exposure to direct natural or artificial sunlight including exposure through glass windows. Instruct patients to protect skin from exposure to sunlight by wearing sun-protective clothing and/or the use of sunscreen products. If a skin reaction or rash develops, dermatologic consultation should be considered.

Embryo-Fetal Toxicity

Based on its mechanism of action, ZYNLONTA can cause embryo-fetal harm when administered to a pregnant woman because it contains a genotoxic compound (SG3199) and affects actively dividing cells.

Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with ZYNLONTA and for 9 months after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with ZYNLONTA and for 6 months after the last dose.

ADVERSE REACTIONS

In a pooled safety population of 215 patients (Phase 1 and LOTIS-2), the most common (>20%) adverse reactions, including laboratory abnormalities, were thrombocytopenia, increased gamma-glutamyltransferase, neutropenia, anemia, hyperglycemia, transaminase elevation, fatigue, hypoalbuminemia, rash, edema, nausea, and musculoskeletal pain.

In LOTIS-2, serious adverse reactions occurred in 28% of patients receiving ZYNLONTA. The most common serious adverse reactions that occurred in ≥2% receiving ZYNLONTA were febrile neutropenia, pneumonia, edema, pleural effusion, and sepsis. Fatal adverse reactions occurred in 1%, due to infection.

Permanent treatment discontinuation due to an adverse reaction of ZYNLONTA occurred in 19% of patients. Adverse reactions resulting in permanent discontinuation of ZYNLONTA in ≥2% were gamma-glutamyltransferase increased, edema, and effusion.

Dose reductions due to an adverse reaction of ZYNLONTA occurred in 8% of patients. Adverse reactions resulting in dose reduction of ZYNLONTA in ≥4% was gamma-glutamyltransferase increased.

Dosage interruptions due to an adverse reaction occurred in 49% of patients receiving ZYNLONTA. Adverse reactions leading to interruption of ZYNLONTA in ≥5% were gamma-glutamyltransferase increased, neutropenia, thrombocytopenia, and edema.

You may report side effects to the FDA at (800) FDA-1088 or www.fda.gov/medwatch. You may also report side effects to ADC Therapeutics at 1-855-690-0340.

Please see accompanying full Prescribing Information, including Patient Information.

ADVANCING Patient Support

Offers personalized assistance from ADC Therapeutics

Dedicated case managers can provide the access and reimbursement support and resources to help patients get started and stay on ZYNLONTA.

Coverage Support

Financial Support[a]

Nursing Support

To get started and enroll your patient, visit **ADVANCINGPatientSupport.com** or contact one of our case managers at **1-855-690-0340** Monday-Friday (8 AM–8 PM ET)

[a] Eligibility restrictions apply.

www.zynlontahcp.com

Full Prescribing Information PDF