Adjusted Body Weight Formula

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Indication and Usage

Loncastuximab tesirine (Lonca) 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 the overall response rate. Continued approval for this indication may be contingent upon the verification and description of the clinical benefit in a confirmatory trial(s).

Lonca Dosing and Administration Overview

Recommended Dose

0.15 mg/kg first 2 cycles

0.075 mg/kg subsequent cycles

In LOTIS-2, Lonca was administered until progressive disease or unacceptable toxicity

Premedication

Dexamethasone 4 mg (oral or intravenous) twice daily for 3 days beginning the day before Lonca infusion (unless contraindicated)

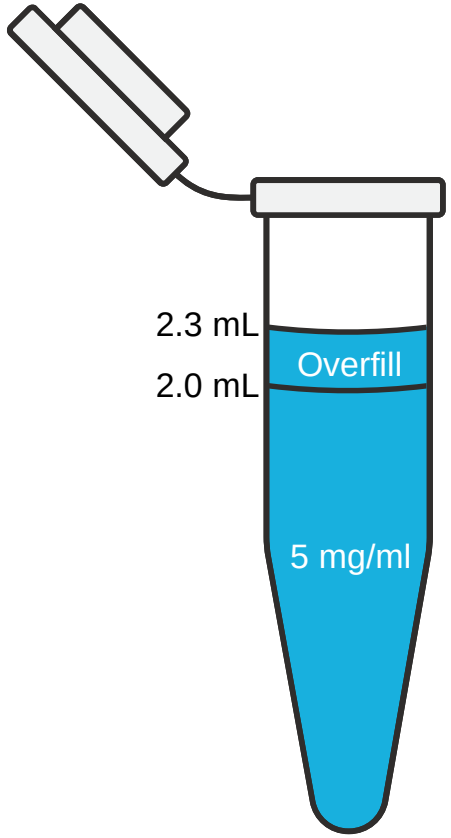
If dexamethasone administration does not begin the day before Lonca, it should begin at least 2 hours prior to Lonca infusion

Administration

Administer by intravenous infusion over 30 minutes every 3 weeks

Lonca Reconstitution and Dilution

- Lonca is supplied as a lyophilized powder in a 10-mg single-dose vial for reconstitution and further dilution[1]
- Reconstitute each Lonca vial using 2.2 mL of sterile water for injection to obtain a final concentration of 5 mg/mL[1]
  - The overfill amount of Lonca is approximately 0.3 mL after reconstitution[2]
  - The overfill ensures that approximately 2 mL of the drug at a concentration of 5 mg/mL can be extracted from the vial
- Withdraw the required volume of the reconstituted solution from the Lonca vial using a sterile syringe[1]
- Add the calculated dose volume of the Lonca solution into a 50-mL infusion bag of 5% dextrose injection, USP[1]



Dosing & Administration

Lonca Dose Calculation

- Calculate the total dose (mg) required based on the patient's weight and prescribed dose
- For patients with a body mass index ≥35 kg/m^2, calculate the dose based on an adjusted body weight (ABW) as follows:
  - ABW in kg = 35 kg/m^2 × (height in meters)^2
- More than one vial may be needed to achieve the calculated dose
- Convert the calculated dose (mg) to volume using 5 mg/mL, which is the concentration of Lonca after reconstitution

Lonca Administration

- Administer Lonca as an infusion over 30 minutes on Day 1 of each cycle (every 3 weeks); recommended dosage:
  - 0.15 mg/kg every 3 weeks for 2 cycles
  - 0.075 mg/kg every 3 weeks for subsequent cycles
- Administer 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
- Do not mix Lonca or administer as an infusion with other drugs

Rationale for Adjusted Body Weight Formula

Rationale for the Adjusted Body Weight Formula

- Body weight-based dosing is associated with a physiological bias, which can lead to higher exposure of therapeutic proteins in patients who are obese and lower exposure in patients with lower body weight[1]
- A BMI threshold of ≥35 kg/m^2 was chosen during clinical development to mitigate the potential toxicity associated with treatment in patients who were obese[1]
  - A BMI of 35 to <40 kg/m^2 is categorized as Class 2 obesity[2]
- The adjusted body weight formula was applied in the phase 2 LOTIS-2 study due to the risk of overdose with weight-normalization administration, cumulative toxicity in patients who received doses >150 µg/kg in the phase 1 study, and the identification of BMI as a significant covariate on Lonca exposure in the population pharmacokinetic modeling of the phase 1 LOTIS-1 study[1,3]

Dosing Calculation Examples

Dosing Calculation Example: Patients with a BMI <35 kg/m^2

Recommended Dose	Patient Body Weight, Height, and BMI	Calculated Lonca Dose	Required Vials (10 mg/vial)	Required Volume of Reconstituted Solution (5 mg/mL)
Cycles 1 and 2 (0.15 mg/kg)	**Weight**: 134 lbs (60.9 kg) **Height**: 5' 1'' (1.55 m) **BMI**: 25.3 kg/m^2	60.9 kg x 0.15 mg/kg = **9.1 mg**	1 vial	$9.1\ \text{mg} \times \frac{1\ \text{mL}}{5\ \text{mg}}$ = **1.82 mL**
Cycle 3 and Beyond (0.075 mg/kg)	**Weight**: 134 lbs (60.9 kg) **Height**: 5' 1'' (1.55 m) **BMI**: 25.3 kg/m^2	60.9 kg x 0.075 mg/kg = **4.6 mg**	1 vial	$4.6\ \text{mg} \times \frac{1\ \text{mL}}{5\ \text{mg}}$ = **0.92 mL**

Dosing Calculation Example: Patients with a BMI ≥35 kg/m^2

Recommended Dose	Patient Body Weight, Height, and BMI	Calculated Lonca Dose*	Required Vials (10 mg/vial)	Required Volume of Reconstituted Solution (5 mg/mL)
Cycles 1 and 2 (0.15 mg/kg)	**Weight**: 250 lbs (113.6 kg) **Height**: 5’ 9’’ (1.75 m) **BMI**: 36.9 kg/m^2	35 kg/m^2 × (1.75 m)^2 = 107.2 kg 107.2 kg x 0.15 mg/kg = **16.1 mg**	2 vials	$16.1\ \text{mg} \times \frac{1\ \text{mL}}{5\ \text{mg}}$ = **3.22 mL**
Cycle 3 and Beyond (0.075 mg/kg)	**Weight**: 250 lbs (113.6 kg) **Height**: 5’ 9’’ (1.75 m) **BMI**: 36.9 kg/m^2	35 kg/m^2 × (1.75 m)^2 = 107.2 kg 107.2 kg x 0.075 mg/kg = **8 mg**	1 vial	$8\ \text{mg} \times \frac{1\ \text{mL}}{5\ \text{mg}}$ = **1.6 mL**

*Patients with a BMI ≥35 kg/m^2 would require using the ABW formula to calculate the Lonca dose.

ABW in kg = 35 kg/m^2 × (height in meters)^2