ZYNLONTA® (loncastuximab tesirine-lpyl) – Stability with Alternative Dilution

Summary

- ZYNLONTA should be administered using a 50 mL infusion bag of 5% Dextrose Injection, United States Pharmacopeia (USP).[4]
- Zynlonta is compatible with dextrose (D5W) as diluent, while it is NOT compatible with normal saline (NS) as diluent.
    - Compatibility studies were conducted for ZYNLONTA use in both intravenous (IV) dextrose (D5W) and normal saline (NS) bags. These evaluations were based on a clinical dose range of 1 mg to 25 mg and 50 mL infusion volume. The range of concentration evaluated was 0.02 mg/mL to 0.5 mg/mL.[2]
- No incompatibility was observed with ZYNLONTA for the following intravenous (IV) material types: polyolefin (PO), partial additive bag (PAB®), polyvinylchloride (PVC). Any commercial product made of similar material is acceptable for ZYNLONTA administration.[1]
- Zynlonta is compatible with 50 mL filled in 100 mL IV bags and 50 mL in 150 mL IV bags.[2]
- To ensure that the patient receives the full dose of ZYNLONTA, the tubing should be flushed with sufficient volume of D5W/glucose according to local institutional guidelines/policies.[3]
- ADC Therapeutics does not recommend the administration of ZYNLONTA outside of what is approved in the US Prescribing Information. See **Relevant Prescribing Information** for additional information.

Non-Clinical Data

Stability in Normal Saline Bags

- Compatibility studies were conducted for ZYNLONTA use in both intravenous (IV) dextrose (D5W) and normal saline (NS) bags. These evaluations were based on a clinical dose range of 1 mg to 25 mg and 50 mL infusion volume. The range of concentration evaluated was 0.02 mg/mL to 0.5 mg/mL.[2]
- Normal saline, and D5W were evaluated as diluent for ZYNLONTA administration. Upon diluting ZYNLONTA in saline, there was immediate loss in conjugated drug to antibody ratio (DAR) species and corresponding increase in unconjugated antibody percentage, resulting in reduction in average DAR.[2]
    - Loss of conjugated DAR species in saline were potentially due to absorption to surface as a result of the high salt concentration. These results indicate that loncastuximab tesirine is not compatible with normal saline.[2]

Stability in Lactated Ringer's 5% Dextrose in Water (D5LRS) or Ringer's Solution

- The stability of ZYNLONTA has not been evaluated with Lactated Ringer's 5% Dextrose in Water or Ringer's solution. Please refer to the Prescribing Information which only recommends the use of 50 mL D5W IV bags.[1,2.]

Stability in IV Bags and In-Line Filters

- Due to multiple administration components for IV preparations, it is not possible to test every component which is commercially available. Materials were tested for compatibility based on material type instead of the individual components. If ZYNLONTA was found to be compatible

with the material type, then the use of all commercially available products in the material category may be used.[1,2.]

- Please see Table 1 below for a summary of material types utilized for compatibility studies. ZYNLONTA compatibility was tested for pH, color/appearance, osmolality, and DAR. No incompatibility was observed for any of the material types, or the components made from these material types.

Table 1: Compatibility in IV Bags, CSTD, In-Line Filters, and Catheters. Adapted from Data on File. ADC Therapeutics.[1]

Dose Concentration (mg/mL)	Diluent	IV Bag	CSTD	In-Line Filter	Catheter
0.02	D5W	PO	PhaSeal™	PES	Vialon
0.02	D5W	PAB®	OnGuard®	PES	Teflon
0.105	D5W	PVC	PhaSeal™	PES	N/A
0.105	D5W	PVC	OnGuard®	PES	N/A
0.105	D5W	PVC	Equashield®	PES	N/A
0.105	D5W	PVC	Chemolock™	PES	N/A
0.5	D5W	PO	Equashield®	PES	Teflon
0.5	D5W	PAB®	Chemolock™	PES	Vialon

CSTD -closed system transfer device; D5W-5% dextrose in water; IV-intravenous; N/A-not applicable; PAB- partial additive bag; PES-polyethersulfone; PO-polyolefin; PVC-polyvinyl chloride

Stability in partial filled 100 mL and 150 mL IV D5W Bags

- Zynlonta is compatible with 50 mL filled in 100 mL IV bags and 50 mL in 150 mL IV bags.[2]
    - Protein recovery was confirmed at both low (0.02 mg/mL) and high (0.5 mg/mL) concentrations in the configuration of 50 mL filled in 100 mL IV bag and 50 mL filled in 150 mL bag respectively.
    - Cytotoxicity was tested at high (0.5 mg/mL) in 50 mL filled in 150 IV bag and at low concentration (0.02 mg/mL) in 50 mL filled in 50 mL bags per the bracketing design of the study.[2]

Flushing of Tubing

- To ensure that the patient receives the full dose of ZYNLONTA, the tubing should be flushed with sufficient volume of D5W/glucose according to local institutional guidelines/policies.[3]
- Because of the potentially low volumes of ZYNLONTA to be added to the IV bag, if a CSTD is used we recommend a flush of D5W/glucose through the injection port to ensure the dose is effectively mixed in the IV bag.[1,2.]

Literature Search

- A PubMed biomedical literature search conducted on February 28, 2025, yielded no further relevant information regarding alternative dilution with ZYNLONTA.

Relevant Prescribing Information

Section 2: Dosage and Administration[4]

2.4: Reconstitution and Administration Instructions

Dilution in Infusion Bag

- Withdraw the required volume of reconstituted solution from the ZYNLONTA vial using a sterile syringe. Discard any unused portion left in the vial.
- Add the calculated dose volume of ZYNLONTA solution into a 50 mL infusion bag of **5% Dextrose Injection, USP**.
- Gently mix the intravenous bag by slowly inverting the bag. Do not shake.
- If not used immediately, store the diluted ZYNLONTA infusion solution 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. No incompatibilities have been observed between ZYNLONTA and intravenous infusion bags with product-contacting materials of polyvinylchloride (PVC), polyolefin (PO), and PAB® (copolymer of ethylene and propylene).

Administration

- Administer by intravenous infusion over 30 minutes 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 [see Adverse Reactions (6.1)]. Monitor the infusion site for possible subcutaneous infiltration during drug administration.
- Do not mix ZYNLONTA with or administer as an infusion with other drugs.

References

[1] Data on File, BLA761196, Pharmaceutical Development. ADC Therapeutics.
[2] Data on File, Quality Memo. ADC Therapeutics.
[3] Data on File, Pharmacy Manual. ADC Therapeutics.
[4] ZYNLONTA® (loncastuximab tesirine-lpyl) FDA Prescribing Information, October 2022.

ADC Therapeutics encourages all health care professionals to report any adverse events and product quality complaints to medical information at 855-690-0340. Please consult the ZYNLONTA Prescribing Information.