ELZONRIS® (tagraxofusp-erzs) DOSE PREPARATION AND ADMINISTRATION INSTRUCTIONS

ELZONRIS®
(tagraxofusp-erzs) Injection

INDICATION

ELZONRIS is a CD123-directed cytotoxin indicated for the treatment of blastic plasmacytoid dendritic cell neoplasm (BPDCN) in adults and in pediatric patients 2 years and older

Boxed WARNING: CAPILLARY LEAK SYNDROME

Capillary Leak Syndrome (CLS) which may be life-threatening or fatal, can occur in patients receiving ELZONRIS. Monitor for signs and symptoms of CLS and take actions as recommended.

Please see **Important Safety Information, including Boxed WARNING** on the last page and accompanying **Full Prescribing Information**, **including Boxed WARNING** in the pocket insert.

This information is intended as educational and should not replace a healthcare professional's judgement or clinical expertise.

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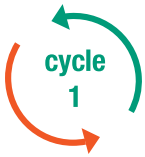
Scan the QR code to contact your ELZONRIS representative.

Treatment Requirements

Before initiating treatment

Review the treatment requirements below to ensure that the patient meets all the requirements prior to ELZONRIS preparation and administration.

Prior to first dose: Cycle[1]



- ☐ Ensure that the patient has adequate cardiac function*
- ☐ Ensure that the patient's serum albumin ≥3.2 g/dL

*In the clinical studies, patients had a left ventricular ejection fraction ≥ institutional lower limit of normal as measured by multigated acquisition scan or 2-dimensional echocardiography within 28 days prior to the start of therapy. No clinically significant abnormalities on a 12-lead electrocardiogram.[2]

Review and record the below parameters prior to each dose of ELZONRIS administration. Alert the treating physician if any of the below parameters exceed the limits for dose modification per the recommended dose modification guidelines and CLS management guidelines.[1]

Parameters	
Body weight (kg)	☐
Systolic blood pressure (mmHg)	☐
Heart rate (bpm)	☐
Body temperature (°C)	☐
Serum albumin (g/dL)	☐
Aspartate aminotransferase [AST] (U/L)	☐
Alanine aminotransferase [ALT] (U/L)	☐
Serum creatinine (mg/dL)	☐

Recommended dosage of ELZONRIS[1]:

12 mcg/kg/day administered intravenously via a syringe pump over 15 minutes once daily on days 1 through 5 of a 21-day cycle.

Dosing delays may be extended up to day 10 of the cycle.

The total infusion time will be controlled using a syringe pump to deliver the entire dose and the 0.9% Sodium Chloride Injection, USP flush over 15 minutes.

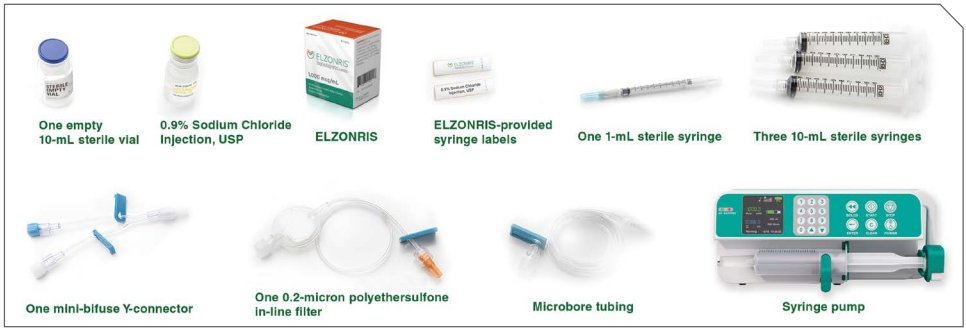
Dose Preparation

Key considerations before ELZONRIS preparation

- To get started, lay out all your components to ensure that you have everything you need. Your components may vary depending on their manufacturer. However, all the components pictured here are required for the assembly of the ELZONRIS administration system. All components must be sterile.

Before initiating the ELZONRIS dose preparation process, make sure you have everything you need, including your institution's preferred syringe pump.

Dose preparation components



- Please ensure that all of the following components are available prior to thawing ELZONRIS[1]:

Empty 10-mL sterile vial

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Mini-bifuse Y-connector

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0.2-micron polyethersulfone in-line filter

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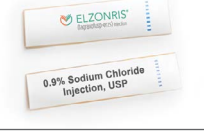
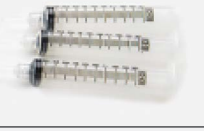
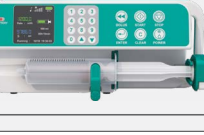
Dose Preparation

Microbore tubing	4 	☐
ELZONRIS-provided syringe label	5 	☐
Three 10-mL sterile syringes	6 	☐
One 1-mL sterile syringe	7 	☐
0.9% Sodium Chloride Injection, USP	8 	☐
ELZONRIS	9 	☐
Infusion syringe pump	10 	☐

Dose Preparation

Calculate the required dose based on the recommended dosage of ELZONRIS[1]*:

Dose calculation = 12 mcg/kg X patient's body weight (kg)

*Ensure that the required components are available to support the dilution of a second vial, if the calculated dose based on the patient's weight exceeds 10 mL of ELZONRIS.[1]

ELZONRIS Injection Instructions for Intravenous Use[1]

1

1,000 mcg/mL

ELZONRIS injection for intravenous use is a preservative-free, sterile, clear, colorless, 1,000 mcg/mL solution supplied in a single-dose glass vial.

2

Freezer temp -25ºC to -15ºC

ELZONRIS vials should be stored in a freezer between -25° Celsius and -15° Celsius (or between -13° Fahrenheit and 5° Fahrenheit) and protected from light.

3

Prior to thawing, the patient's vital signs, serum albumin, transaminases, and serum creatinine levels should be checked to ensure patient is able to receive ELZONRIS.

4

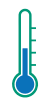
To prepare the first dose, first calculate the required volume of diluted ELZONRIS based on the patient's body weight and then determine what components you need for preparation.

5

Room temp 15ºC to 25ºC

Prior to dose preparation, thaw at room temperature between 15° Celsius and 25° Celsius for 15 to 30 minutes in the original carton, and verify thaw visually.

6



~1 hr at room temp

Thawed vials may be held at room temperature for approximately 1 hour prior to dosage preparation.

7

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

8

Thawed ELZONRIS appearance should be a clear, colorless liquid that may contain a few white to translucent particles. Do not force thaw. Do not refreeze.

9

Administer ELZONRIS within 4 hours of completing the dose preparation. During this 4-hour window, the prepared dose should remain at room temperature.

10

Use aseptic technique for preparation of ELZONRIS dose.

Please see Important Safety Information, **including Boxed WARNING** on the last page.

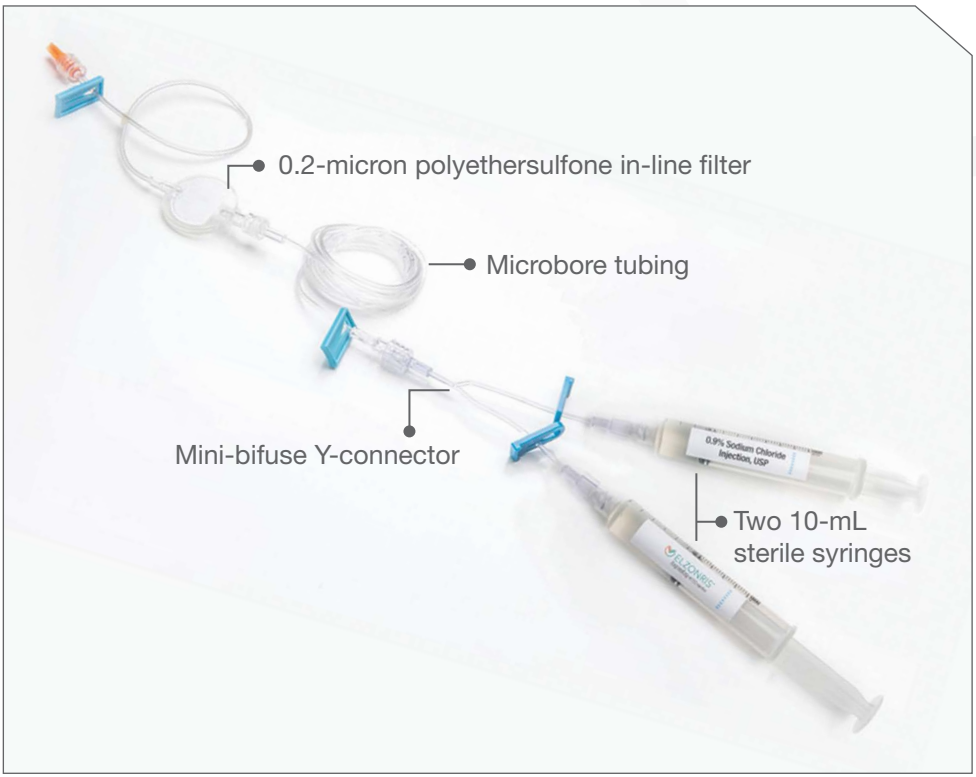
ELZONRIS® (tagraxofusp-erzs) Injection

Dose Preparation

Dose preparation steps[1]

Prepare ELZONRIS under a laminar flow hood using aseptic technique.

This is one example of an assembled administration system:



Some of the components may look slightly different depending on the manufacturer. If the pharmacy did not include one or more of these components, such as a full syringe for the flush, you should procure your own.

Dose Preparation

Step 1 Using a sterile 10-mL syringe, withdraw 9 mL 0.9% Sodium Chloride Injection USP, and transfer into the empty 10-mL sterile vial.

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Step 2 Next, gently swirl the ELZONRIS vial to mix the contents.

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Step 3 Remove the cap and, using a sterile 1-mL syringe, withdraw 1 mL of thawed ELZONRIS from the product vial.

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Step 4 Transfer the 1 mL of ELZONRIS into the 10-mL vial containing the 9 mL of 0.9% Sodium Chloride Injection, USP.

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Step 5 To ensure adequate mixing of the diluted ELZONRIS, gently invert the vial containing the 0.9% Sodium Chloride Injection, USP and ELZONRIS at least 3 times. Do not shake vigorously; avoid foaming.

☐

Dose Preparation

Step 6 Following dilution, the final concentration of ELZONRIS is 100 mcg/mL.

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Step 7 The recommended dose of ELZONRIS is 12 mcg/kg diluted to 100 mcg/mL. If more than 10 mL of ELZONRIS is calculated based on the patient's weight, ensure that the required components are available to support the dilution of a second vial and use a 20-mL sterile syringe when delivering ELZONRIS.

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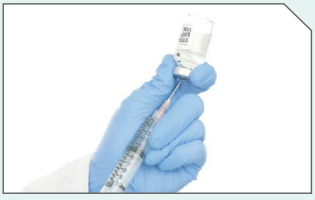
Step 8 Using a new 10-mL syringe, withdraw the correct dosage volume from the vial containing the diluted ELZONRIS.



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Step 9 Cap and label the ELZONRIS-filled syringe with the ELZONRIS-provided label, and set it aside. Each label will have a unique item code number.

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Step 10 Next, take a new 10-mL sterile syringe...

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Dose Preparation

and fill it with at least 3 mL of 0.9% Sodium Chloride Injection, USP. This will be the 0.9% Sodium Chloride Injection, USP flush syringe. The 0.9% Sodium Chloride Injection, USP flush will be used to push out the full required dose of ELZONRIS to the patient at the end of the infusion.

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Step 11 Cap and label this syringe with the 0.9% Sodium Chloride Injection, USP provided label.

☐

Step 12 Attach the ELZONRIS-filled syringe to one arm of the Y-connector.

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Attach the 0.9% Sodium Chloride Injection, USP syringe to the other arm of the Y-connector. Clamp off both arms until needed.

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Step 13 Connect the terminal end of the Y-connector to the microbore tubing.

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Dose Preparation

Step 14 Remove the cap from the supply side of the 0.2-micron filter and…

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attach it to the terminal end of the microbore tubing.

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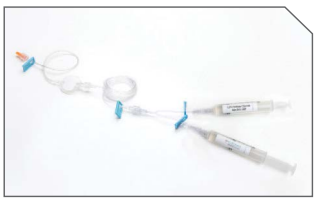
Step 15 All components are now attached.



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Step 16 Next, prime the 0.9% Sodium Chloride Injection, USP and ELZONRIS-filled lines. Unclamp the arm of the Y-connector connected to the 0.9% Sodium Chloride Injection, USP flush syringe.

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Prime the Y-connector up to the intersection. Do not prime the full infusion set with 0.9% Sodium Chloride Injection, USP. Re-clamp the Y-connector line of the 0.9% Sodium Chloride Injection flush arm.

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Dose Preparation

Step 17 Remove the cap from the opposite side of the in-line filter and set it aside.

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Next, prime the ELZONRIS side of the Y-connector, the microbore tubing, and the in-line filter.

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Step 18 Put the cap back onto the in-line filter to ensure that ELZONRIS will not leak out.

☐

Step 19 The infusion set is now ready for delivery for dose administration. Finally, label the administration setup according to your institutional guidelines.

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Visit ELZONRIS.com/hcp for a detailed video on how to properly prepare ELZONRIS.

Dose Administration

Key considerations for ELZONRIS administration

The first cycle of ELZONRIS should be administered in an inpatient setting, while the subsequent cycles can be administered in the inpatient setting or a suitable outpatient ambulatory care setting equipped with appropriate observation for patients with hematopoietic malignancies undergoing treatment.[1]

Cycle 1

Prepare to observe patients through at least 24 hours after the last infusion during cycle 1 in the inpatient setting[1]

Cycle 2

In cycle two and beyond, prepare to observe patients for at least 4 hours following each infusion for any adverse events[1]

Factors to consider before dose administration[1]

Prior to administration, ELZONRIS is diluted to 100 micrograms per milliliter according to the patient's weight.

Do not reuse excess ELZONRIS. Any excess material should be thrown away immediately following infusion.

Administer ELZONRIS until disease progression or unacceptable toxicity occurs. Do not administer as an IV push or bolus.

Refer to the Package Insert for a complete list of Warnings and Precautions and recommended dose modifications.

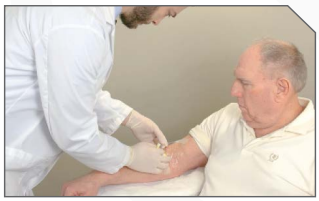
Pre-medicate patients ~60 minutes prior to each infusion with[1]:

- H1-histamine antagonist (eg, diphenhydramine hydrochloride)
- Acetaminophen (paracetamol)
- Corticosteroid (eg, 50 mg IV methylprednisolone or equivalent)
- H2-histamine antagonist (eg, famotidine)

Dose Administration

Dose administration steps[1]

Step 1 Prior to infusion, check the patient's ID band, establish venous access, and maintain with sterile 0.9% Sodium Chloride Injection, USP.



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Step 2 Insert the syringe containing the diluted ELZONRIS dose into the programmable syringe pump, following the pump's instructions. Please refer to the manufacturer's instructions for your pump to ensure proper use.

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Step 3 The total infusion time will be controlled using a programmable pump to deliver the entire diluted ELZONRIS dose over 15 minutes. This time frame includes the 0.9% Sodium Chloride Injection, USP flush.

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Step 4 The pump must have settings that enable you to input the total dose amount required for infusion and the time required for delivery.

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Step 5 Before you connect the administration setup to the patient's IV line, determine where you will place the 0.9% Sodium Chloride Injection, USP flush so it can be conveniently accessed upon completion of the diluted ELZONRIS dose.

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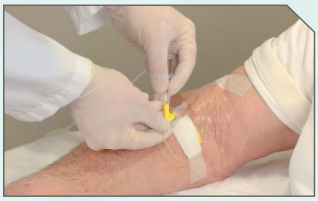
Dose Administration

Step 6 Attach the outlet of the in-line filter to the Y-connector of the patient's IV line.



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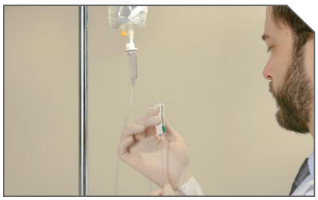
Step 7 Stop the patient's running 0.9% Sodium Chloride Injection, USP line by clamping it and then start the infusion pump.



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Run the infusion syringe pump until the diluted ELZONRIS-filled syringe is empty. This will take less than 15 minutes.

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Step 8 A healthcare professional should closely observe the patient during infusion for any potential adverse or site reactions.

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Step 9 Depending on the type of pump you are using, alarms may sound to indicate that the syringe is almost empty. Visually verify that the syringe is completely empty.

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Step 10 When the diluted ELZONRIS-filled syringe is completely empty, remove it from the pump, following the pump's instructions. Do not turn off the pump.

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Dose Administration

☐

Step 11 Clamp the ELZONRIS side of the Y-connector.

☐

Step 12 Open the clamp on the 0.9% Sodium Chloride Injection, USP flush side of the Y-connector.

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☐

Step 13 Place the 0.9% Sodium Chloride Injection, USP flush syringe in the programmable pump.

☐

Then resume infusion via the programmable pump at the pre-specified flow rate to completely deliver the diluted ELZONRIS dose remaining in the microbore tubing line.

☐

Dose Administration

Step 14 You should ensure that the full recommended dose of diluted ELZONRIS has been sufficiently administered during the 15-minute time frame.

☐

Step 15 When that has happened, remove the 0.9% Sodium Chloride Injection, USP flush syringe from the programmable pump. The 0.9% Sodium Chloride Injection, USP flush syringe will not be emptied entirely at the end of the 15-minute infusion, since it is just intended to push the remaining ELZONRIS dose out of the infusion line to complete dose delivery.

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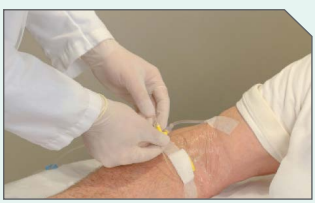
Power off the pump by following the pump's instructions.

☐

Step 16 Disconnect the in-line filter port from the patient's IV line. Prepare to monitor the patient through at least 24 hours after the last infusion during Cycle 1 in the inpatient setting, and at least 4 hours following each infusion in the subsequent cycles for any adverse events.



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Dose Modification Guidelines

Well-defined dose modification guidelines have been established for ELZONRIS administration[1]

Parameter	Severity Criteria	Dosage Modification
Serum albumin	Serum albumin <3.5 g/dL or reduced ≥0.5 g/dL from value measured prior to initiation of the current cycle	See CLS Management Guidelines section on the next page
Body weight	Body weight increase ≥1.5 kg over pretreatment weight on prior treatment day	See CLS Management Guidelines section on the next page
AST or ALT	ALT or AST increase >5 times the upper limit of normal	Withhold ELZONRIS until transaminase elevations are ≤2.5 times the upper limit of normal
Serum creatinine	Serum creatinine >1.8 mg/dL (159 micromol/L) or creatinine clearance <60 mL/min	Withhold ELZONRIS until serum creatinine resolves to ≤1.8 mg/dL (159 micromol/L) or creatinine clearance ≥60 mL/min
Systolic blood pressure	Systolic blood pressure ≥160 mmHg or ≤80 mmHg	Withhold ELZONRIS until systolic blood pressure is <160 mmHg or >80 mmHg
Heart rate	Heart rate ≥130 bpm or ≤40 bpm	Withhold ELZONRIS until heart rate is <130 bpm or >40 bpm
Body temperature	Body temperature ≥38°C	Withhold ELZONRIS until body temperature is <38°C
Hyper-sensitivity reactions	Mild or moderate	Withhold ELZONRIS until resolution of any mild or moderate hypersensitivity reaction. Resume ELZONRIS at the same infusion rate
	Severe or life-threatening	Discontinue ELZONRIS permanently

Visit ELZONRIS.com/hcp for a detailed video on how to administer ELZONRIS.

CLS Management Guidelines

Management of CLS is an important part of treating patients with ELZONRIS[1]

Time of presentation	CLS sign/symptom	Recommended action	ELZONRIS dosing management
Prior to first dose of ELZONRIS in cycle 1	**Serum albumin <3.2 g/dL**	Administer ELZONRIS **when serum albumin ≥3.2 g/dL**	
During ELZONRIS dosing	**Serum albumin <3.5 g/dL**	Administer **25 g intravenous albumin** (q12h or more frequently as practical) until serum albumin is **≥3.5 g/dL AND not more than 0.5 g/dL lower than** the value measured prior to dosing initiation of the current cycle	**Interrupt ELZONRIS dosing until the relevant CLS sign/symptom has resolved***
	Serum albumin reduced by ≥0.5 g/dL from the albumin value measured prior to ELZONRIS dosing initiation of the current cycle		
	A predose body weight that is increased by ≥1.5 kg over the previous day's predose weight	Administer **25 g intravenous albumin** (q12h or more frequently as practical) and manage fluid status as clinically indicated (eg, generally with intravenous fluids and vasopressors if hypotensive and with diuretics if normotensive or hypertensive) until body weight increase has resolved (ie, the increase is no longer **≥1.5 kg** greater than the previous day's predose weight)	
	Edema, fluid overload, and/or hypotension	Administer **25 g intravenous albumin** (q12h, or more frequently as practical) until serum albumin is **≥3.5 g/dL** Administer **1 mg/kg of methylprednisolone** (or an equivalent) per day until resolution of CLS sign/symptom or as clinically indicated **Aggressive management of fluid status** and hypotension if present, which could include intravenous fluids and/or diuretics or other blood pressure management, until resolution of CLS sign/symptom or as clinically indicated	

*If ELZONRIS dose is held:

- ELZONRIS administration may resume in the same cycle if all CLS signs/symptoms have resolved and the patient did not require measures to treat hemodynamic instability
- ELZONRIS administration should be held for the remainder of the cycle if CLS signs/symptoms have not resolved or the patient required measures to treat hemodynamic instability (eg, required administration of intravenous fluids and/or vasopressors to treat hypotension) (even if resolved)
- ELZONRIS administration may only resume in the next cycle if all CLS signs/symptoms have resolved and the patient is hemodynamically stable

IMPORTANT SAFETY INFORMATION

INDICATION

- ELZONRIS is a CD123-directed cytotoxin indicated for the treatment of blastic plasmacytoid dendritic cell neoplasm (BPDCN) in adults and in pediatric patients 2 years and older

IMPORTANT SAFETY INFORMATION

Boxed WARNING: CAPILLARY LEAK SYNDROME

- Capillary Leak Syndrome (CLS) which may be life-threatening or fatal, can occur in patients receiving ELZONRIS. Monitor for signs and symptoms of CLS and take actions as recommended.

WARNINGS AND PRECAUTIONS

Capillary Leak Syndrome

- Capillary leak syndrome (CLS), including life-threatening and fatal cases, has been reported among patients treated with ELZONRIS. In patients receiving ELZONRIS in clinical trials, the overall incidence of CLS was 53% (65/122), including Grade 1 or 2 in 43% (52/122) of patients, Grade 3 in 7% (8/122) of patients, Grade 4 in 1% (1/122) of patients, and four fatalities (3%). The median time to onset was 4 days (range - 1 to 46 days), and all but 5 patients experienced an event in Cycle 1.
- Before initiating therapy with ELZONRIS, ensure that the patient has adequate cardiac function and serum albumin is greater than or equal to 3.2 g/dL. During treatment with ELZONRIS, monitor serum albumin levels prior to the initiation of each dose of ELZONRIS and as indicated clinically thereafter, and assess patients for other signs or symptoms of CLS, including weight gain, new onset or worsening edema, including pulmonary edema, hypotension or hemodynamic instability.

Hypersensitivity Reactions

- ELZONRIS can cause severe hypersensitivity reactions. In patients receiving ELZONRIS in clinical trials, hypersensitivity reactions were reported in 43% (53/122) of patients treated with ELZONRIS and were Grade ≥ 3 in 7% (9/122). Manifestations of hypersensitivity reported in ≥ 5% of patients include rash, pruritus, and stomatitis. Monitor patients for hypersensitivity reactions during treatment with ELZONRIS. Interrupt ELZONRIS infusion and provide supportive care as needed if a hypersensitivity reaction should occur.

Hepatotoxicity

- Treatment with ELZONRIS was associated with elevations in liver enzymes. In patients receiving ELZONRIS in clinical trials, elevations in ALT occurred in 79% (96/122) and elevations in AST occurred in 76% (93/122). Grade 3 ALT elevations were reported in 26% (32/122) of patients. Grade 3 AST elevations were reported in 30% (36/122) and Grade 4 AST elevations were reported in 3% (4/122) of patients. Elevated liver enzymes occurred in the majority of patients in Cycle 1 and were reversible following dose interruption.
- Monitor alanine aminotransferase (ALT) and aspartate aminotransferase (AST) prior to each infusion with ELZONRIS. Withhold ELZONRIS temporarily if the transaminases rise to greater than 5 times the upper limit of normal and resume treatment upon normalization or when resolved.

ADVERSE REACTIONS:

Most common adverse reactions (incidence ≥ 30%) are capillary leak syndrome, nausea, fatigue, pyrexia, peripheral edema, and weight increase. Most common laboratory abnormalities (incidence ≥ 50%) are decreases in albumin, platelets, hemoglobin, calcium, and sodium, and increases in glucose, ALT and AST.

Please see **Full Prescribing Information, including Boxed WARNING** in the pocket insert.

To report SUSPECTED ADVERSE REACTIONS, contact Stemline Therapeutics, Inc. at 1-877-332-7961 or contact the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; CLS, capillary leak syndrome; IV, intravenous; q12h, every 12 hours.

References: 1. ELZONRIS [prescribing information]. New York, NY: Stemline Therapeutics, Inc.; July 2023.
2. Data on file. Stemline Therapeutics, Inc.

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