CAPILLARY LEAK SYNDROME (CLS) MANAGEMENT GUIDE

ELZONRIS®
(tagraxofusp-erzs) Injection

INDICATION

ELZONRIS® (tagraxofusp-erzs) is a CD123-directed cytotoxin 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 full Important Safety Information on back cover and accompanying full Prescribing Information, including Boxed WARNING.

ELZONRIS and CLS

In clinical studies of ELZONRIS, 53% of patients experienced CLS of any grade, including 4 fatal events (N=122).[1]

- >90% of CLS occurred in cycle 1

Common signs and symptoms of CLS with ELZONRIS[1]

- Hypoalbuminemia
- Edema, including pulmonary edema
- Weight gain
- Hypotension
- Hemodynamic instability

Assess all patients appropriately before and throughout ELZONRIS treatment[1]

- **Before initiating therapy with ELZONRIS (first dose of first cycle):**
  - Ensure patient has adequate cardiac function*
  - Ensure patient has serum albumin ≥3.2 g/dL
  - Weigh patient to establish baseline weight for subsequent dose
- **During treatment with ELZONRIS:**
  - Monitor serum albumin levels prior to the initiation of each dose of ELZONRIS and as clinically indicated thereafter
    - Serum albumin <3.5 g/dL or reduced by ≥0.5 g/dL from the albumin value measured prior to ELZONRIS dosing initiation of the current cycle
  - Assess patients for signs/symptoms of CLS, including:
    - Weight gain ≥1.5 kg from the previous day's predose weight
    - New onset or worsening edema, including pulmonary edema
    - Hypotension or hemodynamic instability

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

Observe patients during ELZONRIS administration[1]

- **Cycle 1**
  - Administer in the inpatient setting, and observe patients for at least 24 hours after the last infusion
- **Subsequent cycles**
  - Administer in the inpatient setting or an appropriate outpatient setting
  - Observe patients for at least 4 hours after each infusion

Counsel patients upon discharge[1]

- Advise patients of the risk of CLS and to contact their healthcare provider for signs and symptoms associated with CLS, including:
  - New or worsening edema
  - Weight gain
  - Shortness of breath and/or
  - Hypotension after infusion
- Advise patients to weigh themselves daily

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Guidance for CLS management with ELZONRIS[1]

CLS management guidelines

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 indicated clinically (eg, generally with intravenous fluids and vasopressors if hypotensive and with diuretics if normotensive or hypertensive), until body weight increase has resolved (eg, 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 indicated clinically. **Aggressively manage 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), and
- ELZONRIS administration may only resume in the next cycle if all CLS signs/symptoms have resolved and the patient is hemodynamically stable.

q12h, every 12 hours.

ELZONRIS infusion should be withheld for common signs/symptoms of CLS, including:

- Hypoalbuminemia (serum albumin <3.5 g/dL or reduced by ≥0.5 g/dL below the level at the start of the current cycle)
- Body weight increased by ≥1.5 kg over the pretreatment weight on the previous treatment day
- New onset or worsening edema, including pulmonary edema
- Hypotension (systolic blood pressure ≤80 mm Hg) or hemodynamic instability

ELZONRIS guidance	
RESUME ELZONRIS administration in the same cycle if:	• All CLS signs/symptoms have resolved AND • The patient did NOT require measures to treat hemodynamic instability—eg, intravenous fluid boluses and/or vasopressors to treat hypotension
HOLD ELZONRIS administration for the remainder of the cycle if:	• CLS signs/symptoms have NOT resolved OR • The patient requires/required measures to treat hemodynamic instability (even if resolved)—eg, intravenous fluid boluses and/or vasopressors to treat hypotension
ELZONRIS administration may only resume in the next cycle if all CLS signs/symptoms have resolved and the patient is hemodynamically stable.	

This is intended as educational information for healthcare providers. It does not replace a healthcare provider's judgment or clinical diagnosis.

Visit ELZONRIS.com/hcp for more information

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INDICATION

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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.

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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.

References: 1. ELZONRIS [prescribing information]. New York, NY: Stemline Therapeutics, Inc.; November 2022. **2.** Data on file. Stemline Therapeutics, Inc.

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