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**This document has been reviewed and approved by The Saudi Food and Drug Authority (SFDA).**

## CAPILLARY LEAK SYNDROME (CLS) MANAGEMENT GUIDE FOR HEALTHCARE PROFESSIONALS



This Healthcare Professional Guide is provided to ensure the safe and effective use of ELZONRIS Injection 1000 µg/mL and is essential for managing important selected risks.

### Indication

ELZONRIS is indicated as monotherapy in patients with blastic plasmacytoid dendritic cell neoplasm (BPDCN) in the following:

Adults and pediatric patients 2 years and older as induction therapy to bridge to hematopoietic stem cell transplantation (SCT) and adults who are ineligible to SCT as first-line maintenance therapy.

This indication is approved under accelerated approval based on the response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in either clinical trial(s) or real world evidence in both adults and pediatrics.

Please see full Summary of Product Characteristics.

CLS Healthcare Professional Guide KSA v. 1.2  
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## ELZONRIS and CLS

### 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.

In clinical studies, ELZONRIS was shown to cause capillary leak syndrome (CLS), which in some cases may be life-threatening or fatal. Most CLS events were reported as occurring during the first five days of the first cycle of treatment. In clinical studies, CLS was reported in 18 % of patients. Common signs and symptoms associated with CLS that were reported during treatment with ELZONRIS include:

- Hypoalbuminemia
- Oedema
- Weight gain
- Hypotension

### Assess all patients appropriately before and throughout ELZONRIS treatment

- Before initiating therapy with ELZONRIS (first dose of first cycle):
  - Ensure patient has adequate cardiac function
  - Ensure patient has serum albumin  $\geq 3.2$  g/dL
  - Weigh patient to establish baseline weight for subsequent dose
- During treatment with ELZONRIS:
  - Assess patients for signs/symptoms of CLS, including:
    - Serum albumin  $< 3.5$  g/dL or reduced by  $\geq 0.5$  g/dL from the albumin value measured prior to ELZONRIS dosing initiation of the current cycle
    - New onset or worsening oedema, including pulmonary oedema
    - Weight gain  $\geq 1.5$  kg from the previous day's pre-dose weight
    - Hypotension or haemodynamic instability

### Observe patients during ELZONRIS administration

- Cycle 1
  - The first cycle must be administered in the in-patient setting
  - Observe patients for at least 24 hours after the last infusion of the first cycle
- Subsequent cycles
  - Subsequent cycles may be administered in an in-patient setting or an appropriate out-patient ambulatory care setting

### Counsel patients upon discharge

- Advise patients of the risk of CLS, and to contact their healthcare provider for signs and symptoms associated with CLS. Advise patients to weigh themselves daily
- A Patient Alert Card must be given to patients to remind them of the signs and symptoms of CLS, and to provide contact details for reporting where CLS is suspected, as well as advice patients to carry the card with them at all times

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 $\geq 3.2$ g/dL	
During ELZONRIS dosing	Serum albumin $< 3.5$ g/dL	Administer 25 g intravenous albumin every 12 hours (or more frequently as practical) until serum albumin is $\geq 3.5$ g/dL AND not reduced by $\geq 0.5$ g/dL from the value measured prior to dosing initiation of the current cycle	Hold dosing until the relevant CLS sign/symptom has resolved <sup>1</sup>
	Serum albumin reduced by $\geq 0.5$ g/dL from the albumin value measured prior to ELZONRIS dosing initiation of the current cycle		
	A pre-dose body weight that is increased by $\geq 1.5$ kg over the previous day's pre-dose weight	Administer 25 g intravenous albumin (every 12 hours or more frequently as practical), and manage fluid status as indicated clinically (e.g., generally with intravenous fluids and vasopressors if hypotensive and with diuretics if normotensive or hypertensive), until body weight increase has resolved (i.e. the increase is no longer $\geq 1.5$ kg greater than the previous day's pre-dose weight)	
	Oedema, fluid overload and/or hypotension	Administer 25 g intravenous albumin (every 12 hours, or more frequently as practical) until serum albumin is $\geq 3.5$ g/dL  Administer 1 mg/kg of methylprednisolone (or an equivalent) per day, until resolution of CLS sign/symptom or as indicated clinically  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:<sup>1</sup>

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