CAPILLARY LEAK SYNDROME (CLS) MANAGEMENT GUIDE FOR HEALTHCARE PROFESSIONALS

ELZONRIS
Concentrate for solution for infusion, tagraxofusp 1 mg/mL

Indication
ELZONRIS is a CD123-directed cytotoxin for the treatment of blastic plasmacytoid dendritic cell neoplasm (BPDCN) in adults.

Adverse event reporting
Reporting about adverse events to the Israeli Ministry of Health can be done via the portal for Reporting Side Effects, found on the home page of the Israeli Ministry of Health website www.health.gov.il, or by entering the link: https://sideeffects.health.gov.il/

Please see the Full Prescribing Information.
The Full Prescribing Information is available on the website of the Israeli Ministry of Health

ELZONRIS and CLS

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 ≥ 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 ≥ 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 ≥ 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. Advise patients to carry the card with them at all times.

<table>
<tr><th>Time of Presentation</th><th>CLS Sign/Symptom</th><th>Recommended Action</th><th>ELZONRIS Dosing Management</th></tr>
<tr><td>Prior to first dose of ELZONRIS in cycle 1</td><td>Serum albumin < 3.2 g/dL</td><td colspan="2">Administer ELZONRIS when serum albumin ≥ 3.2 g/dL</td></tr>
<tr><td rowspan="4">During ELZONRIS dosing</td><td>Serum albumin < 3.5 g/dL</td><td rowspan="2">Administer 25 g intravenous albumin every 12 hours (or more frequently as practical) until serum albumin is ≥ 3.5 g/dL AND not reduced by ≥ 0.5 g/dL from the value measured prior to dosing initiation of the current cycle</td><td rowspan="4">Interrupt ELZONRIS dosing until the relevant CLS sign/symptom has resolved [1]</td></tr>
<tr><td>Serum albumin reduced by ≥ 0.5 g/dL from the albumin value measured prior to ELZONRIS dosing initiation of the current cycle</td></tr>
<tr><td>A pre-dose body weight that is increased by ≥ 1.5 kg over the previous day’s pre-dose weight</td><td>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 ≥ 1.5 kg greater than the previous day’s pre-dose weight).</td></tr>
<tr><td>Oedema, fluid overload and/or hypotension</td><td>Administer 25 g intravenous albumin (every 12 hours, 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.

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.</td></tr>
</table>

[1] 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 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.

To order additional copies of this information please contact: EUmedinfo@stemline.com
To report an adverse event please contact: EUPV@stemline.com

This guide was checked and approved by Israeli Ministry of Health in March 2024.