# YOUR GUIDE TO

# stemline arc®

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## Stemline ARC®: Committed to helping you get the support you need

Once enrolled in Stemline ARC, you will receive ongoing support from ARC Patient Advocates throughout the course of your treatment.

ARC Patient Advocates are available to answer questions and connect you to resources during your treatment journey. ARC Patient Advocate support is not intended to replace discussions between you and your healthcare provider.

### About ELZONRIS® (tagraxofusp-erzs)

ELZONRIS is a prescription medicine used to treat blastic plasmacytoid dendritic cell neoplasm (BPDCN) in adults and pediatric patients 2 years and older.

### IMPORTANT SAFETY INFORMATION

ELZONRIS can cause serious side effects, including:

- **Capillary Leak Syndrome (CLS)**. ELZONRIS can cause fluid to leak from small blood vessels into your body's tissues. This is called "Capillary Leak Syndrome." CLS can quickly cause you to have symptoms that may become life-threatening or fatal (ie, lead to death). **Get emergency medical help immediately if you develop any of the following symptoms:**
  - fast weight gain
  - swelling of your face, arms, hands, legs, or feet
  - shortness of breath or difficulty breathing
  - low blood pressure (dizziness or lightheadedness, headache, feeling tired, or shortness of breath)

Your healthcare provider will check your weight and test your blood before you receive each dose of ELZONRIS and as needed during treatment.

Stemline®

ELZONRIS® (tagraxofusp-erzs) Injection

**Please see accompanying full Prescribing Information, including Boxed WARNING.**

# Stemline ARC: Help and Support When You Need It Most

**You may be able to receive financial assistance through several support programs. Talk to your treatment team about which programs you may be eligible for.**


## Stemline Commercial Co-Pay Program*

- Eligible patients may pay as little as $0 for ELZONRIS Injection for IV Use

Please see page 5 for the full terms and conditions.

## Stemline Patient Assistance Program†

- The Stemline Patient Assistance Program provides ELZONRIS Injection for IV Use to eligible patients who are under- or uninsured. Patients must meet certain criteria to qualify

Call 1-833-4-STEMLINE (1-833-478-3654) for more information.

## Independent Third-Party Foundations‡

- Stemline ARC can provide information about independent third-party foundations

**Before you enroll in Stemline ARC, talk to your doctor about which documents you may need, and remember to sign all required forms.**

*Patients must meet eligibility criteria. In order to be eligible for the Stemline Commercial Co-Pay Program, the patient must not have government-funded health insurance (eg, Medicare, Medicaid, or any other federal or state program), must be taking ELZONRIS Injection for IV Use for an FDA-approved indication, and must confirm that they meet all of the eligibility criteria and agree to the rules set forth in the terms and conditions for the program. Patients and healthcare providers are responsible for completing and submitting enrollment forms and coverage or reimbursement documentation. Stemline Therapeutics, Inc. makes no representation or guarantee concerning coverage or reimbursement of any service or item.

†To be eligible for this program, insured patients must have exhausted all other forms of patient assistance and meet financial criteria. Insured and uninsured patients must also meet certain eligibility criteria.

‡Stemline Therapeutics, Inc. does not influence or control the operations or eligibility criteria of any independent charitable assistance foundation and cannot guarantee assistance after information has been provided by Stemline ARC. The information is provided as a resource to patients. The foundations that we discuss with patients are not exhaustive or indicative of Stemline Therapeutics, Inc.'s endorsement or financial support. There may be other foundation support available to patients.

# Support and Connection to Resources Throughout Your Treatment

ARC Patient Advocates are here to provide ongoing support, connect you to helpful resources, and answer questions during your treatment journey.

**ARC Patient Advocates provide a single point of contact**

## Here are some of the questions ARC Patient Advocates can help answer:

- How can I get financial assistance during my treatment?
- How can I get help with transportation or meals?
- How can I get coverage for ELZONRIS?
- How do I handle getting reimbursed by insurance?
- Where can I learn more about BPDCN?
- Where can I find mental health support?
- Where can I find patient, family, or caregiver support groups?
- What kind of resources can I find online?

ARC Patient Advocates are available to provide resource information and answer questions about financial assistance, insurance benefits, and coverage for ELZONRIS. This supplemental support is not intended to replace discussions between you and your healthcare provider.

**If you have questions throughout your treatment, ARC Patient Advocates are available to take your call Monday - Friday, from 9:00 AM to 6:00 PM EST at 1-833-4-STEMLINE (1-833-478-3654).**

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## Enrolling in Stemline ARC Is Simple

Together with your doctor, follow these simple steps to enroll in Stemline ARC:

Fill out the enrollment form with your doctor.

Together with your doctor, sign and date **Stemline ARC** enrollment form authorizations, certifications, and consent fields.

Provide your doctor with all required documentation.

Your doctor will send all required documentation to **Stemline ARC**.

- Your ARC Patient Advocate will call you within 1 business day of enrollment

## Enrollment Reminders

Please use the checklist below to ensure all of the required documentation is included:

- **Sign all necessary forms provided to you by your doctor**
- **Your doctor will let you know if you need to provide your most recent W2, 1099, or other proof of income**
- **Copy both sides of your insurance card(s) and give them to your doctor**

**For questions or more information about Stemline ARC, call 1-833-4-STEMLINE (1-833-478-3654) from 9:00 AM to 6:00 PM EST, Monday through Friday.**

## Stemline Commercial Co-Pay Program Terms and Conditions

By using the Stemline Commercial Co-Pay Program, the patient acknowledges and confirms that, at the time of usage, (s)he is currently eligible and meets the criteria set forth in the terms and conditions described. The Stemline Commercial Co-Pay Program is valid ONLY for patients with commercial (private or nongovernmental) insurance who are taking the medication for an FDA-approved indication. Patients using Medicare, Medicaid, or any other federal or state government-funded program to pay for their medications are not eligible. Patients who start utilizing their government coverage during their enrollment period will no longer be eligible for the program. Patients may pay as little as $0 per month and Stemline Therapeutics, Inc. will pay the remaining out-of-pocket cost up to a maximum of $25,000 per calendar year. Any costs exceeding the maximum of $25,000 are the responsibility of the patient. This Commercial Co-Pay Program is not health insurance or a benefit plan. Distribution or use of the Stemline Commercial Co-Pay Program does not obligate use or continuing use of any specific product or provider. Patient or guardian is responsible for reporting the receipt of all Commercial Co-Pay Program benefits or reimbursement received to any insurer, health plan, or other third party who pays for or reimburses any part of the prescription filled using the Commercial Co-Pay Program, as may be required. The Commercial Co-Pay Program is not valid for medications the patient receives for free or that are eligible to be reimbursed by private insurance plans or other healthcare or pharmaceutical assistance programs that reimburse the patient in part or for the entire cost of his/her Stemline medication. Patient, guardian, pharmacist, prescriber, and any other person using the Commercial Co-Pay Program agree not to seek reimbursement for all or any part of the benefit received by the recipient through the offer.

The Stemline Commercial Co-Pay Program will be accepted by participating pharmacies, physician offices, or hospitals. To qualify for the benefits of this Commercial Co-Pay Program, the patient may be required to pay out-of-pocket expenses for each treatment. This Commercial Co-Pay Program is only available with a valid prescription and cannot be combined with any other rebate/coupon, free trial, or similar offer for the specified prescription. Use of this Commercial Co-Pay Program must be consistent with all relevant health insurance requirements and payer agreements. Participating patients, pharmacies, physician offices, and hospitals are obligated to inform third-party payers about the use of the Commercial Co-Pay Program as provided for under the applicable insurance or as otherwise required by contract or law. ELZONRIS Injection for IV Use provided by the Commercial Co-Pay Program may not be sold, purchased, traded, or offered for sale, purchase, or trade. Program eligibility period is contingent upon the patient's ability to meet and maintain all requirements as set forth by the program. Stemline Therapeutics, Inc. may periodically verify eligibility and will terminate patients without obligation to pay claims if change to status is detected. This program is not valid where prohibited by law and shall follow state restrictions in relation to AB-rated generic equivalents where applicable (eg, MA, CA). The patient must be 18 years or older to receive Commercial Co-Pay Program assistance. This Commercial Co-Pay Program is (1) void if reproduced; (2) void where prohibited by law; (3) only valid in the United States and Puerto Rico; and (4) only valid for FDA-approved on-label indications of Stemline products. Healthcare providers may not advertise or otherwise use the program as a means of promoting their services or Stemline Therapeutics, Inc. products to patients. Stemline Therapeutics, Inc. reserves the right to rescind, revoke, amend, or terminate the program without notice at any time.

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## Visit ELZONRIS.com/stemline-arc for more information

### IMPORTANT SAFETY INFORMATION (cont'd)

- **Hypersensitivity reactions** may occur with ELZONRIS. Symptoms may include rash, itching (pruritus), wheezing, or swelling in your face, including around your eyes and/or in and around your mouth
- **Liver damage** is usually detected through blood tests. Symptoms may include feeling tired (fatigue), loss of appetite, yellowing of your skin or the whites of your eyes (jaundice), or upper right abdominal pain or discomfort

Your healthcare provider will periodically test your blood while you are on ELZONRIS to check for liver damage.

Contact your healthcare provider immediately if you have any of these symptoms.

**Getting medical treatment right away may help keep these problems from becoming more serious.**

If you have any side effects during treatment with ELZONRIS, your healthcare provider may hold your treatment for a period of time or completely stop your treatment with ELZONRIS.

**The most common side effects of ELZONRIS include** CLS, nausea, feeling tired (fatigue), swelling in your legs or feet, fever, and weight gain.

These are not all of the possible side effects of ELZONRIS. If any new side effects start or an existing one gets worse, contact your healthcare provider immediately. For more information, talk to your treatment team.

Be sure to tell your treatment team about:

- all of your medical conditions, including if you
  - are pregnant or plan to become pregnant. ELZONRIS may harm your unborn baby
    - If you are a female who can become pregnant, you should use effective birth control during ELZONRIS treatment and for at least 1 week after the last dose
    - Tell your healthcare provider right away if you become pregnant during treatment with ELZONRIS
  - are breastfeeding or plan to breastfeed. It is not known if ELZONRIS passes into breast milk. You and your healthcare provider should decide if you will receive ELZONRIS or breastfeed. You should not do both
- all of the medicines you take, including prescription medicines, over-the-counter medicines, vitamins, and herbal supplements

You can report any side effects to Stemline Therapeutics, Inc. at 1-877-332-7961 or contact the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

**Please see full Prescribing Information, including Boxed WARNING, for ELZONRIS to learn more.**

The risk information provided here is not comprehensive. To learn more, talk about ELZONRIS (tagraxofusp-erzs) with your healthcare provider or pharmacist. The FDA-approved product labeling can be found on this website.

ELZONRIS and Stemline ARC are registered trademarks of Stemline Therapeutics, Inc.

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ELZONRIS®
(tagraxofusp-erzs) Injection

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**HIGHLIGHTS OF PRESCRIBING INFORMATION**
**These highlights do not include all the information needed to use ELZONRIS™ safely and effectively. See full prescribing information for ELZONRIS.**

**ELZONRIS (tagraxofusp-erzs) injection, for intravenous use**
**Initial U.S. Approval: 2018**

## WARNING: CAPILLARY LEAK SYNDROME

***See full prescribing information for complete boxed warning.***

**Capillary Leak Syndrome (CLS), which may be life-threatening or fatal if not properly managed, can occur in patients receiving ELZONRIS. (5.1)**

**----------INDICATIONS AND USAGE----------**

ELZONRIS 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. (1)

**----------DOSAGE AND ADMINISTRATION----------**

- Premedicate with an H1-histamine antagonist, acetaminophen, corticosteroid and H2-histamine antagonist prior to each ELZONRIS infusion. (2.1)
- Administer ELZONRIS intravenously at 12 mcg/kg over 15 minutes once daily on days 1 to 5 of a 21-day cycle. (2.1)
- Administer the first cycle of ELZONRIS in the inpatient setting. Subsequent cycles may be administered in the inpatient or appropriate outpatient setting. (2.1)
- Additional important preparation and administration information is in full prescribing information. See full prescribing information for instructions on preparation and administration. (2.3, 2.4)

**----------DOSAGE FORMS AND STRENGTHS----------**

Injection: 1,000 mcg in 1 mL in a single-dose vial. (3)

**----------CONTRAINDICATIONS----------**

- None. (4)

**----------WARNINGS AND PRECAUTIONS----------**

- Hypersensitivity: Monitor patients for signs/symptoms and treat appropriately. (5.2)
- Hepatotoxicity: Monitor ALT and AST. Interrupt ELZONRIS if the transaminases rise to greater than 5 times the upper limit of normal. (5.3)

**----------ADVERSE REACTIONS----------**

Most common adverse reactions (incidence ≥ 30%) are capillary leak syndrome, nausea, fatigue, peripheral edema, pyrexia 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. (6.1)

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

**----------USE IN SPECIFIC POPULATIONS----------**

Lactation: Advise women not to breastfeed (8.2)

**See 17 for PATIENT COUNSELING INFORMATION**

**Revised: 12/2018**

**FULL PRESCRIBING INFORMATION: CONTENTS***



* Sections or subsections omitted from the full prescribing information are not listed.

## FULL PRESCRIBING INFORMATION

**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 [*see Warnings and Precautions* (5.1)].**

## 1 INDICATIONS AND USAGE

ELZONRIS 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.

## 2 DOSAGE AND ADMINISTRATION

### 2.1 Recommended Dose

- Administer ELZONRIS at 12 mcg/kg intravenously over 15 minutes once daily on days 1 to 5 of a 21-day cycle. The dosing period may be extended for dose delays up to day 10 of the cycle. Continue treatment with ELZONRIS until disease progression or unacceptable toxicity.
- Prior to the first dose of the first cycle, ensure serum albumin is greater than or equal to 3.2 g/dL before administering ELZONRIS.
- Premedicate patients with an H1-histamine antagonist (e.g., diphenhydramine hydrochloride), H2-histamine antagonist (e.g., ranitidine), corticosteroid (e.g., 50 mg intravenous methylprednisolone or equivalent) and acetaminophen (or paracetamol) approximately 60 minutes prior to each ELZONRIS infusion.
- Administer Cycle 1 of ELZONRIS in the inpatient setting with patient observation through at least 24 hours after the last infusion.
- Administer subsequent cycles of ELZONRIS in the inpatient setting or in a suitable outpatient ambulatory care setting that is equipped with appropriate monitoring for patients with hematopoietic malignancies undergoing treatment. Observe patients for a minimum of 4 hours following each infusion.

### 2.2 Dose Modifications

Monitor vital signs and check albumin, transaminases, and creatinine prior to preparing each dose of ELZONRIS. See Table 1 for recommended dose modifications and Table 2 for CLS management guidelines.

**Table 1. Recommended ELZONRIS Dose Modifications**

| Parameter | Severity Criteria | Dose 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 (Table 2) |
| Body weight | Body weight increase ≥ 1.5 kg over pretreatment weight on prior treatment day | See CLS Management Guidelines (Table 2) |
| Aspartate aminotransferase (AST) or alanine aminotransferase (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/minute | Withhold ELZONRIS until serum creatinine resolves to ≤ 1.8 mg/dL (159 micromol/L) or creatinine clearance ≥ 60 mL/minute. |

| Parameter | Severity Criteria | Dose Modification |
|---|---|---|
| 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. |
| Hypersensitivity 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. |

## Table 2. 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 25g 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[1]. |
| | 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 25g intravenous albumin (q12h 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 predose weight). | |
| | Edema, fluid overload and/or hypotension | Administer 25g intravenous albumin (q12h, or more frequently as practical) until serum albumin is ≥ 3.5 g/dL.<br><br>Administer 1 mg/kg of methylprednisolone (or an equivalent) per day, until resolution of CLS sign/symptom or as indicated clinically.<br><br>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. | |

[1] 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 (e.g. 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.

### 2.3 Preparation for Administration

Assure the following components required for dose preparation and administration are available prior to thawing ELZONRIS:

- One empty 10 mL sterile vial
- 0.9% Sodium Chloride Injection, USP (sterile saline)
- Three 10 mL sterile syringes
- One 1 mL sterile syringe
- One mini-bifuse Y-connector
- Microbore tubing
- One 0.2 micron polyethersulfone in-line filter

- Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Thawed ELZONRIS appearance should be a clear, colorless liquid that may contain a few white to translucent particles.
- Prior to dose preparation thaw at room temperature, between 15°C and 25°C (59°F and 77°F), for 15 to 30 minutes in original carton, and verify thaw visually. Thawed vials may be held at room temperature for approximately 1 hour prior to dosage preparation. Do not force thaw. Do not refreeze vial once thawed.
- Use aseptic technique for preparation of the ELZONRIS dose.
- A 2-step process is required for preparation of the final ELZONRIS dose:
  - Step 1 - Prepare 10 mL of 100 mcg/mL ELZONRIS
    - Using a sterile 10 mL syringe, transfer 9 mL of 0.9% Sodium Chloride Injection, USP to an empty sterile 10 mL vial.
    - Gently swirl the ELZONRIS vial to mix the contents, remove the cap, and using a sterile 1 mL syringe, withdraw 1 mL of thawed ELZONRIS from the product vial.
    - Transfer the 1 mL of ELZONRIS into the 10 mL vial containing the 0.9% Sodium Chloride Injection. Gently invert the vial at least 3 times to mix the contents. Do not shake vigorously.
    - Following dilution the final concentration of ELZONRIS is 100 mcg/mL.
  - Step 2 – Prepare the ELZONRIS infusion set.
    - Calculate the required volume of diluted ELZONRIS (100 mcg/mL) according to patient's weight.
    - Draw up the required volume into a new syringe (if more than 10 mL of diluted ELZONRIS (100 mcg/mL) is required for the calculated patient dose, repeat step 1 with a second vial of ELZONRIS). Label the ELZONRIS syringe.
    - Prepare a separate syringe with at least 3 mL of 0.9% Sodium Chloride Injection, USP (saline flush) to be used to flush the administration set once the ELZONRIS dose is delivered.
    - Label the saline flush syringe.
    - Connect the saline flush syringe to one arm of the Y-connector and ensure the clamp is closed.
    - Connect the product syringe to the other arm of the Y-connector and ensure the clamp is closed.
    - Connect the terminal end of the Y-connector to the microbore tubing.
    - Remove the cap from the supply side of the 0.2 micron filter and attach it to the terminal end of the microbore tubing.
    - Unclamp the arm of the Y-connector connected to the saline flush syringe. Prime the Y-connector up to the intersection (do not prime the full infusion set with saline). Re-clamp the Y-connector line on the saline flush arm.
    - Remove the cap on the terminal end of the 0.2 micron filter and set it aside. Unclamp the arm of the Y-connector connected to the product syringe, and prime the entire infusion set, including the filter. Recap the filter, and re-clamp the Y-connector line on the product side. The infusion set is now ready for delivery for dose administration.
- Administer ELZONRIS within 4 hours. During this 4-hour window, the prepared dose should remain at room temperature.

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

### 2.4 Administration

- Establish venous access and maintain with sterile 0.9% Sodium Chloride Injection, USP.
- Administer the prepared ELZONRIS dose via infusion syringe pump over 15 minutes. The total infusion time will be controlled using a syringe pump to deliver the entire dose and the saline flush over 15 minutes.
- Insert the ELZONRIS syringe into the syringe pump, open the clamp on the ELZONRIS side of the Y-connector and deliver the prepared ELZONRIS dose.
- Once the ELZONRIS syringe has been emptied, remove it from the pump and place the saline flush syringe in the syringe pump.
- Open the clamp on the saline flush side of the Y-connector and resume infusion via the syringe pump at the pre-specified flow to push remaining ELZONRIS dose out of the infusion line to complete delivery.

## 3 DOSAGE FORMS AND STRENGTHS

Injection: 1,000 mcg in 1 mL clear colorless solution in a single-dose vial.

## 4 CONTRAINDICATIONS

None.

## 5 WARNINGS AND PRECAUTIONS

### 5.1 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 55% (52/94), including Grade 1 or 2 in 46% (43/94), Grade 3 in 6% (6/94), Grade 4 in 1% (1/94) and 2 fatal events (2/94, 2%). Common signs and symptoms (incidence ≥ 20%) associated with CLS that were reported during treatment with ELZONRIS include hypoalbuminemia, edema, weight gain, and hypotension.

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 *[see Dose Modifications (2.2)]*.

### 5.2 Hypersensitivity Reactions

ELZONRIS can cause severe hypersensitivity reactions. In patients receiving ELZONRIS in clinical trials, hypersensitivity reactions were reported in 46% (43/94) of patients treated with ELZONRIS and were Grade ≥ 3 in 10% (9/94). Manifestations of hypersensitivity reported in ≥ 5% of patients include rash, pruritus, stomatitis, and wheezing. Monitor patients for hypersensitivity reactions during treatment with ELZONRIS. Interrupt ELZONRIS infusion and provide supportive care as needed if a hypersensitivity reaction should occur *[see Dose Modifications (2.2)]*.

### 5.3 Hepatotoxicity

Treatment with ELZONRIS was associated with elevations in liver enzymes. In patients receiving ELZONRIS in clinical trials, elevations in liver enzymes occurred in 88% (83/94) of patients, including Grade 1 or 2 in 48% (45/94), Grade 3 in 36% (34/94), and Grade 4 in 4% (4/94). 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 *[see Dose Modifications (2.2)]*.

## 6 ADVERSE REACTIONS

The following serious adverse drug reactions are described elsewhere in the labeling:

- Capillary Leak Syndrome [*see Warnings and Precautions (5.1)*]
- Hypersensitivity Reactions [*see Warnings and Precautions (5.2)*]
- Hepatotoxicity [*see Warnings and Precautions (5.3)*]

### 6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Safety of ELZONRIS was assessed in a single-arm clinical trial that included 94 adults with newly-diagnosed or relapsed/refractory myeloid malignancies, including 58 with BPDCN, treated with ELZONRIS 12 mcg/kg daily for 5 days of a 21-day cycle. The overall median number of cycles administered was 2 (range, 1-43), and 4 in patients with BPDCN (range, 1-43).

Two (2%) patients had fatal adverse reaction, both capillary leak syndrome. Overall, 10 (11%) patients discontinued treatment with ELZONRIS due to an adverse reaction; the most common adverse reactions resulting in treatment discontinuation were hepatic toxicities and CLS.

Table 3 summarizes the common (≥ 10%) adverse reactions with ELZONRIS in patients with myeloid malignancies. The rate of any given adverse reaction or lab abnormality was derived from all the reported events of that type.

**Table 3. Adverse Reactions in ≥ 10% of Patients Receiving 12 mcg/kg of ELZONRIS**

| | N=94 | |
|---|---|---|
| | **All Grades %** | **Grade ≥ 3 %** |
| **Vascular disorders** | | |
| Capillary leak syndrome[1] | 55 | 9 |
| Hypotension | 29 | 9 |
| Hypertension | 15 | 6 |
| **Gastrointestinal disorders** | | |
| Nausea | 49 | 0 |
| Constipation | 23 | 0 |
| Vomiting | 21 | 0 |
| Diarrhea | 20 | 0 |

| | N=94 | |
|---|---|---|
| | **All Grades %** | **Grade ≥ 3 %** |
| **General disorders and administration site conditions** | | |
| Fatigue | 45 | 7 |
| Peripheral edema | 43 | 1 |
| Pyrexia | 43 | 0 |
| Chills | 29 | 1 |
| **Investigations** | | |
| Weight increase | 31 | 0 |
| **Nervous system disorders** | | |
| Headache | 29 | 0 |
| Dizziness | 20 | 0 |
| **Metabolism and nutrition disorders** | | |
| Decreased appetite | 24 | 0 |
| **Blood and lymphatic system disorders** | | |
| Febrile neutropenia | 20 | 18 |
| **Musculoskeletal and connective tissue disorders** | | |
| Back pain | 20 | 2 |
| Pain in extremity | 10 | 2 |
| **Respiratory, thoracic and mediastinal disorders** | | |
| Dyspnea | 19 | 2 |
| Cough | 14 | 0 |
| Epistaxis | 14 | 1 |
| Oropharyngeal pain | 12 | 0 |
| **Psychiatric disorders** | | |
| Insomnia | 17 | 0 |
| Anxiety | 15 | 0 |
| Confusional state | 11 | 0 |
| **Cardiac disorders** | | |
| Tachycardia | 17 | 0 |
| **Skin and subcutaneous tissue disorders** | | |
| Petechiae | 10 | 0 |
| Pruritus | 10 | 0 |
| **Renal and urinary disorders** | | |
| Hematuria | 10 | 0 |

[1] Capillary leak syndrome defined as any event reported as CLS during treatment with ELZONRIS or the occurrence of at least 2 of the following CLS manifestations within 7 days of each other: hypoalbuminemia (including albumin value less than 3.0 g/dL), edema (including weight increase of 5 kg or more), hypotension (including systolic blood pressure less than 90 mmHg).

Table 4 summarizes the clinically-important laboratory abnormalities that occurred in ≥ 10% patients with myeloid malignancies treated with ELZONRIS.

**Table 4. Selected Laboratory Abnormalities in Patients Receiving 12 mcg/kg of ELZONRIS**

| | Treatment-Emergent Laboratory Abnormalities | |
|---|---|---|
| | **All Grades %** | **Grade ≥ 3 %** |
| **Hematology** | | |
| Platelets decrease | 67 | 53 |
| Hemoglobin decrease | 60 | 35 |
| Neutrophils decrease | 37 | 31 |
| **Chemistry** | | |
| Glucose increase | 87 | 20 |
| ALT increase | 82 | 30 |
| AST increase | 79 | 37 |
| Albumin decrease | 77 | 0 |
| Calcium decrease | 57 | 2 |
| Sodium decrease | 50 | 10 |
| Potassium decrease | 39 | 4 |
| Phosphate decrease | 30 | 11 |
| Creatinine increase | 27 | 0 |
| Alkaline phosphatase increase | 26 | 1 |
| Potassium increase | 21 | 2 |
| Magnesium decrease | 20 | 0 |
| Magnesium increase | 14 | 3 |
| Bilirubin increase | 14 | 0 |
| Glucose decrease | 11 | 0 |
| Sodium increase | 10 | 0 |

## 6.2 Immunogenicity

As with all therapeutic proteins, there is potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to ELZONRIS with the incidences of antibodies to other products may be misleading.

Immune response to ELZONRIS was evaluated by assessment of serum binding reactivity against ELZONRIS (anti-drug antibodies; ADA) and neutralizing antibodies by inhibition of functional activity. Immune response to ELZONRIS was assessed using two immunoassays. The first assay detected reactivity directed against ELZONRIS (ADA), and the second assay detected reactivity against the interleukin-3 (IL-3) portion of ELZONRIS. Two cell-based assays were used to investigate the presence of neutralizing antibodies by inhibition of a cell-based functional activity.

The presence of ADA had a clinically significant effect on the pharmacokinetics of tagraxofusp-erzs *[see Clinical Pharmacology (12.2)]*. In 130 patients treated with ELZONRIS in 4 clinical trials:

- 96% (115/120) of patients evaluable for the presence of pre-existing ADA at baseline before treatment were confirmed positive with 21% being positive for the presence of neutralizing antibodies. The high prevalence of ADA at baseline was anticipated due to diphtheria immunization.

- 99% (107/108) of patients evaluable for treatment-emergent ADA tested positive with most patients showing an increase in ADA titer by the end of Cycle 2 of ELZONRIS.

- 85% (86/101) of ADA-positive patients evaluable for the presence of neutralizing antibodies were neutralizing antibody-positive.

- 68% (73/108) of patients evaluable for treatment-emergent anti-IL-3 antibodies tested positive with most patients testing positive by Cycle 3 of ELZONRIS.

## 8 USE IN SPECIFIC POPULATIONS

### 8.1 Pregnancy

Risk Summary

Based on its mechanism of action, ELZONRIS has the potential for adverse effects on embryo-fetal development *[see Clinical Pharmacology (12.1)]*. There are no available data on ELZONRIS use in pregnant women to inform a drug-associated risk of adverse developmental outcomes. Animal reproduction or developmental toxicity studies have not been conducted with tagraxofusp-erzs. Advise pregnant women of the potential risk to the fetus.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4%, and 15% to 20%, respectively.

### 8.2 Lactation

Risk Summary

No data are available regarding the presence of ELZONRIS in human milk, the effects on the breastfed child, or the effects on milk production. Because of the potential for serious adverse reactions in breastfed children from ELZONRIS, breast feeding is not recommended during treatment and for 1 week after the last dose.

### 8.3 Females and Males of Reproductive Potential

Based on its mechanism of action, ELZONRIS may cause fetal harm when administered to a pregnant woman *[see Use in Specific Populations (8.1)]*.

Pregnancy Testing:

Conduct pregnancy testing in females of reproductive potential within 7 days prior to initiating ELZONRIS treatment.

Contraception:

Advise females to use acceptable contraceptive methods during ELZONRIS treatment and for at least 1 week after the last dose of ELZONRIS.

### 8.4 Pediatric Use
The safety and effectiveness of ELZONRIS for treatment of BPDCN have been established in pediatric patients 2 years of age and older (no data for pediatric patients less than 2 years of age). Use of ELZONRIS in these age groups is supported by evidence from an adequate and well-controlled study of ELZONRIS in adults with BPDCN and additional safety data from three pediatric patients with BPDCN, including 1 child (2 years to < 12 years old) and 2 adolescents (12 years to < 17 years old), treated with ELZONRIS at the recommended dosage. The safety profile of ELZONRIS in the pediatric patients was similar to that seen in the adults. Efficacy for pediatric patients is extrapolated from the results of STML-401-0114 *[see Clinical Studies 14.1, 14.2]*.

### 8.5 Geriatric Use
Of the 94 patients who received ELZONRIS at the labeled dose in STML-401-0114, 23% were 75 years and older. The older patients experienced a higher incidence of altered mental status (including confusional state, delirium, mental status changes, dementia, and encephalopathy) than younger patients.

## 11 DESCRIPTION
Tagraxofusp-erzs, a CD123-directed cytotoxin, is a fusion protein comprised of a recombinant human interleukin-3 (IL-3) and truncated diphtheria toxin (DT). Tagraxofusp-erzs has an approximate molecular weight of 57,695 Daltons. Tagraxofusp-erzs is constructed by recombinant DNA technology and produced in *Escherichia coli* cells.

ELZONRIS (tagraxofusp-erzs) injection is a preservative-free, sterile, clear, colorless solution that may contain a few white to translucent particles and requires dilution prior to intravenous infusion. ELZONRIS is supplied at a concentration of 1,000 mcg/mL in a single-dose vial. Each mL of ELZONRIS contains 1,000 mcg tagraxofusp-erzs, sodium chloride (4.38 mg), sorbitol (50 mg), tromethamine (2.42 mg) and Water for Injection, USP and pH is 7.5.

## 12 CLINICAL PHARMACOLOGY

### 12.1 Mechanism of Action
Tagraxofusp-erzs is a CD123-directed cytotoxin composed of recombinant human interleukin-3 (IL-3) and truncated diphtheria toxin (DT) fusion protein that inhibits protein synthesis and causes cell death in CD123-expressing cells.

### 12.2 Pharmacokinetics
Following administration of tagraxofusp-erzs 12 mcg/kg via 15-minute infusion in patients with BPDCN, the mean (SD) area under the plasma drug concentration over time curve (AUC) was 231 (123) hr·mcg/L and maximum plasma concentration (Cmax) was 162 (58.1) mcg/L.

Distribution
Mean (SD) volume of distribution of tagraxofusp-erzs is 5.1 (1.9) L in patients with BPDCN.

Elimination
Mean (SD) clearance is 7.1 (7.2) L/hr in patients with BPDCN. Mean (SD) terminal half-life of tagraxofusp-erzs is 0.7 (0.3) hours.

Anti-Product Antibody Formation Affecting Pharmacokinetics

Pharmacokinetic data obtained following doses given in Cycle 3 showed increased titers of anti-drug antibodies and reduced free ELZONRIS concentration in most plasma samples. Following administration of tagraxofusp-erzs 12 mcg/kg via 15-minute infusion in patients with pre-existing anti-drug antibodies, the mean (SD) volume of distribution of tagraxofusp-erzs is 21.2 (25.4) L, clearance is 13.9 (19.4) L/hr, AUC is 151 (89.2) hr·mcg/L and Cmax is 80.0 (82.2) mcg/L.

Specific Populations

No clinically significant differences in the pharmacokinetics of tagraxofusp-erzs were observed based on age (22 to 84 years), sex, mild to moderate renal impairment (eGFR 30 to 89 mL/min/1.73 $m^2$, estimated by MDRD), mild (total bilirubin ≤ ULN and AST >ULN, or total bilirubin 1 to 1.5 times ULN and any AST) or moderate (total bilirubin >1.5 to 3 times ULN and any AST) hepatic impairment or body weight after adjusting dose by body weight. The effect of severe renal impairment (eGFR 15 to 29 mL/min/1.73 $m^2$), or severe hepatic impairment (total bilirubin >3 times ULN and any AST) on tagraxofusp-erzs pharmacokinetics is unknown.

Drug Interaction Studies

No drug-drug interaction studies have been conducted with ELZONRIS.

## 13 NONCLINICAL TOXICOLOGY

### 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

No studies have been conducted to assess the carcinogenic or genotoxic potential of tagraxofusp. Animal fertility studies have not been conducted with tagraxofusp-erzs.

### 13.2 Animal Toxicology and/or Pharmacology

At human equivalent doses greater than or equal to 1.6 times the recommended dose based on body surface area, severe kidney tubular degeneration/necrosis was observed in cynomolgus monkeys. At human equivalent doses equal to the recommended dose, degeneration/necrosis of the choroid plexus in the brain was observed in cynomolgus monkeys. The reversibility of this finding was not assessed at lower doses, but the finding was irreversible and became progressively more severe at a human equivalent dose 1.6 times the recommended dose, 3 weeks after dosing stopped.

## 14 CLINICAL STUDIES

### 14.1 First-Line Treatment of Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN)

STML-401-0114 (NCT 02113982; Study 0114) was a multicenter, open-label, single-arm, clinical trial that included a prospective cohort of 13 patients with treatment-naive BPDCN. Treatment consisted of ELZONRIS 12 mcg/kg intravenously over 15 minutes once daily on days 1 to 5 of a 21-day cycle. Patient baseline characteristics are presented in Table 5.

**Table 5. Baseline Demographics of Patients with Treatment-Naive BPDCN**

| Parameter | N=13 |
|---|---|
| Gender, N (%) | |
| Male | 11 (84.6) |
| Female | 2 (15.4) |
| Age (years), N (%) | |
| Median | 65.0 |
| Minimum, Maximum | 22, 84 |
| ECOG, N (%) | |
| 0 | 8 (61.5) |
| 1 | 5 (38.5) |
| BPDCN at Baseline, N (%) | |
| Skin | 13 (100.0) |
| Bone Marrow | 7 (53.8) |
| Peripheral Blood | 3 (23.1) |
| Lymph Nodes | 6 (46.2) |
| Viscera | 2 (15.4) |

The efficacy of ELZONRIS in patients with treatment-naive BPDCN was based on the rate of complete response or clinical complete response (CR/CRc). Key efficacy measures are presented in Table 6. The median time to CR/CRc was 57 days (range: 14 to 107).

**Table 6. Efficacy Measures in Patients with Treatment-Naive BPDCN**

| Parameter | N=13 |
|---|---|
| CR/CRc* Rate, N (%) | 7 (53.8) |
| (95% CI) | (25.1, 80.8) |
| Duration of CR/CRc (months) | |
| Median | Not Reached |
| Minimum, Maximum | 3.9, 12.2 |
| Duration of follow up (months) | |
| Median | 11.5 |
| Minimum, Maximum | 0.2, 12.7 |

* CRc is defined as complete response with residual skin abnormality not indicative of active disease.

## 14.2 Relapsed or Refractory Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN)

STML-401-0114 (NCT02113982; Study 0114) was a multicenter, open-label, single-arm, clinical trial that included 15 patients with relapsed or refractory BPDCN. Treatment consisted of ELZONRIS 12 mcg/kg on days 1 to 5 of each 21-day cycle. Patient baseline characteristics are presented in Table 7.

**Table 7. Baseline Demographics of Patients with Relapsed or Refractory BPDCN**

| Parameter | (N=15) |
|---|---|
| Gender, N (%) | |
| Male | 13 (86.7) |
| Female | 2 (13.3) |
| Age (years) | |
| Median | 72 |
| Minimum, Maximum | 44, 80 |
| ECOG, N (%) | |
| 0 | 5 (33.3) |
| 1 | 10 (66.7) |
| BPDCN at Baseline, N (%) | |
| Skin | 13 (86.7) |
| Bone marrow | 9 (60.0) |
| Lymph node | 8 (53.3) |
| Visceral | 4 (26.7) |
| Peripheral blood | 1 (6.7) |

In the 15 patients with relapsed/refractory BPDCN, one patient achieved a CR (duration: 111 days) and one patient achieved a CRc (duration: 424 days).

## 16 HOW SUPPLIED/STORAGE AND HANDLING

### 16.1 How Supplied

ELZONRIS (tagraxofusp-erzs) injection is a preservative-free, sterile, clear, colorless, 1,000 mcg in 1 mL solution supplied in a single-dose glass vial. Each carton contains one vial (NDC 72187-0401-1).

### 16.2 Storage and Handling

Store in freezer between -25°C and -15°C (-13°F and 5°F). Protect ELZONRIS from light by storing in the original package until time of use. Thaw vials at room temperature between 15°C and 25°C (59°F and 77°F) prior to preparation *[see Preparation for Administration (2.3)]*. Do not refreeze the vial once thawed. Do not use beyond expiration date on container.

## 17 PATIENT COUNSELING INFORMATION

Capillary Leak Syndrome

Advise patients of the risk of capillary leak syndrome (CLS), and to contact their health care professional 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 *[see Warnings and Precautions (5.1)]*.

Hypersensitivity

Advise patients of the risk of hypersensitivity reactions, and to contact their healthcare professional for signs and symptoms associated with hypersensitivity reactions including rash, flushing, wheezing and swelling of the face *[see Warnings and Precautions (5.2)]*.

Hepatic Toxicity
Advise patients to report symptoms that may indicate elevated liver enzymes including fatigue, anorexia and/or right upper abdominal discomfort *[see Warnings and Precautions (5.3)]*.

Contraception
Advise females to avoid pregnancy and to use acceptable contraceptive methods during ELZONRIS treatment and for at least 1 week after the last dose of ELZONRIS.

Lactation
Advise women not to breastfeed *[see Use in Specific Populations (8.2)]*.

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