

## Corporate Medical Policy

### Tagraxofusp-erzs (Elzonris™)

<b>File Name:</b>	tagraxofusp_elzonris
<b>Origination:</b>	3/2019
<b>Last CAP Review:</b>	4/2020
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#### Description of Procedure or Service

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Tagraxofusp-erzs (Elzonris™) is a CD123-directed cytotoxin for the treatment of blastic plasmacytoid dendritic cell neoplasm (BPDCN) in adults and pediatric patients 2 years of age and older.

BPDCN is a rare and aggressive hematologic malignancy that usually manifests as cutaneous lesions, with or without involvement of the bone marrow and leukemic dissemination in the peripheral blood. The histologic classification of this entity has evolved from blastic natural killer (NK) lymphoma to being of dendritic cell origin (plasmacytoid type 2 dendritic cells) in the 2008 WHO classification. BPDCN is most common in older adults, with a median age at diagnosis of 65 years. Approximately 10-20% of individuals with BPDCN have a history of a prior hematologic malignancy, including myelodysplasia, and acute or chronic myeloid leukemia. Diagnosis of BPDCN requires histopathologic examination of skin lesions, if present, and immunophenotypic confirmation on tissue or blood, either by immunohistochemistry or flow cytometry.

Optimal treatment of BPDCN is not well defined, and the approach may differ depending upon patient age. Treatment for remission induction, with or without central nervous system prophylaxis, may include tagraxofusp. Post first remission management may include allogeneic hematopoietic cell transplantation in adults. Treatment of relapsed and refractory disease is influenced by prior therapy, and salvage may include tagraxofusp as first time or repeat use.

Tagraxofusp-erzs (Elzonris) is a fusion protein consisting of a recombinant human interleukin-3 (IL-3) and truncated diphtheria toxin (DT) that was approved by the U.S. Food and Drug Administration (FDA) in December 2018 for the treatment of BPDCN. It works by inhibiting protein synthesis and causing cell death in CD123-expressing cells.

**\*\*\*Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.**

#### Policy

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**BCBSNC will provide coverage for tagraxofusp-erzs (Elzonris™) when it is determined to be medically necessary because the medical criteria and guidelines noted below are met.**

#### Benefits Application

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This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit

# Tagraxofusp-erzs (Elzonris™)

design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

## When Tagraxofusp-erzs (Elzonris) is covered

### Initial Therapy

Tagraxofusp-erzs (Elzonris) is considered medically necessary as initial or salvage treatment of blastic plasmacytoid dendritic cell neoplasm (BPDCN) when the following criteria are met:

- The patient is 2 years of age or older, and
- There is immunophenotypic confirmation of the diagnosis, including CD-123 expression, and
- The patient has a serum albumin level of at least 3.2 g/dL prior to each course of therapy

Initial authorization: 6 months

### Continuation Therapy

Continuation of treatment with tagraxofusp-erzs (Elzonris) beyond 6 months after initiation of therapy, and every 6 months thereafter, is considered medically necessary for the treatment of blastic plasmacytoid dendritic cell neoplasm (BPDCN) when the following criteria are met:

- The patient has been receiving tagraxofusp-erzs treatment previously, and
- The patient has not had disease progression or unacceptable toxicity while receiving tagraxofusp-erzs

Use of tagraxofusp-erzs (Elzonris) may be considered medically necessary for clinical indications not listed above when the drug is prescribed for the treatment of cancer either:

- In accordance with FDA label (when clinical benefit has been established, (see Policy Guidelines); **OR**
- In accordance with specific strong endorsement or support by nationally recognized compendia, when such recommendation is based on strong/high levels of evidence, and/or uniform consensus of clinical appropriateness has been reached

## When Tagraxofusp-erzs (Elzonris) is not covered

Tagraxofusp-erzs (Elzonris) is considered **investigational** and therefore not covered when the above criteria are not met.

Tagraxofusp-erzs (Elzonris) is considered investigational when used for:

1. Non-cancer indications; **OR**
2. When criteria are not met regarding FDA labeling **OR** strong endorsement/support by nationally recognized compendia, as stated under “When Tagraxofusp-erzs (Elzonris) is covered.”

# Tagraxofusp-erzs (Elzonris™)

## Policy Guidelines

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Tagraxofusp may be used as part of initial (remission induction) and/or salvage therapy, depending upon patient age and other therapies used.

The recommended dose of Elzonris is 12 mcg/kg administered intravenously over 15 minutes once daily on days 1 to 5 of a 21-day cycle and continued until disease progression or unacceptable toxicity.

According to the manufacturer's safety information for Elzonris, the most common adverse reactions ( $\geq 30\%$  incidence) include capillary leak syndrome, nausea, fatigue, peripheral edema, fever, and weight gain. The most common laboratory abnormalities ( $\geq 50\%$  incidence) include decreases in platelets, albumin, hemoglobin, calcium and sodium, and increases in glucose, AST and ALT.

Capillary leak syndrome may be life-threatening or fatal. Therefore, the patient's serum albumin must be greater than or equal to 3.2 g/dL prior to administering the first Elzonris dose of the first cycle. Patients should also be premedicated with an H1-histamine antagonist (e.g., diphenhydramine), acetaminophen, corticosteroid (e.g., 50 mg intravenous methylprednisolone or equivalent), and H2-histamine antagonist (e.g., ranitidine) before each Elzonris infusion.

The efficacy and safety of tagraxofusp-erzs (Elzonris) for the treatment of blastic plasmacytoid dendritic cell neoplasm (BPDCN) has been described in two multicenter, open-label, single arm trials that included 13 patients with treatment-naïve BPDCN (Study 1) and 15 patients with relapsed or refractory BPDCN (Study 2). In study 1, median patient age was 65 years, and all patients had skin involvement; 54% had bone marrow involvement, 23% had leukemic dissemination and 46% had nodal involvement. The efficacy was based on clinical complete response (CR/CRC, with CRC defined as CR with residual skin abnormality not indicative of active disease). CR/CRC rate was 53.8% (95% confidence interval 25.1-80.8). Median duration of CR/CRC was not reached (range 3.9-12.2 months) after a median duration of follow-up of 11.5 months (range 0.2-12.7 months). Patients in study 2 were a median age of 72 years. Only one patient achieved a CR, for a duration of 111 days, and one patient achieved a CRC for a duration of 424 days.

Drugs prescribed for treatment of cancer in accordance with FDA label may be considered medically necessary when clinical benefit has been established, and should not be determined to be investigational as defined in Corporate Medical Policy (CMP), "Investigational (Experimental) Services."

Please refer to CMP "Investigational (Experimental) Services" for a summary of evidence standards from nationally recognized compendia.

## Billing/Coding/Physician Documentation Information

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This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at [www.bcbsnc.com](http://www.bcbsnc.com). They are listed in the Category Search on the Medical Policy search page.

*Applicable codes: J9269, S0353, S0354*

# Tagraxofusp-erzs (Elzonris™)

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

## Scientific Background and Reference Sources

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Stemline Therapeutics, Inc. Elzonris (tagraxofusp-erzs) injection for intravenous use. Highlights of prescribing information. December 2018. Available at: [https://www.elzonris.com/hcp/resources/ELZONRIS\\_US\\_Full\\_Prescribing\\_Information.pdf](https://www.elzonris.com/hcp/resources/ELZONRIS_US_Full_Prescribing_Information.pdf). Accessed March 2019.

U.S. Food and Drug Administration. FDA approves first treatment for rare blood disease. Available at: <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm629020.htm>. Accessed March 2019.

Pemmaraju N, Sweet KL, Lane AA, et al. Results of a pivotal phase 2 trial of SL-401 in patients with blastic plasmacytoid dendritic cell neoplasm (BPDCN). *Blood*. 2017;130:1298.

Medical Director review 4/2019

Specialty Matched Consultant Advisory Panel 11/2019

Specialty Matched Consultant Advisory Panel 4/2020

## Policy Implementation/Update Information

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4/16/19 New policy developed. Elzonris is considered medically necessary as initial or salvage treatment of blastic plasmacytoid dendritic cell neoplasm (BPDCN). Added HCPCS codes C9399, J3490, J3590, J9999, S0353, and S0354 to Billing/Coding section. References added. Medical Director review 4/2019. (krc)

7/1/19 Added HCPCS code C9049 to Billing/Coding section and deleted code C9399. (krc)

10/1/19 Added HCPCS code J9269 to Billing/Coding section and deleted codes C9049, J3490, J3590, and J9999 effective 10/1/19. (krc)

12/2/19 Specialty Matched Consultant Advisory Panel review 11/20/2019. No change to policy intent. (krc)

6/9/20 Specialty Matched Consultant Advisory Panel review 4/15/2020. No change to policy intent. (krc)

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Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.