Elzonris™ (tagraxofusp-erzs)
(Intravenous)

-E-

Document Number: IC-0539

Last Review Date: 05/03/2021
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I. Length of Authorization

Coverage will be provided for 6 months and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Elzonris 1000 mcg/1 mL single dose vial: 10 vials per 21 day cycle

B. Max Units (per dose and over time) [HCPCS Unit]:

- 200 billable units on days 1-5 of every 21 day cycle

III. Initial Approval Criteria [1-6]

Coverage is provided in the following conditions:

- Patient is 2 at least years of age; **AND**
- Patient has a baseline serum albumin level of at least 3.2 g/dL; **AND**

Universal Criteria [1-6]

- Patient has CD-123 positive/expressing disease; **AND**
- Patient does not have significant cardiovascular disease (e.g., uncontrolled or any NYHA Class 3 or 4 congestive heart failure, uncontrolled angina, history of myocardial infarction or stroke within 6 months of initiating therapy, uncontrolled hypertension or clinically significant arrhythmias not controlled by medication, baseline left ventricular ejection fraction < 40%); **AND**
- Patient does not have active or suspected CNS leukemia; **AND**

Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN) † Φ [1-6]

- Must be used as a single agent; **AND**
- Patient must have a definitive diagnosis of BPDCN in the peripheral blood, bone marrow, spleen, lymph nodes, skin, and/or other sites; **AND**

- Used as induction therapy in treatment-naïve patients who are candidates for intensive remission therapy; **OR**
- Used as treatment until progression if a complete response (CR) was achieved after induction; **OR**
- Used as treatment for relapsed/refractory disease if not already used

Preferred therapies and recommendations are determined by review of clinical evidence. NCCN category of recommendation is taken into account as a component of this review. Regimens deemed equally efficacious (i.e., those having the same NCCN categorization) are considered to be therapeutically equivalent.

† FDA-labeled indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1-6]

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: capillary leak syndrome, severe hypersensitivity reactions, severe hepatotoxicity, etc.; **AND**
- Disease stabilization or improvement as evidenced by a complete response [CR] *(i.e., morphologic, cytogenetic or molecular complete response)* or clinical complete response [CRc] (*i.e., complete response with residual skin abnormality not indicative of active disease*)

V. Dosage/Administration[1,2,6]

Indication	Dose
BPDCN	Administer 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 until disease progression or unacceptable toxicity. • Administer Cycle 1 in the inpatient setting with patient observation through at least 24 hours after the last infusion. Subsequent cycles are suitable for administration in the outpatient ambulatory care setting with appropriate monitoring.

**Store in a freezer between-25°C and -15°C (-13°F and 5°F).*

VI. Billing Code/Availability Information

HCPCS code:

- J9269 – Injection, tagraxofusp-erzs, 10 micrograms; 1 billable unit = 10 mcg

NDC:

- Elzonris 1000 mcg/1 mL single-dose vials: 72187-0401-xx

VII. References (STANDARD)

1. Elzonris [package insert]. New York, NY; Stemline Therapeutics; December 2018. Accessed April 2021.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) tagraxofusp-erzs. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed April 2021.
3. Pemmaraju N, Sweet KL, Lane AA, et al. Results of Pivotal Phase 2 Trial of SL-401 in Patients with Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN). Blood 2017 130:1298
4. Sweet KL, Pemmaraju N, Lane AA, et al. Lead-in Stage Results of a Pivotal Trial of SL-401, an Interleukin-3 Receptor (IL-3R) Targeting Biologic, in Patients with Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN) or Acute Myeloid Leukemia (AML). Blood 2015 126:3795
5. Pemmaraju N, Lane AA, Sweet KL, et al. Results from Phase 2 Trial Ongoing Expansion Stage of SL-401 in Patients with Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN). Blood 2016 128:342
6. Pemmaraju N, Lane AA, Sweet KL, et al. Tagraxofusp in Blastic Plasmacytoid Dendritic-Cell Neoplasm. N Engl J Med. 2019 Apr 25;380(17):1628-1637. doi: 10.1056/NEJMoa1815105.

VIII. References (ENHANCED)

1e. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Acute Myeloid Leukemia, Version 3.2021. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed April 2021.

2e. Pagano L, Valentini CG, Pulsoni A, et al. Blastic plasmacytoid dendritic cell neoplasm with leukemic presentation: an Italian multicenter study. Haematologica. 2013;98(2):239–246. doi:10.3324/haematol.2012.072645.

3e. Montero J, Stephansky J, Cai T, et al. Blastic Plasmacytoid Dendritic Cell Neoplasm Is Dependent on BCL2 and Sensitive to Venetoclax. Cancer Discov. 2017;7(2):156–164. doi:10.1158/2159-8290.CD-16-0999.

4e. DiNardo CD, Rausch CR, Benton C, et al. Clinical experience with the BCL2-inhibitor venetoclax in combination therapy for relapsed and refractory acute myeloid leukemia and related myeloid malignancies. Am J Hematol. 2018;93(3):401–407. doi:10.1002/ajh.25000.

5e. Magellan Health, Magellan Rx Management. Elzonris Clinical Literature Review Analysis. Last updated April 2021. Accessed April 2021.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C86.4	Blastic NK-cell lymphoma

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC

Appendix 3 – CLINICAL LITERATURE REVIEW

OS = overall survival; PFS = progression-free survival; ORR = objective response rate; CR = complete response; PR = partial response; DoR = duration of response; TTP = time to progression; FFS = failure-free survival; EFS = event-free survival; PFR = progression free rate; SCT = stem-cell transplant

Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN)

Induction therapy							
Regimen	**NCCN Category**	**FDA Approved**	**Trial Design**	**Comparator**	**Primary End-Point**	**Line of Therapy**	**Conclusion**
Tagraxofusp-erzs	2A	Yes	Phase 2, open-label, multi-cohort	N/A	CR + clinical CR	Previously untreated disease	• In adult patients with untreated BPDCN, tagraxofusp led to an ORR of 90%.
Cytarabine + idarubicin or daunorubicin *AML induction*	2A	No	Retrospective multi-center study	N/A	-----	Induction therapy	• Out of 26 patients who received AML-type induction therapy, 7 patients achieved complete remission.
Hyper CVAD (cyclophosphamide + vincristine + doxorubicin + dexamethasone + methotrexate + cytarabine) *ALL induction* CHOP (cyclophosphamide + doxorubicin +	2A	No	Retrospective multi-center study	N/A	-----	Induction therapy	• Out of 15 patients who received ALL/Lymphoma-type induction therapy, 10 patients achieved complete remission.

vincristine + prednisone) *Lymphoma induction*							
Relapsed or refractory disease							
Regimen	**NCCN Category**	**FDA Approved**	**Trial Design**	**Comparator**	**Primary End-Point**	**Line of Therapy**	**Conclusion**
Tagraxofusp-erzs	2A	Yes	Phase 2, open-label, multi-cohort	N/A	CR + clinical CR	Persistent, refractory, or recurrent disease	• In adult patients with relapsed BPDCN, tagraxofusp led to an ORR of 67%.
Venetoclax	2A	No	Case report	N/A	-----	Relapsed or refractory disease	• 2 patients with relapsed/ refractory BPDCN who received venetoclax off-label and experienced significant disease responses.
Venetoclax-based therapy (in combination with a hypomethylating agent or low-dose cytarabine)	2A	No	Retrospective study	N/A	-----	Relapsed or refractory disease	• Low-intensity chemotherapy, including hypomethylating agents or low-dose cytarabine, in combination with venetoclax is a viable salvage option with an ORR 21%, even in relapsed/refractory patients with AML, MDS, and BPDCN.