I. PURPOSE
To define and describe the accepted indications for Elzonris (tagraxofusp) usage in the treatment of cancer.

II. DEFINITIONS
Elzonris (tagraxofusp): is a CD123-directed cytotoxin. Tagraxofusp consists of a cytotoxic agent, truncated diphtheria toxin (DT), attached to a recombinant fusion protein, IL3. The IL3 domain binds to its natural receptor, DT is released into the cytosol and causes protein synthesis inhibition and cell death in CD123-expressing cells. Blastic plasmacytoid dendritic cell neoplasm blast cells have high CD123 or interleukin-3 receptor (IL3)-alpha surface expression.

Elzonris (tagraxofusp) is FDA approved for the treatment of blastic plasmacytoid dendritic cell neoplasm (BPDCN) in adults and in pediatric patients 2 years and older.

Elzonris (tagraxofusp) is available in 1,000 mcg in 1 mL in a single-dose vial for injection.

III. POLICY
New Century Health is responsible for processing all medication requests from network ordering providers. Medications not authorized by New Century Health may be deemed as not approvable and therefore not reimbursable. Treatment request outside the approved FDA manufacturer labeling or CMS approved compendia must follow CMS Medicare Beneficiary Policy Manual Chapter 15. If references are not produced, delays may occur to the processing of such request.

Inclusion Criteria: Elzonris (tagraxofusp) may be considered medically necessary when any of the following selection criteria are met:

1. Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN)
   a. The member has BPDCN and Elzonris (tagraxofusp) is being used as a single agent AND
   b. Has adequate cardiac function with a left ventricular ejection fraction (LVEF) ≥ 40% as measured by MUGA scan or 2-D ECHO AND
   c. Prior to administering the first dose in cycle 1 ALL of the following:
      i. A serum albumin level of 3.2 g/dL or greater
      ii. Serum creatinine ≤ 1.5 mg/dl
      iii. Bilirubin ≤ 1.5 mg/dl
iv. AST and ALT ≤ 2.5 times the upper limit of normal (ULN).

Exclusion Criteria: Elzonris (tagraxofusp) is not considered medically necessary when any of the following selection criteria are met:

1. Elzonris (tagraxofusp) is being used after disease progression with the same regimen.
2. Concurrent use with other chemotherapy.
3. Dosing exceeds single dose limit of Elzonris (tagraxofusp) 12 mcg/kg.
4. Indications not supported by CMS recognized compendia or acceptable peer reviewed literature may be deemed as not approvable and therefore not reimbursable.

IV. PROCEDURE

Requests for Elzonris (tagraxofusp) shall be reviewed for appropriateness per FDA approved product labeling, the National Comprehensive Cancer Network (NCCN) and American Society of Clinical Oncology (ASCO) clinical guidelines, or CMS approved compendia.

1. **Dosage and Administration:** 12 micrograms/kg IV once daily on days 1, 2, 3, 4, and 5 repeated every 21 days until disease progression. Premedicate patients with an H1-histamine antagonist (e.g., diphenhydramine), H2-histamine antagonist (e.g., ranitidine), corticosteroid (e.g., methylprednisolone 50 mg IV or equivalent), and acetaminophen about 60 minutes prior to each infusion. Administer the first cycle in the inpatient setting. Subsequent cycles may be administered in the inpatient or appropriate outpatient setting.

2. **Dosage Adjustments:**
   a. AST or ALT elevation (increases greater than 5 times ULN): Withhold therapy until transaminase elevations are 2.5 times ULN or less; resume treatment upon normalization or when resolved.
   b. Body temperature increase (38 degrees C or higher): Withhold therapy until body temperature is less than 38 degrees C.
   c. Body weight increase (predose weight increased by 1.5 kg or greater over the previous day’s predose weight): Follow capillary leak syndrome (CLS) management; administer albumin 25 g IV every 12 hours or more frequently and manage fluid status as indicated clinically (e.g., generally with IV fluids and vasopressors if hypotensive and with diuretics if normotensive or hypertensive) until body weight increase has resolved (the increase is no longer 1.5 kg or greater than the previous day's predose weight). Interrupt tagraxofusp-erzs dosing until the relevant CLS sign/symptom has resolved; may resume in same cycle if all CLS signs/symptoms have resolved without treatment for hemodynamic instability or withheld for remainder of cycle if CLS signs/symptoms have not resolved or patient required treatment for hemodynamic instability (e.g., IV fluids and/or vasopressors to treat hypotension) even if resolved. Administration may only resume in next cycle if all CLS signs/symptoms have resolved and patient is hemodynamically stable.
   d. Edema, fluid overload and/or hypotension: Follow capillary leak syndrome (CLS) management; administer albumin 25 g IV every 12 hours or more frequently until serum albumin is 3.5 g/dL or greater. Administer methylPREDNISolone 1 mg/kg/day (or an equivalent), and aggressively manage fluid status and hypotension if present (IV fluids and/or diuretics or other blood pressure management), until resolution of CLS
sign/symptom or as clinically indicated. Interrupt tagraxofusp-erzs dosing until relevant CLS sign/symptom has resolved; may resume in same cycle if all CLS signs/symptoms have resolved without treatment for hemodynamic instability or withheld for remainder of cycle if CLS signs/symptoms have not resolved or patient required treatment of hemodynamic instability (eg, IV fluids and/or vasopressors to treat hypotension) even if resolved. Administration may only resume in next cycle if all CLS signs/symptoms have resolved and patient is hemodynamically stable.

e. Heart rate (130 beats per minute (bpm) or higher or 40 bpm or less): Withhold therapy until heart rate is less than 130 bpm or greater than 40 bpm

f. Hypersensitivity reaction (mild or moderate): Withhold therapy until resolution; resume at same infusion rate

g. Hypersensitivity reaction (severe or life threatening): Permanently discontinue therapy

h. Serum albumin (less than 3.2 g/dL) prior to first dose in cycle 1: Do not administer until level is 3.2 g/dL or greater

i. Serum albumin (less than 3.5 g/dL or reduced by 0.5 g/dL or more measured prior to initiation of current cycle): Follow capillary leak syndrome (CLS) management; administer albumin 25 g IV every 12 hours or more frequently until serum albumin is 3.5 g/dL or greater and is not more than 0.5 g/dL lower than the value measured prior to dosing initiation of the current cycle. Interrupt tagraxofusp-erzs dosing until relevant CLS sign/symptom has resolved; may resume in same cycle if all CLS signs/symptoms have resolved without treatment for hemodynamic instability or withheld for remainder of cycle if CLS signs/symptoms have not resolved or patient required treatment of hemodynamic instability (eg, IV fluids and/or vasopressors to treat hypotension) even if resolved. Administration may only resume in next cycle if all CLS signs/symptoms have resolved and patient is hemodynamically stable.

j. Serum creatinine greater than 1.8 mg/dL (159 micromol/L) or CrCl 60 mL/min or lower: Withhold therapy until serum creatinine resolves to 1.8 mg/dL (159 micromol/L) or lower or CrCl resolves to 60 mL/min or greater

k. Systolic blood pressure (160 mmHg or greater or 80 mmHg or lower): Withhold therapy until systolic blood pressure is less than 160 mmHg or greater than 80 mmHg

3. Monitoring

a. Evidence of disease response or stabilization is indicative of efficacy.

b. AST and ALT: Prior to each infusion.

c. Creatinine: Prior to each infusion.

d. Pregnancy test: In females with reproductive potential within 7 days prior to initiation of therapy.

e. Serum albumin: Prior to initiation, ensure that level is 3.2 g/dL or greater and during treatment monitor serum albumin levels prior to the initiation of each dose and as indicated clinically thereafter.

f. Adequate cardiac function: Prior to initiation.
g. Clinical observation: Through at least 24 hours after the last infusion of cycle 1 (inpatient) and for at least 4 hours following each infusion of subsequent cycles (inpatient or suitable outpatient setting).

h. Hypersensitivity reactions: During treatment.

i. Signs or symptoms of capillary leak syndrome: Including weight gain, new onset or worsening edema, including pulmonary edema, hypotension or hemodynamic instability during treatment.

j. Vital signs: Prior to each dose.

V. APPROVAL AUTHORITY

1. Review – UM Department
2. Final Approval – UM Committee

VI. ATTACHMENTS

None

VII. REFERENCES