CODING AND BILLING GUIDE FOR

ELZONRIS®
(tagraxofusp-erzs) Injection

Permanent J-Code and NTAP designation for ELZONRIS® (tagraxofusp-erzs) Injection for Intravenous (IV) Use, effective October 1, 2019

ELZONRIS INJECTION FOR IV USE			
Permanent J-Code[1]:	**ICD-10-PCS[2]:**	**Revenue Code[3]:**	**CPT Codes[4]:**
J9269 Injection, tagraxofusp-erzs, 10 mcg	**XW033Q5** or **XW043Q5***	**0636**	**96413** or **96409**

Centers for Medicare & Medicaid Services (CMS) granted ELZONRIS Injection for IV Use a New Technology Add-On Payment (NTAP) designation for inpatient utilization.†

*Procedure code required to initiate NTAP payment.

†Medicare beneficiaries at qualified facilities that report an appropriate diagnosis code and ICD-10-PCS for the inpatient administration of ELZONRIS Injection for IV Use may be eligible for additional payment. NTAP as defined by CMS is issued to new technology meeting specific criteria and thresholds. The technology must be: 1) New: 2 or 3 years following FDA approval; 2) Existing MS-DRG must be inadequate; and 3) Technology must have substantial clinical improvement over existing services. The amount of payment is the lesser of 65% of the cost of ELZONRIS Injection for IV Use **OR** 65% of the amount by which the cost of the case exceeds the MS-DRG payment.

The information contained in this guide is intended to provide a general understanding of the coding and billing process and is not intended to assist healthcare providers in obtaining reimbursement for any specific claim. This guide is for informational purposes only and does not represent legal or billing advice. The content here is based on information as of October 1, 2019 and is subject to change.

Please see accompanying full Prescribing Information, including Boxed WARNING.

Stemline®

This guide is designed to help healthcare providers, hospital staff, and coding and billing managers by providing information on coding and billing for ELZONRIS Injection for IV Use, in the hospital settings for all insurance types, including Medicare, Medicare Advantage, Medicaid, and commercial payers.

FIND IN THIS GUIDE

- Coding and billing overview, processing a claim, overview of codes (NDC, ICD-10-CM, CPT, and HCPCS)
- Payer specifics: Medicare, Medicare Advantage, Medicaid, commercial payers
- Stemline ARC®
- Appendix:
  - Sample annotated physician office billing CMS-1500
  - Sample annotated hospital outpatient billing CMS-1450/UB-04
  - Summary of billing codes

SUMMARY OF CODING AND BILLING FOR ELZONRIS INJECTION FOR IV USE

DISPENSING PACK QUANTITY	**1 vial/box**
NDC	72187-0401-1 or 72187-0401-01
PERMANENT J-CODE	J9269 Injection, tagraxofusp-erzs, 10 mcg
CPT CODES[4]	96413 or 96409
DESCRIPTION[5]	Single-dose, sterile glass vial containing 1 mL of solution

NTAP DESIGNATION: ICD-10-PCS CODES LISTED BELOW FOR MEDICAL NECESSITY OF ELZONRIS INJECTION FOR IV USE

- C86.4, the principal diagnosis code for blastic plasmacytoid dendritic cell neoplasm (BPDCN)
- Procedure: Required ICD-10-PCS
- Procedure code: XW033Q5 or XW043Q5

For Medicare patients, non-exempt hospitals that report the correct ICD-10-PCS procedure and diagnosis codes may qualify for additional reimbursement the lesser of 65% of the cost of ELZONRIS Injection for IV Use **OR** 65% of the amount by which the cost of the case exceeds the MS-DRG payment.

ELZONRIS Injection for IV Use NTAP and J-Code effective October 1, 2019.

CODING AND BILLING FOR ELZONRIS INJECTION FOR IV USE

Processing a claim

To process a claim, it is important to:

- Complete the correct form (CMS-1500, CMS-1450/UB-04)
- Include correct codes: NDC, ICD-10-CM, CPT, and HCPCS
- Ensure all patient information (name, address, insurance ID number) is accurate
- Verify the name of the healthcare provider and National Provider Identifier (NPI)
- Use the most appropriate ICD-10-CM diagnosis and CPT procedure codes associated with each patient's diagnosis and care
- Specify the setting or place of service (POS) where the infusion was provided (eg, hospital setting) and dose given (10-mcg increments)
- Ensure patient medical records contain documentation that supports the diagnosis and procedure codes submitted on the claim
- Complete all claim form fields accurately and provide information upon request

Overview of codes

Once you have administered ELZONRIS Injection for IV Use to your patient, you may submit a claim to the patient's health plan. Correct coding is essential for timely claims processing and reimbursement. Important codes include the following:

National Drug Codes (NDCs)[6]
NDCs help healthcare providers and health plans identify specific product package sizes. Some health plans require healthcare providers to use an 11-digit NDC when reporting a drug on a claim form. Converting the 10-digit NDC for ELZONRIS Injection for IV Use to an 11-digit NDC requires the use of a leading zero in the product code.

International Classification of Disease, 10th Revision, Clinical Modification (ICD-10-CM) diagnosis code[7]
Use the current ICD-10-CM codes to report a patient's diagnosis on claim submissions. Be sure to use the correct coding when submitting a claim for the item or service.

Healthcare Common Procedure Coding System (HCPCS) codes[8,9]
Most health plans cover IV therapies under their medical benefit. CPT codes are used to identify services and procedures provided by a physician.

NDCs[6]

ELZONRIS Injection for IV Use NDC numbers are listed below. Please note that converting the 10-digit NDC to an 11-digit NDC requires the use of a leading zero in the product code.

ELZONRIS INJECTION FOR IV USE PACKAGE SIZE	NDC	FORMS
2.25 in. × 2 in.	10-digit: 72187-0401-1	CMS-1500; CMS-1450/UB-04
	11-digit: 72187-0401-01	CMS-1500; UB-04

Always confirm coding requirements with each patient's individual health plan, as the information required may vary.

ELZONRIS® (tagraxofusp-erzs) Injection

CODING AND BILLING OVERVIEW (cont'd)

ICD-10-CM diagnosis codes

It's important to check with the health plan to verify coding and special billing requirements. The ICD-10-CM diagnosis code for ELZONRIS Injection for IV Use is shown below.

The ICD-10-CM diagnosis code for ELZONRIS Injection for IV Use[10]

ICD-10-CM	DESCRIPTION	FORMS	
		CMS-1500	CMS-1450 (UB-04)
C86.4	Blastic NK-cell lymphoma Blastic plasmacytoid dendritic cell neoplasm (BPDCN)	Item 21	Form Locator 67

HCPCS codes[8,9]

Most health plans cover IV therapies under their medical benefit. CPT codes are used to identify services and procedures provided by a physician.

HCPCS LEVEL I CODES[5,6]		DESCRIPTION	FORMS	
		IV	CMS-1500	CMS-1450/UB-04
CPT Code	96413	Chemotherapy administration, IV infusion technique, up to 1 hour, single or initial substance/drug	Item 24D	Form Locator 44
	96409	Chemotherapy administration; intravenous, push technique, single or initial substance/drug		
Revenue Code	0636	Drugs requiring detailed coding	N/A	Form Locators 42 and 43
PERMANENT J-CODE[1]				
J9269		ELZONRIS Injection, tagraxofusp-erzs, 10 mcg	N/A	Form Locator 44 or electronic comment field

Please see accompanying full Prescribing Information, including Boxed WARNING.

PAYER SPECIFICS

Medicare

Medicare Part B[11]

ELZONRIS Injection for IV Use is covered by Medicare Part B in the outpatient setting.

Medicare Administrative Contractors (MACs)[12]

MACs are multistate regional contractors responsible for administering both Medicare Part A and Medicare Part B claims.

MACs are the central point of contact for providers of healthcare services. MACs are the primary operational contact between the Medicare fee-for-service (FFS) program and the healthcare providers enrolled in the program.

To find your Medicare Part B or durable medical equipment (DME) MAC jurisdiction, visit the CMS website.

Medicare Part D[11]

As an infused drug, ELZONRIS Injection for IV Use is not covered under Medicare Part D benefit.

To find your Medicare Part B or DME MAC jurisdiction, visit the CMS website.

Medicaid

ELZONRIS Injection for IV Use may be available under state Medicaid programs. Each state Medicaid program has its own eligibility standards, so coverage will vary from state to state. It's important to understand how your patient's Medicaid coverage works by contacting the Medicaid program or accessing the specific coverage information. Some Medicaid plans require prior authorization.

Commercial Health Plans[7]

Commercial health plans may provide coverage for ELZONRIS Injection for IV Use under the pharmacy or medical benefit. While commercial health plans may provide coverage under either of these benefits, the medical benefit will be utilized for the majority of plans. Please contact your patient's health plan for further guidance. Specific coverage requirements and restrictions depend on a given patient's benefits and may vary by plan type and site of service.

References: 1. Centers for Medicare & Medicaid Services. C-Codes Effective October 1, 2019. Available at https://www.cms.gov/Medicare/Coding/HCPCSReleaseCodeSets/HCPCS-Quarterly-Update.html. Accessed September 5, 2019. **2.** Centers for Medicare & Medicaid Services. Fiscal year 2020 final rule. Available at https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/AcuteInpatientPPS/FY2020-IPPS-Final-Rule-Home-Page-Items/FY2020-IPPS-Final-Rule-Data-Files.html. Accessed August 26, 2019. **3.** MLN Matters article index 2017 through August 2018. Centers for Medicare & Medicaid Services website. https://www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNMattersArticles/Downloads/2017-2018MLNMattersArticlesIndex.pdf. Accessed October 15, 2018. **4.** Optum360. 2018 Coding Companion for Oncology/Hematology. Eden Prairie, MN: Optum360; 2017. **5.** ELZONRIS [prescribing information]. New York, NY, US: Stemline Therapeutics, Inc.; December 2018. **6.** National Drug Code database background information. US Food & Drug Administration website. https://www.fda.gov/drugs/developmentapprovalprocess/ucm070829.htm. Updated March 20, 2017. Accessed October 8, 2018. **7.** ICD-10-CM, ICD-10-PCS, CPT, and HCPCS code sets. Centers for Medicare & Medicaid Services website. https://www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNProducts/Downloads/ICD9-10CM-ICD10PCS-CPT-HCPCS-Code-Sets-Educational-Tool-ICN900943.pdf Published May 2018. Accessed October 8, 2018. **8.** Einodshofer MT, Duren LN. Cost management through care management, part 2: the importance of managing specialty drug utilization in the medical benefit. *Am Health Drug Benefits*. 2012;5(6):359-364. **9.** HCPCS coding questions. Centers for Medicare & Medicaid Services website. https://www.cms.gov/Medicare/Coding/MedHCPCSGenInfo/HCPCS_Coding_Questions.html. Updated July 22, 2013. Accessed October 9, 2018. **10.** 2018 ICD-10 CM and GEMs. Centers for Medicare & Medicaid Services website. https://www.cms.gov/Medicare/Coding/ICD10/2018-ICD-10-CM-and-GEMs.html. Updated August 11, 2018. Accessed October 8, 2018. **11.** Medicare drug coverage under Medicare Part A, Part B, Part C, & Part D. Centers for Medicare & Medicaid Services website. https://www.cms.gov/outreach-and-education/outreach/partnerships/downloads/11315-p.pdf. Updated August 2017. Accessed October 8, 2018. **12.** What is a MAC. Centers for Medicare & Medicaid Services website. https://www.cms.gov/Medicare/Medicare-Contracting/Medicare-Administrative-Contractors/What-is-a-MAC.html. Updated October 26, 2017. Accessed October 9, 2018.

ELZONRIS® (tagraxofusp-erzs) Injection

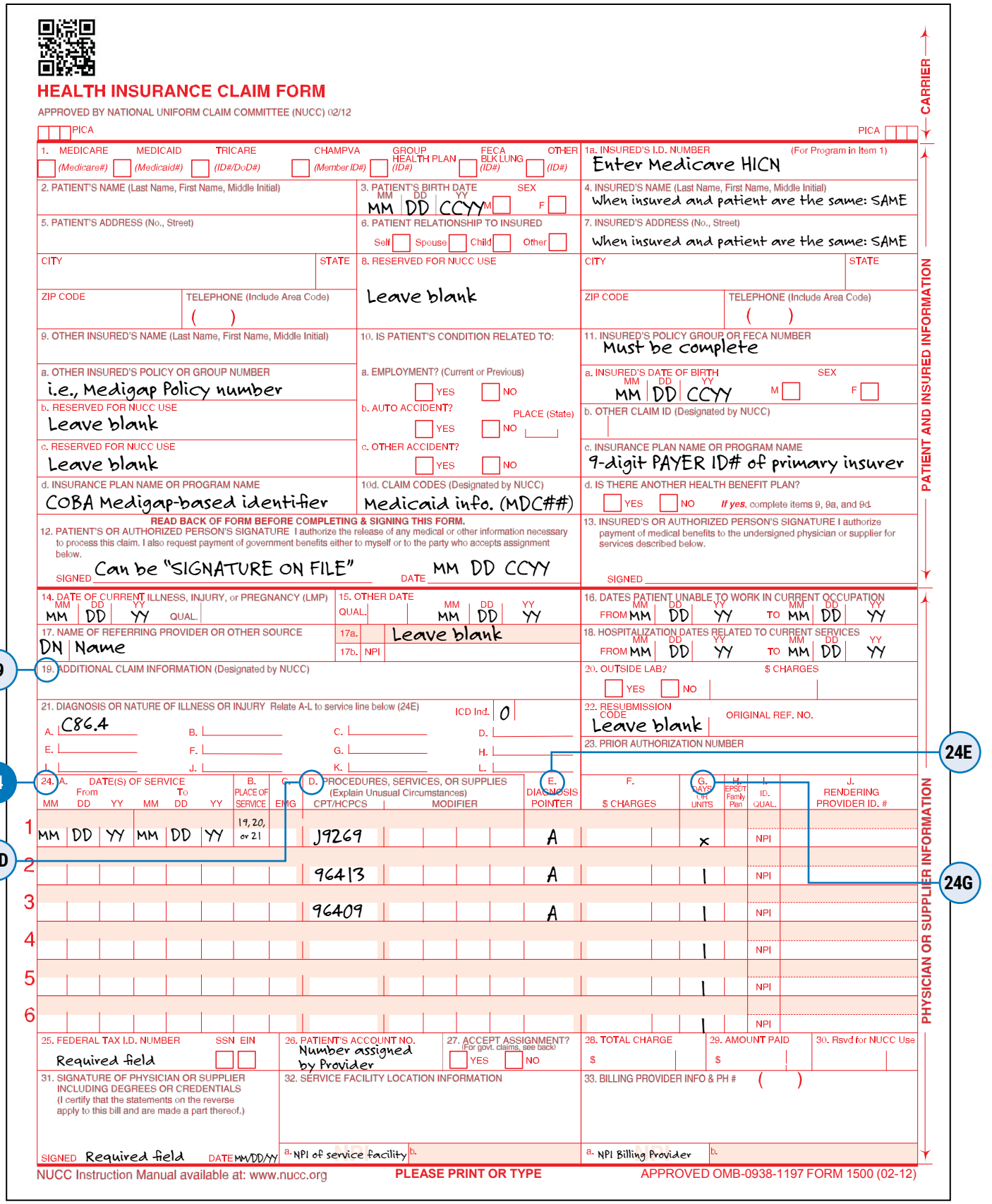
APPENDIX SAMPLE ANNOTATED FORMS

Note: *Sample form and annotations are for example only. Providers must contact their patient's health plan representative to confirm required coding and documentation for individual situations.*

• *Incomplete or invalid information will render form invalid and unable to be processed, causing payment delays*

Sample CMS-1500 physician office billing: ELZONRIS INJECTION FOR IV USE

LINE	TITLE	INFO	CODES
19	**Note:** The reporting field for electronic claims (SV202-2) is limited to 80 characters. However, some payers may allow utilization of Loop 2300 NTE 01 and 02 if additional space is needed. Check with the payer for additional guidance.		
21	**DIAGNOSIS CODE**	Enter appropriate ICD-10-CM diagnosis code(s) corresponding to patient's diagnosis.	**BPDCN ICD-10-CM: C86.4**
24	**DATES, PROCEDURES, POINTER, AND MODIFIER**		
24D	**PROCEDURES, SERVICES, OR SUPPLIES**	**Commercial, Medicare, Medicare Advantage, Medicaid fee-for-service HCPCS codes**	• **J9269** Injection, tagraxofusp-erzs, 10 mcg
		CPT - Chemotherapy and complex drug/biologic infusions	• **96413** Chemotherapy administration, IV infusion technique, up to 1 hour, single or initial substance or drug • **96409** Chemotherapy administration, IV push, single or initial substance or drug
24E	**DIAGNOSIS POINTER**	Specify diagnosis from Item 21, A-L, relating to each CPT/HCPCS code listed in Item 24D.	
24G	**NDC SERVICE UNITS**	Plan requires the number of NDC units J9269 injection, tagraxofusp-erzs, **10 mcg**, used in Item 24G. Specify the appropriate number of service units as designated by individual payers. There may be variation.	



HEALTH INSURANCE CLAIM FORM

APPROVED BY NATIONAL UNIFORM CLAIM COMMITTEE (NUCC) 02/12

PICA

1. MEDICARE (Medicare#) MEDICAID (Medicaid#) TRICARE (ID#/DoD#) CHAMPVA (Member ID#) GROUP HEALTH PLAN (ID#) FECA BLK LUNG (ID#) OTHER (ID#)

1a. INSURED'S I.D. NUMBER (For Program in Item 1): Enter Medicare HICN

2. PATIENT'S NAME (Last Name, First Name, Middle Initial)

3. PATIENT'S BIRTH DATE MM DD YY SEX M F: MM DD CCYY

4. INSURED'S NAME (Last Name, First Name, Middle Initial): When insured and patient are the same: SAME

5. PATIENT'S ADDRESS (No., Street)

6. PATIENT RELATIONSHIP TO INSURED: Self Spouse Child Other

7. INSURED'S ADDRESS (No., Street): When insured and patient are the same: SAME

CITY | STATE

8. RESERVED FOR NUCC USE: Leave blank

CITY | STATE

ZIP CODE | TELEPHONE (Include Area Code) ( )

ZIP CODE | TELEPHONE (Include Area Code) ( )

9. OTHER INSURED'S NAME (Last Name, First Name, Middle Initial)

10. IS PATIENT'S CONDITION RELATED TO:

11. INSURED'S POLICY GROUP OR FECA NUMBER: Must be complete

a. OTHER INSURED'S POLICY OR GROUP NUMBER: i.e., Medigap Policy number

a. EMPLOYMENT? (Current or Previous) YES NO

a. INSURED'S DATE OF BIRTH MM DD YY SEX M F: MM DD CCYY

b. RESERVED FOR NUCC USE: Leave blank

b. AUTO ACCIDENT? YES NO PLACE (State)

b. OTHER CLAIM ID (Designated by NUCC)

c. RESERVED FOR NUCC USE: Leave blank

c. OTHER ACCIDENT? YES NO

c. INSURANCE PLAN NAME OR PROGRAM NAME: 9-digit PAYER ID# of primary insurer

d. INSURANCE PLAN NAME OR PROGRAM NAME: COBA Medigap-based identifier

10d. CLAIM CODES (Designated by NUCC): Medicaid info. (MDC##)

d. IS THERE ANOTHER HEALTH BENEFIT PLAN? YES NO *If yes*, complete items 9, 9a, and 9d.

READ BACK OF FORM BEFORE COMPLETING & SIGNING THIS FORM.

12. PATIENT'S OR AUTHORIZED PERSON'S SIGNATURE I authorize the release of any medical or other information necessary to process this claim. I also request payment of government benefits either to myself or to the party who accepts assignment below.

SIGNED: Can be "SIGNATURE ON FILE" DATE: MM DD CCYY

13. INSURED'S OR AUTHORIZED PERSON'S SIGNATURE I authorize payment of medical benefits to the undersigned physician or supplier for services described below.

SIGNED

14. DATE OF CURRENT ILLNESS, INJURY, or PREGNANCY (LMP) MM DD YY QUAL.: MM DD YY

15. OTHER DATE QUAL. MM DD YY

16. DATES PATIENT UNABLE TO WORK IN CURRENT OCCUPATION MM DD YY FROM MM DD YY TO MM DD YY

17. NAME OF REFERRING PROVIDER OR OTHER SOURCE: DN | Name

17a. Leave blank

17b. NPI

18. HOSPITALIZATION DATES RELATED TO CURRENT SERVICES MM DD YY FROM MM DD YY TO MM DD YY

19. ADDITIONAL CLAIM INFORMATION (Designated by NUCC)

20. OUTSIDE LAB? YES NO $ CHARGES

21. DIAGNOSIS OR NATURE OF ILLNESS OR INJURY Relate A-L to service line below (24E) ICD Ind. 0

A. C86.4 B. C. D. E. F. G. H. I. J. K. L.

22. RESUBMISSION CODE: Leave blank ORIGINAL REF. NO.

23. PRIOR AUTHORIZATION NUMBER

24. A. DATE(S) OF SERVICE From MM DD YY To MM DD YY | B. PLACE OF SERVICE | C. EMG | D. PROCEDURES, SERVICES, OR SUPPLIES (Explain Unusual Circumstances) CPT/HCPCS MODIFIER | E. DIAGNOSIS POINTER | F. $ CHARGES | G. DAYS OR UNITS | H. EPSDT Family Plan | I. ID. QUAL. | J. RENDERING PROVIDER ID. #

	A. DATE(S) OF SERVICE From	To	B.	C.	D. CPT/HCPCS	MODIFIER	E.	F. $ CHARGES	G. DAYS OR UNITS	H.	I. ID. QUAL.	J. RENDERING PROVIDER ID. #
1	MM DD YY	MM DD YY	19, 20, or 21		J9269		A		x		NPI	
2					96413		A		1		NPI	
3					96409		A		1		NPI	
4									1		NPI	
5									1		NPI	
6									1		NPI	

25. FEDERAL TAX I.D. NUMBER SSN EIN: Required field

26. PATIENT'S ACCOUNT NO.: Number assigned by Provider

27. ACCEPT ASSIGNMENT? (For govt. claims, see back) YES NO

28. TOTAL CHARGE $

29. AMOUNT PAID $

30. Rsvd for NUCC Use

31. SIGNATURE OF PHYSICIAN OR SUPPLIER INCLUDING DEGREES OR CREDENTIALS (I certify that the statements on the reverse apply to this bill and are made a part thereof.)

SIGNED Required field DATE MM/DD/YY

32. SERVICE FACILITY LOCATION INFORMATION

a. NPI of service facility b.

33. BILLING PROVIDER INFO & PH # ( )

a. NPI Billing Provider b.

NUCC Instruction Manual available at: www.nucc.org

PLEASE PRINT OR TYPE

APPROVED OMB-0938-1197 FORM 1500 (02-12)

CARRIER

PATIENT AND INSURED INFORMATION

PHYSICIAN OR SUPPLIER INFORMATION

19

24

24D

24E

24G

ELZONRIS®
(tagraxofusp-erzs) Injection

APPENDIX SAMPLE ANNOTATED FORMS

Note: *Sample form and annotations are for example only. Providers must contact their patient's health plan representative to confirm required coding and documentation for individual situations.*

• Incomplete or invalid information will render form invalid and unable to be processed, causing payment delays

Sample CMS-1450/UB-04 hospital outpatient billing: ELZONRIS INJECTION FOR IV USE

LINE	DESCRIPTION		CODES
42	**REVENUE CODE:** Corresponding to HCPCS or CPT© in FL44	**DRUG**	**Medicare:** Revenue code **0636** or **0335** chemotherapy administration IV
		PROCEDURE	Medicare and most payers require a revenue code for each procedure
	Payers vary on revenue code requirements. Please contact the patient's health plan to confirm required coding in individual situations.		
43	**DESCRIPTION:** ELZONRIS INJECTION FOR IV USE	**PRODUCT**	**J9269** Injection, tagraxofusp-erzs, 10 mcg
		PROCEDURE	**Revenue code: 0636**
44	**PRODUCT AND PROCEDURE:** ELZONRIS INJECTION FOR IV USE	**PRODUCT**	**J9269** Injection, tagraxofusp-erzs, 10 mcg **Revenue code: 0636**
		PROCEDURE CPT	**CHEMOTHERAPY AND COMPLEX DRUG/BIOLOGIC INFUSIONS** • **96413** Chemotherapy administration, IV infusion technique, up to 1 hour, single or initial substance/drug • **96409** Chemotherapy administration, IV push, single or initial substance/drug **Revenue code: 0335**
46	**NDC Service Units:** Plan requires the number of NDC units J9269 injection, tagraxofusp-erzs,**10 mcg**, used in Item 46. Specify the appropriate number of service units as designated by individual payers. There may be variation.		
66	**DIAGNOSIS CODE**		**0**
67	**ICD-10-CM**		**C86.4** is the principal diagnosis code for BPDCN
69	**ADMIT DX**		**C86.4**
Note: Enter code reflecting histology of patient's disease diagnosis.			
74	**ICD-10-PCS**		**XW033Q5 or XW043Q5**
80	Plans are different and some may require additional information. Please check with the patient's plan to ensure all required information is provided for timely reimbursement.		

1 Billing provider name Address; city, state, zip code + extension Area code, phone, fax, country code	2 Billing provider designated pay-to Name, address, city, state, ID	3a PAT. CNTL # alpha-numeric code assigned by provider b. MED. REC. # number assigned by provider	4 TYPE OF BILL 0234
		5 FED. TAX NO. 12-3456789	6 STATEMENT COVERS PERIOD FROM MM/DD/YY THROUGH MM/DD/YY	7 Leave blank

8 PATIENT NAME a Last, first, MI, identifier	9 PATIENT ADDRESS a Mailing address
b	b c d e

10 BIRTHDATE	11 SEX	12 ADMISSION DATE	13 HR	14 TYPE	15 SRC	16 DHR	17 STAT	18	19	20	21	22	23	24	25	26	27	28	29 ACDT STATE	30
MM/DD/CCYY		MM/DD/YY																		

31 CODE	31 OCCURRENCE DATE	32 CODE	32 OCCURRENCE DATE	33 CODE	33 OCCURRENCE DATE	34 CODE	34 OCCURRENCE DATE	35 CODE	35 OCCURRENCE SPAN FROM	THROUGH	36 CODE	36 OCCURRENCE SPAN FROM	THROUGH	37
	MM/DD/YY		MM/DD/YY		MM/DD/YY		MM/DD/YY		MM/DD/YY	MM/DD/YY		MM/DD/YY	MM/DD/YY	

38	39 CODE	39 VALUE CODES AMOUNT	40 CODE	40 VALUE CODES AMOUNT	41 CODE	41 VALUE CODES AMOUNT
	a					
	b					
	c					
	d					

42 REV. CD. | 43 DESCRIPTION | 44 HCPCS / RATE / HIPPS CODE | 45 SERV. DATE | 46 SERV. UNITS | 47 TOTAL CHARGES | 48 NON-COVERED CHARGES | 49

	42 REV. CD.	43 DESCRIPTION	44 HCPCS / RATE / HIPPS CODE	45 SERV. DATE	46 SERV. UNITS	47 TOTAL CHARGES	48 NON-COVERED CHARGES	
1	0636	Elzonris Injection for IV Use	J9269	MM/DD/YY	x			1
2								2
3	0335	Elzonris Injection for IV Use	96413	MM/DD/YY	1			3
4								4
5	0335	Elzonris Injection for IV Use	96409	MM/DD/YY	1			5
6								6
7								7
8								8
9								9
10								10
11								11
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21								21
22								22
23		PAGE ____ OF ____ CREATION DATE			TOTALS			23

	50 PAYER NAME	51 HEALTH PLAN ID	52 REL. INFO	53 ASG. BEN.	54 PRIOR PAYMENTS	55 EST. AMOUNT DUE	56 NPI	Billing provider number	
A	Payer identification - Primary (1º)				1º	1º	57	Other provider number	A
B	Payer identification - Secondary (2º)				2º	2º	OTHER	Other provider number	B
C	Payer identification - Tertiary (3º)				3º	3º	PRV ID	Other provider number	C

	58 INSURED'S NAME	59 P REL	60 INSURED'S UNIQUE ID	61 GROUP NAME	62 INSURANCE GROUP NO.
A					
B					
C					

	63 TREATMENT AUTHORIZATION CODES	64 DOCUMENT CONTROL NUMBER	65 EMPLOYER NAME
A			(of the insured) Primary
B			(of the insured) Secondary
C			(of the insured) Tertiary

66 DX: C86.4 (A) | (B) | (C) | (D) | (E) | (F) | (G) | (H) | 68

0 (J) | (K) | (L) | (M) | (N) | (O) | (P) | (Q)

69 ADMIT DX: C86.4 | 70 PATIENT REASON DX: Reason for visit code | b | c | 71 PPS CODE | 72 ECI | 73

74 PRINCIPAL PROCEDURE CODE	DATE	a. OTHER PROCEDURE CODE	DATE	b. OTHER PROCEDURE CODE	DATE	75
XW033Q5	MM/DD/YY		MM/DD/YY		MM/DD/YY	

c. OTHER PROCEDURE CODE	DATE	d. OTHER PROCEDURE CODE	DATE	e. OTHER PROCEDURE CODE	DATE
	MM/DD/YY		MM/DD/YY		MM/DD/YY

80 REMARKS

81CC			
a			
b			
c			
d			

76 ATTENDING	NPI MD Provider number	QUAL	
LAST		FIRST	
77 OPERATING	NPI Operating MD number	QUAL	
LAST		FIRST	
78 OTHER	NPI	QUAL	
LAST		FIRST	
79 OTHER	NPI	QUAL	
LAST		FIRST	

UB-04 CMS-1450 APPROVED OMB NO.

THE CERTIFICATIONS ON THE REVERSE APPLY TO THIS BILL AND ARE MADE A PART HEREOF.

NUBC® National Uniform Billing Committee

LIC9213257

42 43 44 46 67 66 69 74 80

ELZONRIS® (tagraxofusp-erzs) Injection

STEMLINE ARC® PROVIDES ACCESS, REIMBURSEMENT SUPPORT, AND CONNECTION TO RESOURCES FOR ELIGIBLE PATIENTS THROUGHOUT TREATMENT WITH ELZONRIS INJECTION FOR IV USE

stemline arc®
access | reimbursement support | connection

access
Support for benefits investigation and verification, information on alternate support, and co-pay support for eligible patients*

reimbursement support
Information regarding prior authorization, template letter of medical necessity, appeals of denied claims, and coding & billing support

connection
ARC Patient Advocates provide an overview of support services, confirm ELZONRIS coverage and financial assistance, and share helpful resources†

Stemline ARC is here to help patients, hospitals, and offices alike. We provide:

- Hospital and office access/procurement support
- Support for prior authorization, medical exceptions, and appeals of denied claims
- Billing and coding guidance, including J-code, NDC, ICD-10, and MS-DRG

$0

Stemline Commercial Co-Pay Program
- Eligible patients may pay as little as $0 per month supply of ELZONRIS Injection for IV Use

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 for eligible patients

For 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, or visit ELZONRIS.com/hcp/stemline-arc-summary. Fax completed enrollment form to 1-833-329-7836.

*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.

†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 patients and their healthcare providers.

‡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 foundations to support the patient's disease state.

Stemline®

ELZONRIS®
(tagraxofusp-erzs) Injection

stemline arc®
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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. 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.	

[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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