Clinical Policy: Erwinia Asparaginase (Erwinaze, Rylaze)

Reference Number: PA.CP.PHAR.301
Effective Date: 01/2018
Last Review Date: 01/2023

Coding Implications
Revision Log

Description
Asparaginase *Erwinia chrysanthemi* (Erwinaze®) and asparaginase *Erwinia chrysanthem* (recombinant)-rywn (Rylaze™) are asparagine specific enzymes.

FDA Approved Indication(s)
Erwinaze is indicated as a component of a multi-agent chemotherapeutic regimen for the treatment of patients with acute lymphoblastic leukemia (ALL) who have developed hypersensitivity to *E. coli*-derived asparaginase.

Rylaze is indicated as a component of a multi-agent chemotherapeutic regimen for the treatment of ALL and lymphoblastic lymphoma (LBL) in adult and pediatric patients 1 month or older who have developed hypersensitivity to *E. coli*-derived asparaginase.

Policy/Criteria
Provider must submit documentation (including such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of PA Health & Wellness ® that Erwinaze and Rylaze are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Acute Lymphoblastic Leukemia (must meet all):

1. Diagnosis of acute lymphoblastic leukemia (ALL);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. One of the following (a or b):
   a. For Erwinaze, age ≥ 1 year;
   b. For Rylaze, age ≥ 1 month;
4. Prescribed as a component of a multi-agent chemotherapeutic regimen;
5. Member meets (a or b):
   a. Member has developed hypersensitivity to an *E. coli* derived asparaginase product (Elspar® - off-market) or pegaspargase (Oncaspar®);
   b. For Erwinaze, that is prescribed as combination induction therapy and one of the following (i or ii):
      i. Age ≥ 65 years;
      ii. Age ≥ 18 years with substantial comorbidities;
6. Request meets one of the following (a, b, or c):
   a. Erwinaze: dose does not exceed 25,000 International Units/m^2 administered three times per week;
   b. Rylaze: dose does not exceed 25 mg/ m^2 every 48 hours;
   c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence).*

Approval duration: 3 months

B. Lymphoblastic Lymphoma (must meet all)**:**
1. Diagnosis of LBL;
2. Request is for Rylaze;
3. Prescribed by or in consultation with an oncologist or hematologist;
4. Age ≥ 1 month;
5. Prescribed as a component of a multi-agent chemotherapeutic regimen;
6. Member has developed hypersensitivity to an *E. coli* derived asparaginase product (Elspar - off-market) or pegaspargase (Oncaspar);
7. Request meets one of the following (a or b):
   a. Dose does not exceed 25 mg/ m^2 every 48 hours;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence).*

Approval duration: 3 months

C. T-Cell Lymphoma (off-label) (must meet all)**:**
1. Diagnosis of extranodal NK/T-cell lymphoma;
2. Request is for Rylaze;
3. Prescribed by or in consultation with an oncologist or hematologist;
4. Age ≥ 1 month;
5. Member has developed hypersensitivity to an *E. coli* derived asparaginase product (Elspar - off-market) or pegaspargase (Oncaspar);
6. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 3 months

D. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Approval

A. All Indications in Section I(must meet all)**:**
1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a, b, or c):
   a. Erwinaze: new dose should not exceed 25,000 International Units per m^2 administered three times per week;
   b. Rylaze: new dose does not exceed 25 mg/ m^2 every 48 hours;
   c. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence).*

Approval duration: 6 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to PA.CP.PMN.53

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
ALL: acute lymphoblastic leukemia
FDA: Food and Drug Administration
LBL: lymphoblastic lymphoma

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Oncaspar (pegaspargase)	• Administered IM or IV no more frequently than every 14 days. • Patients ages 21 years and younger: 2,500 International Units/m^2. • Patients ages over 21 years: 2,000 International Units/m^2. •	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): History of serious hypersensitivity reactions to Erwinaze/Rylaze, including anaphylaxis, serious pancreatitis with prior L-asparaginase therapy, serious thrombosis with prior L-asparaginase therapy, serious hemorrhagic events with prior L-asparaginase therapy.
- Boxed warning(s): None reported.

IV. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Erwinaze	ALL	To substitute for pegaspargase: the recommended dose for each planned dose of pegaspargase is 25,000 International Units/m^2 administered IM or IV TIW (Monday/Wednesday/Friday) for six doses. To substitute for a dose of native *E. coli* asparginase: the recommended dose is 25,000 International Units/m^2 administered	25,000 IU/m^2/dose

Drug Name	Indication	Dosing Regimen	Maximum Dose
		intramuscularly or intravenously for each scheduled dose of native *E. coli* asparginase	
Rylaze	ALL, LBL	When replacing a long-acting asparginase product the recommended dose is: • 25 mg/m^2 IM every 48 hours OR 25 mg/m^2 IM on Monday morning and Wednesday morning, and 50 mg/m^2 IM on Friday afternoon	25 mg/m^2/dose

V. Product Availability

Drug Name	Availability
Erwinaze	10,000 International Units lyophilized powder per vial
Rylaze	10 mg/0.5 ml solution in single-dose vial

VI. References

1. Erwinaze Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; December 2019. Available at https://pp.jazzpharma.com/pi/erwinaze.en.USPI.pdf. Accessed November 11, 2022.
2. Rylaze Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; November 2022. Available at: https://pp.jazzpharma.com/pi/rylaze.en.USPI.pdf. Accessed November 22, 2022.
3. Oncaspar Prescribing InformationBoston, MA: Servier Pharmaceuticals, LLC.; November 2021. Available at https://www.oncaspar.com/prescribing_information.pdf. Accessed November 11, 2022.
4. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at ww.nccn.org/professionals/drug_compendium. Accessed November 11, 2022.
5. National Comprehensive Cancer Network. Acute Lymphoblastic Leukemia Version 1.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/all.pdf. Accessed November 11, 2022.
6. National Comprehensive Cancer Network. Pediatric Acute Lymphoblastic Leukemia Version 1.2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf. Accessed November 11, 2022.
7. National Comprehensive Cancer Network. T-Cell Lymphomas Version 2.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf. Accessed November 11, 2022.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9019	Injection, asparaginase, (Erwinaze), 1,000 IU
J9020	Injection, asparaginase, not otherwise specified, 10,000 units

HCPCS Codes	Description
J9021	Injection, asparaginase, recombinant, (Rylaze), 0.1 mg

Reviews, Revisions, and Approvals	Date	Approval Date
Combined FDA approved criteria and NCCN recommendations, FDA indication covers both. References reviewed and updated	02/2018	
1Q 2019 annual review; specialist added; per Recordati Rare Diseases, who acquired Elspar from Lundbeck in January 2013, Elspar was discontinued in 2012, there are currently no plans to reintroduce Elspar, there is no residual Elspar supply remaining on the current market, and Recordati Rare Diseases has not provided Elspar to any other territory within the global market; references reviewed and updated.	01/2019	
1Q 2020 annual review: induction therapy added per NCCN for members 65 or older; references reviewed and updated.	01/2020	
1Q 2021 annual review: Oncospar dosing updated; references reviewed and updated.	01/2021	
RT4: added Rylaze to policy with new criteria set for LBL indication	10/2021	
1Q 2022 annual review: specified only Erwinaze recommended for ALL induction therapy per NCCN; references reviewed and updated.	01/2022	
1Q 2023 annual review: added age requirements for ALL and LBL indication; added usage of Erwinaze for ALL for those age ≥18 years with substantial comorbidities per NCCN; added criterion for T-cell lymphoma per NCCN; references reviewed and updated.	01/2023	