Clinical Policy: Erwinia Asparaginase (Erwinaze, Rylaze)

Reference Number: ERX.SPA.305
Effective Date: 03.01.19
Last Review Date: 11.21
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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 ALL;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Prescribed as a component of a multi-agent chemotherapeutic regimen;
4. Member meets (a or b):
   a. Member has developed hypersensitivity to an *E. coli* derived asparaginase product (Elspar® - off-market) or pegaspargase (Oncaspar®);
   b. Age ≥ 65 years and prescribed as combination induction therapy;
5. Request meets one of the following (a, b, or c):*
   a. Erwinaze: Dose does not exceed 25,000 International Units/m^2 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*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

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. Prescribed as a component of a multi-agent chemotherapeutic regimen;

5. Member has developed hypersensitivity to an *E. coli* derived asparaginase product (Elspar - off-market) or pegaspargase (Oncaspar);
6. 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).*

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration: 3 months

C. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, or documentation supports that member is currently receiving Erwinaze or Rylaze for a covered indication and has received this medication for at least 30 days;
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 does not exceed 25,000 International Units/m^2 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).*

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration: 6 months

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. 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.	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	• Patients ages 21 years and younger: 2,500 International Units/m^2. • Patients ages over 21 years: 2,000 International Units/m^2. • For IM administration, limit the volume at a single injection site to 2 mL; if greater than 2 mL, use multiple injection sites. • For IV administration, give over a period of 1 to 2 hours in 100 mL of 0.9% Sodium Chloride Injection, USP or 5% Dextrose Injection, USP through an infusion that is already running. • Do not administer Oncaspar if drug has been frozen, stored at room temperature for more than 48 hours, or shaken or vigorously agitated.	

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 1) serious hypersensitivity reactions to Erwinaze/Rylaze, including anaphylaxis, 2) serious pancreatitis with prior L-asparaginase therapy, 3) serious thrombosis with prior L-asparaginase therapy, 4) serious hemorrhagic events with prior L-asparaginase therapy
- Boxed warning(s): none reported

V. 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 6 doses.	25,000 IU/m^2/dose
Rylaze	ALL, LBL	To substitute for pegaspargase: 25 mg/m^2 IM every 48 hours to complete the intended duration of pegaspargase therapy	25 mg/m^2/dose

VI. 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

VII. 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 October 12, 2020.
2. Rylaze Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; June 2021. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/761179s000lbl.pdf. Accessed July 13, 2021.
3. Oncaspar Prescribing Information. Gaithersburg, MD: Sigma-Tau Pharmaceuticals, Inc.; August 2019. Available at https://www.oncaspar.com/prescribing_information.pdf. Accessed October 12, 2020.
4. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at ww.nccn.org. Accessed July 13, 2021.
5. Acute Lymphoblastic Leukemia Version 1.2021. National Comprehensive Cancer Network Guidelines. Available at www.nccn.org. Accessed July 13, 2021.

6. Pediatric Acute Lymphoblastic Leukemia Version 2.2021. National Comprehensive Cancer Network Guidelines. Available at www.nccn.org. Accessed July 13, 2021.
7. B-Cell Lymphomas Version 4.2021. National Comprehensive Cancer Network Guidelines. Available at https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed July 13, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	11.13.18	02.19
1Q 2020 annual review: induction therapy added per NCCN for members 65 or older; references reviewed and updated.	11.19.19	02.20
1Q 2021 annual review: no significant changes; Oncospar dosing updated in Appendix B; references reviewed and updated.	10.12.20	02.21
RT4: added Rylaze to policy with new criteria set for LBL indication.	07.13.21	11.21

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.