Clinical Policy: Erwinia Asparaginase (Erwinaze, Rylaze)

Reference Number: CP.PHAR.301
Effective Date: 02.01.2017
Last Review Date: 11.22
Line of Business: Commercial, HIM, Medicaid

Coding Implications
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.

It is the policy of health plans affiliated with Centene Corporation® 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. For Erwinaze, 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 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)*.

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

Approval duration:

Commercial/HIM/Medicaid – 3 months
Legacy WellCare – 2 weeks

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:
Commercial/HIM/Medicaid – 3 months
Legacy WellCare – 2 weeks

C. Other diagnoses/indications
1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via Centene benefit, 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 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)*.

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

Approval duration:
Commercial/HIM/Medicaid – 6 months
Legacy WellCare – 2 weeks

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, 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. • 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 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 IU/m^2/dose

Drug Name	Indication	Dosing Regimen	Maximum Dose
		25,000 International Units/m^2 administered IM or IV TIW (Monday/Wednesday/Friday) for six doses.	
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 November 10, 2021.
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 November 10, 2021.
3. Oncaspar Prescribing Information. Boston, MA: Servier Pharmaceuticals LLC.; June 2020. Available at https://www.oncaspar.com/prescribing_information.pdf. Accessed November 10, 2021.
4. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at ww.nccn.org. Accessed November 10, 2021.
5. Acute Lymphoblastic Leukemia Version 2.2021. National Comprehensive Cancer Network Guidelines. Available at www.nccn.org. Accessed November 10, 2021.

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
J9021	Injection, asparaginase, recombinant, (Rylaze), 0.1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2019 annual review; HIM line of business added; specialist added; per Recordati Rare Diseases, who acquired Elspar from Lundbeck in	11.13.18	02.19

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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.		
1Q 2020 annual review: removed HIM disclaimer for HIM NF drugs; 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; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	10.12.20	02.21
RT4: added Rylaze to policy with new criteria set for LBL indication; added legacy WellCare to policy maintaining current authorization limits; retire WCG.CP.PHAR.301.	07.13.21	11.21
1Q 2022 annual review: specified only Erwinaze recommended for ALL induction therapy per NCCN; added commercial line of business; updated HCPCS codes; references reviewed and updated.	11.10.21	02.22

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a

discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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