Clinical Policy: Erwinia Asparaginase (Rylaze)

Reference Number: CP.PHAR.301
Effective Date: 02.01.17
Last Review Date: 02.26
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 chrysanthem* (recombinant)-rywn (Rylaze®) is an asparagine specific enzyme.

FDA Approved Indication(s)

Rylaze is indicated as a component of a multi-agent chemotherapeutic regimen for the treatment of acute lymphoblastic leukemia (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 Rylaze is **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. Age ≥ 1 month;
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), pegaspargase (Oncaspar®), or calaspargase pegol-mknl (Asparlas®);
6. Request meets one of the following (a, b, or c):*
   a. Dose does not exceed 25 mg/m^2 every 48 hours;
   b. Dose does not exceed 25 mg/m^2 on Monday and Wednesday and 50 mg/m^2 on Friday;
   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:
Medicaid/HIM – 12 months
Commercial – 6 months or duration of request, whichever is less

B. Lymphoblastic Lymphoma (must meet all)**:**
1. Diagnosis of LBL;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 1 month;
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, b, c):*
   a. Dose does not exceed 25 mg/m^2 every 48 hours;
   b. Dose does not exceed 25 mg/m2 on Monday and Wednesday and 50 mg/m2 on Friday;
   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:
Medicaid/HIM – 12 months
Commercial – 6 months or duration of request, whichever is less

C. T-Cell Lymphoma (off-label) (must meet all)**:**
1. Diagnosis of extranodal NK/T-cell lymphoma;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Member has developed hypersensitivity to an *E. coli* derived asparaginase product (Elspar - off-market) or pegaspargase (Oncaspar);
5. 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*).*

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

Approval duration:
Medicaid/HIM – 12 months
Commercial – 6 months or duration of request, whichever is less

D. Other diagnoses/indications (must meet 1 or 2):
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: 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 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. Dose does not exceed 25 mg/m^2 every 48 hours;
   b. Dose does not exceed 25 mg/m^2 on Monday and Wednesday and 50 mg/m^2 on Friday;
   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:
Medicaid/HIM – 12 months
Commercial – 6 months or duration of request, whichever is less

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: 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
Not applicable

Appendix C: Contraindications/Boxed Warnings
- Contraindication(s): history of serious hypersensitivity reactions to 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, severe hepatic impairment.
- Boxed warning(s): None reported.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
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	50 mg/m^2/dose

VI. Product Availability

Single-dose vial for injection: 10 mg/0.5 ml

VII. References

1. Rylaze Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; July 2025. Available at: https://pp.jazzpharma.com/pi/rylaze.en.USPI.pdf. Accessed October 21, 2024.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at ww.nccn.org/professionals/drug_compendium. Accessed November 19, 2025.
3. National Comprehensive Cancer Network. Acute Lymphoblastic Leukemia Version 2.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/all.pdf. Accessed November 19, 2025.
4. National Comprehensive Cancer Network. Pediatric Acute Lymphoblastic Leukemia Version 1.2026. Available at: https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf. Accessed November 19, 2025.
5. National Comprehensive Cancer Network. T-Cell Lymphomas Version 2.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf. Accessed November 19, 2025.

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

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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
Template changes applied to other diagnoses/indications.	09.21.22	
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; For ALL and LBL, added Rylaze MWF dosing regimen; revised commercial approval duration to the current standard for injectables of "6 months or to member's renewal date, whichever is longer"; Legacy WellCare approval durations consolidated to 3 or 6 months; references reviewed and updated.	11.10.22	02.23
1Q 2024 annual review: for ALL, added Asparlas to criteria that member was developed hypersensitivity to; removed discontinued Erwinaze product from policy; references reviewed and updated.	10.16.23	02.24
1Q 2025 annual review: no significant changes; added "severe hepatic impairment" to contraindications section per PI; references reviewed and updated.	10.21.24	02.25
1Q 2026 annual review: no significant changes; for Medicaid/HIM lines of business, extended both initial and continued therapy approval durations from 6 to 12 months for this maintenance medication for a chronic condition; references reviewed and updated. Removed HCPCS code [J9020].	01.06.26	02.26

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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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.