Rylaze [asparaginase erwinia chrysanthemi (recombinant)-rywn]
PAM – 043

Iowa Medicaid Program	Prior Authorization	**Effective Date**	01/01/2022
Revision Number	4	**Last Reviewed**	07/18/2025
Reviewed By	Medicaid Medical Director	**Next Review**	07/17/2026
Approved By	Medicaid Clinical Advisory Committee	**Approved Date**	07/15/2022

Overview

Medication: [1]	asparaginase erwinia chrysanthemi (recombinant)-rywn
Brand Name:	Rylaze®
Pharmacologic Category:	Antineoplastic agent; asparaginase specific enzyme
FDA-Approved Indication(s):	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.
How Supplied:	One carton contains 3 single-dose vials (10 mg/0.5 mL per vial)
Dosage and Administration:	Two regimens that can be utilized when using Rylaze® [administered intramuscularly (IM)] to replace a long-acting asparaginase product: 1. Administer every 48 hours ▪ 25 mg/m^2 every 48 hours (IM injection) 2. Administer on a Monday-Wednesday-Friday schedule ▪ Monday morning: 25 mg/m^2 (IM injection) ▪ Wednesday morning: 25 mg/m^2 (IM injection) ▪ Friday afternoon: 50 mg/m^2 (IM injection) administered 53 to 58 hours after the Wednesday morning dose See prescribing information for the long-acting asparaginase product to determine the treatment duration with Rylaze® as replacement therapy.
Benefit Category:	Medical

Descriptive Narrative

Asparaginase specific enzymes work by depleting blood plasma levels of asparagine. Normal cells create more asparagine; however, some leukemic cells are not able to synthesize this amino acid and die. Asparaginase specific enzymes are primarily used to treat acute lymphoblastic leukemia (ALL).

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 one (1) month or older who have developed hypersensitivity to E. coli-derived asparaginase.

Guidelines

The National Comprehensive Cancer Network (NCCN) publishes guidelines for the prevention, diagnosis, and management of malignancies across the continuum of care. The NCCN Guidelines® are a comprehensive set of guidelines detailing the sequential management decisions and interventions that currently apply to 97 percent of cancers affecting patients in the United States. The guidelines are developed and updated by 61 individual panels, comprising over 1,700 clinicians and oncology researchers from the 33 NCCN Member Institutions.

Guidelines are reviewed and updated on a continual basis to ensure that the recommendations take into account the most current evidence. To view the most recent and complete version of the guidelines, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.[2,3]

The information referenced at the time of this policy writing/revision is from the NCCN Guidelines® for (note version number and effective date):[4]

- Acute Lymphoblastic Leukemia (v.2.2025 – June 27, 2025)

NCCN Guidelines® Recommendation(s)
(1) Acute Lymphoblastic Leukemia (ALL) or Lymphoblastic Lymphoma (LBL) a. Supportive Care – Asparaginase Toxicity Management i. Asparaginase erwinia chrysanthemi (recombinant)-rywn: second-line agent in patients who have developed a systemic allergic reaction or anaphylaxis due to pegaspargase (PEG) hypersensitivity (Category 2A)

NCCN Categories of Evidence and Consensus (all recommendations are category 2A unless otherwise indicated)	
Category 1	Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A	Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B	Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3	Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

NCCN Categories of Preference (all recommendations are considered appropriate)	
Preferred intervention	Interventions that are based on superior efficacy, safety, and evidence; and, when appropriate, affordability.
Other recommended intervention	Other interventions that may be somewhat less efficacious, more toxic, or based on less mature data; or significantly less affordable for similar outcomes.
Useful in certain circumstances	Other interventions that may be used for select patient populations (defined with recommendation).

Criteria

Prior authorization is required.

Rylaze® is considered medically necessary when **ALL** of the following are met:

1. Diagnosis of acute lymphoblastic leukemia (ALL) or lymphoblastic lymphoma; **AND**
2. Prescribed as a component of a multi-agent chemotherapeutic regimen; **AND**
3. Member has developed sensitivity to an *E. Coli*-derived asparaginase product; **AND**
4. Prescribed by, or in consultation with, an oncologist; **AND**
5. Request meets one of the following (a, b, or c):
    a. Dose is administered every 48 hours and does not exceed 25 mg/m^2; or,
    b. Dose is administered every Monday, Wednesday, and Friday, and:
        i. Monday dose is given in the MORNING and does not exceed 25 mg/m^2; **AND**
        ii. Wednesday dose is given in the MORNING and does not exceed 25 mg/m^2; **AND**
        iii. Friday dose is given in the AFTERNOON and does not exceed 50 mg/m^2; or,
    c. Regimen is supported by clinical practice guidelines (i.e., must be recommended in NCCN Guidelines®). Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Rylaze® is considered medically necessary for continuation of therapy when **ALL** of the following are met:

1. Member is currently receiving medication through the Iowa Medicaid benefit or has previously met initial approval criteria; **AND**
2. Documentation of positive clinical response to therapy, as demonstrated by tumor response or lack of disease progression, and an acceptable toxicity profile; **AND**
3. Prescribed by, or in consultation with, an oncologist; **AND**
4. Request meets one of the following (a, b, or c):
    a. Dose is administered every 48 hours and does not exceed 25 mg/m^2; or,
    b. Dose is administered every Monday, Wednesday, and Friday, and:
        i. Monday dose is given in the MORNING and does not exceed 25 mg/m^2; **AND**
        ii. Wednesday dose is given in the MORNING and does not exceed 25 mg/m^2; **AND**
        iii. Friday dose is given in the AFTERNOON and does not exceed 50 mg/m^2; or,
    c. Regimen is supported by clinical practice guidelines (i.e., must be recommended in NCCN Guidelines®). Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Approval Duration and Quantity Limits

	Initial Authorization	Subsequent Authorization(s)
Approval Duration	3 months	6 months
Quantity Limits	Dose may not exceed: A. 25 mg/m^2 every 48 hours (when following the 48-hour dosing regimen); **OR** B. 25 mg/m^2 on Monday & Wednesday and 50 mg/m^2 on Friday (when following the Mon-Wed-Fri dosing regimen)	

Coding and Product Information

The following list(s) of codes and product information are provided for reference purposes only and may not be all inclusive. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment, nor does the exclusion of a code imply that its association to the HCPCS code is inappropriate.

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

ICD-10	Description
C83.50 – C83.59	Lymphoblastic (diffuse) lymphoma
C91.00 – C91.02	Acute lymphoblastic leukemia (ALL)

NDC (Strength)	Labeler	Dosage	Pkg Size	Pkg Qty	Units/ Pkg
68727-0900-01 (single-dose vial, 10 mg/0.5 mL)	Jazz Pharmaceuticals, Inc. (68727)	0.1 mg	1	EA	100
68727-0900-03 (carton of 3 single-dose vials)	Jazz Pharmaceuticals, Inc. (68727)	0.1 mg	1	EA	300

Compliance

1. Should conflict exist between the policy and applicable statute, the applicable statute shall supersede.
2. Federal and State law, as well as contract language, including definitions and specific contract provisions or exclusions, take precedence over medical policy and must be considered first in determining eligibility for coverage.
3. Medical technology is constantly evolving, and Iowa Medicaid reserves the right to review and update medical policy on an annual or as-needed basis.

Medical necessity guidelines have been developed for determining coverage for member benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. Medical necessity guidelines are developed for selected physician-administered medications found to be safe and proven to be effective in a limited, defined population or clinical circumstances. They include concise clinical coverage criteria based on current

literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. Criteria are revised and updated annually, or more frequently if new evidence becomes available that suggests needed revisions.

References

[1] Rylaze® prescribing information (04/2024). Jazz Pharmaceuticals, Inc.: Palo Alto, CA. Available online: www.rylaze.com. Accessed June 9, 2025.

[2] National Comprehensive Cancer Network (NCCN). Guidelines Process: About Clinical Practice Guidelines. Available online at www.nccn.org. Accessed July 29, 2024.

[3] National Comprehensive Cancer Network (NCCN). Guidelines Process: Development and Update of Guidelines. Available online at www.nccn.org. Accessed July 29, 2024.

[4] NCCN Clinical Practice Guidelines in Oncology. The NCCN Guidelines® are a work in progress that may be refined as often as new significant data becomes available. To view the most recent and complete version, go online to NCCN.org. NCCN Guidelines® referenced (note version number and effective date):

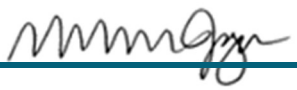
- Acute Lymphoblastic Leukemia (v.2.2025 – June 27, 2025)

Development of utilization management criteria may also involve research into other state Medicaid programs, other payer policies, consultation with experts and review by the Medicaid Clinical Advisory Committee (CAC). These sources may not be referenced individually unless they are specifically published and are otherwise applicable to the criteria at issue.

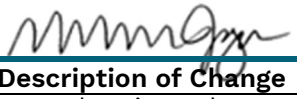
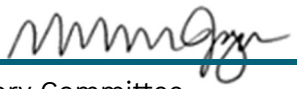
Criteria Change History

Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]	CAC		
Signature			

Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]	CAC		
Signature			

Change Date	Changed By	Description of Change	Version
07/18/2025	CAC	Annual review. Updated references.	4
Signature William (Bill) Jagiello, DO			

Criteria Change History *(continued)*

Change Date	Changed By	Description of Change	Version
07/19/2024	CAC	Annual review. Added dosing information into criteria. Reviewed NCCN Guidelines and updated references.	3
Signature William (Bill) Jagiello, DO			
Change Date	**Changed By**	**Description of Change**	**Version**
07/21/2023	CAC	Annual review. Alternative dosing regimen approved by FDA, added to Overview section and updated in Quantity Limits.	2
Signature William (Bill) Jagiello, DO			
Change Date	**Changed By**	**Description of Change**	**Version**
07/15/2022	CAC	Criteria implementation.	1
Signature William (Bill) Jagiello, DO			

CAC = Medicaid Clinical Advisory Committee