# Rylaze® (asparaginase Erwinia chrysanthemi (recombinant)-rywn)
## (Intramuscular)

-E-

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## I. Length of Authorization

- Initial: Prior authorization validity will be provided initially for 6 months.
- Renewal: Prior authorization validity may be renewed every 6 months thereafter.

## II. Dosing Limits

**Max Units (per dose and over time) [HCPCS Unit]:**

- 2,500 billable units (250 mg) per week

## III. Initial Approval Criteria [1]

Prior authorization validity is provided in the following conditions:

- Patient is at least 1 month of age; **AND**
- Patient must not have a history of serious pancreatitis, thrombosis, or hemorrhagic events with prior L-asparaginase therapy; **AND**

**Universal Criteria [1]**

- Patient must not have severe hepatic impairment; **AND**
- Used as a component of multi-agent chemotherapy regimen; **AND**
- Patient will receive premedication prior to administration of Rylaze to decrease the risk and severity of hypersensitivity reactions§ (e.g., acetaminophen, an H-1 receptor blocker [such as diphenhydramine], and an H-2 receptor blocker [such as famotidine]); **AND**

**Acute Lymphoblastic Leukemia (ALL)/Lymphoblastic Lymphoma (LBL) † Φ [1-3,5]**

- Used as a substitute for E. coli-derived asparaginase (e.g., pegaspargase calaspargase) in cases of hypersensitivity§ *(e.g., systemic allergic reactions or anaphylaxis)*

**T-Cell Lymphomas ‡ [2]**

- Patient has Extranodal NK/T-Cell Lymphoma; **AND**

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- Used as a substitute for pegaspargase in cases of systemic allergic reaction or anaphylaxis due to hypersensitivity to pegaspargase

| § Definition of Hypersensitivity Reactions (CTCAE v5.0) [7,8] |
|---|
| **Allergic Reaction**<br>– Grade 1: Systemic intervention not indicated<br>– Grade 2: Oral intervention indicated<br>– Grade 3: Bronchospasm; hospitalization indicated for clinical sequelae; IV intervention indicated<br>– Grade 4: Life-threatening consequences; urgent intervention indicated<br>– Grade 5: Death<br>**Anaphylaxis**<br>– Grade 1 or 2: N/A<br>– Grade 3: Symptomatic bronchospasm, with or without urticaria; parenteral intervention indicated; allergy-related edema/angioedema; hypotension<br>– Grade 4: Life-threatening consequences; urgent intervention indicated<br>– Grade 5: Death |

**Preferred therapies and recommendations are determined by review of clinical evidence. NCCN category of recommendation is taken into account as a component of this review. Regimens deemed equally efficacious (i.e., those having the same NCCN categorization) are considered to be therapeutically equivalent.**

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

## IV. Renewal Criteria [1]

Prior authorization validity can be renewed based upon the following criteria:

- Patient continues to meet the universal and indication-specific criteria as identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: severe hypersensitivity reactions including anaphylaxis, pancreatitis, thrombosis, hemorrhage, hepatotoxicity (including hepatic veno-occlusive disease), etc.; **AND**

**Acute Lymphoblastic Leukemia (ALL)/Lymphoblastic Lymphoma (LBL)**

- Disease stabilization or improvement as evidenced by a complete response [CR] (e.g., morphologic, cytogenetic or molecular complete response CR), complete hematologic response or a partial response by CBC, bone marrow cytogenic analysis, QPCR, or FISH

**T-Cell Lymphoma**



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- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread

## V. Dosage/Administration [1]

<table>
<tr><th>Indication</th><th>Dose</th></tr>
<tr><td>All Indications</td><td>When replacing a long-acting asparaginase product, there are two Rylaze regimens that can be used. (See table below for duration of administration as a replacement therapy).<br>• Rylaze 25 mg/m$^2$ administered intramuscularly every 48 hours; OR<br>• Rylaze 25 mg/m$^2$ administered intramuscularly on Monday and Wednesday morning, and 50 mg/m$^2$ on Friday afternoon (Administer the Friday afternoon dose 53 to 58 hours after the Wednesday morning dose (e.g., 8:00 am on Monday and Wednesday, and 1:00 pm to 6:00 pm on Friday)
<table>
<tr><th>When RYLAZE is Administered:</th><th>Recommended Duration of RYLAZE to Replace Calaspargase Pegol Products</th><th>Recommended Duration of RYLAZE to Replace Pegaspargase Products</th></tr>
<tr><td>25 mg/m$^2$ intramuscular every 48 hours</td><td>Replace one dose of calaspargase pegol products with 11 doses of RYLAZE</td><td>Replace one dose of pegaspargase products with 7 doses of RYLAZE</td></tr>
<tr><td>25 mg/m$^2$ intramuscular on Monday morning and Wednesday morning, and 50 mg/m$^2$ intramuscular on Friday afternoon</td><td>Replace one dose of calaspargase pegol products with 9 doses of RYLAZE</td><td>Replace one dose of pegaspargase products with 6 doses of RYLAZE</td></tr>
</table>
Note: Premedicate patients 30-60 minutes prior to administration of therapy. Because of the risk of serious allergic reactions (e.g., life-threatening anaphylaxis), administer in a clinical setting with resuscitation equipment and other agents necessary to treat anaphylaxis (e.g., epinephrine, oxygen, intravenous steroids, antihistamines).</td></tr>
</table>

## VI. Billing Code/Availability Information

HCPCS Code:

- J9021 – Injection, asparaginase, recombinant, (rylaze), 0.1 mg; 1 billable unit = 0.1 mg

NDC(s):

- Rylaze 10 mg/0.5 mL solution in a single-dose vial: 68727-0900-xx



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## VII. References (STANDARD)


1. Rylaze [package insert]. Palo Alto, CA; Jazz Pharmaceuticals, Inc.; July 2025. Accessed November 2025.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Asparaginase Erwinia chrysanthemi (recombinant)-rywn. National Comprehensive Cancer Network, 2025. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed November 2025.
3. Pieters R, Hunger SP, Boos J, et al. L-asparaginase treatment in acute lymphoblastic leukemia: a focus on Erwinia asparaginase. Cancer. 2011 Jan 15; 117(2): 238–249.
4. Raetz EA, Salzer WL. Tolerability and Efficacy of L-Asparaginase Therapy in Pediatric Patients With Acute Lymphoblastic Leukemia, Journal of Pediatric Hematology/Oncology: October 2010 - Volume 32 - Issue 7 - p 554-563 doi: 10.1097/MPH.0b013e3181e6f003
5. Maese L, Rau RE, Raetz EA, et al. A phase II/III study of JZP-458 in patients with acute lymphoblastic leukemia (ALL)/lymphoblastic lymphoma (LBL) who are hypersensitive to E. coli-derived asparaginases. DOI: 10.1200/JCO.2020.38.15_suppl.TPS7568 *Journal of Clinical Oncology* 38, no. 15_suppl
6. Lin T, Hernandez-Illas M, Rey A, Jenkins J, et al. A Randomized Phase I Study to Evaluate the Safety, Tolerability, and Pharmacokinetics of Recombinant Erwinia Asparaginase (JZP-458) in Healthy Adult Volunteers. Clin Transl Sci. 2021 May;14(3):870-879. doi: 10.1111/cts.12947. Epub 2021 Mar 23.
7. Stock W, Douer D, DeAngelo DJ, et al. Prevention and management of asparaginase/pegasparaginase-associated toxicities in adults and older adolescents: recommendations of an expert panel. Leuk Lymphoma 2011:52;2237-2253.
8. Common Terminology Criteria for Adverse Events (CTCAE) v5.0. NIH National Cancer Institute: Division of Cancer Treatment & Diagnosis – Cancer Therapy Evaluation Program. Available at: CTEP Trial Development and Conduct - NCI.


## VIII. References (ENHANCED)


1e. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Acute Lymphoblastic Leukemia. Version 2.2025. National Comprehensive Cancer Network, 2025. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To





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view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed November 2025.

2e. Vrooman LM, Kirov II, Dreyer ZE, et al. Activity and Toxicity of Intravenous Erwinia Asparaginase Following Allergy to E. coli-Derived Asparaginase in Children and Adolescents With Acute Lymphoblastic Leukemia. Pediatr Blood Cancer. 2016 Feb;63(2):228-33. doi: 10.1002/pbc.25757. Epub 2015 Sep 16.

3e. Matsumoto Y, Nomura K, Kanda-Akano Y, et al. Successful treatment with Erwinia L-asparaginase for recurrent natural killer/T cell lymphoma. *Leukemia & lymphoma*. 2003;44(5):879-882. doi:https://doi.org/10.1080/1042819031000067873

4e. Prime Therapeutics Management. Rylaze Clinical Literature Review Analysis. Last updated November 2025. Accessed November 2025.

## Appendix A – Non-Quantitative Treatment Limitations (NQTL) Factor Checklist

Non-quantitative treatment limitations (NQTLs) refer to the methods, guidelines, standards of evidence, or other conditions that can restrict how long or to what extent benefits are provided under a health plan. These may include things like utilization review or prior authorization. The utilization management NQTL applies comparably, and not more stringently, to mental health/substance use disorder (MH/SUD) Medical Benefit Prescription Drugs and medical/surgical (M/S) Medical Benefit Prescription Drugs. The table below lists the factors that were considered in designing and applying prior authorization to this drug/drug group, and a summary of the conclusions that Prime's assessment led to for each.

| Factor | Conclusion |
|---|---|
| Indication | Yes: Consider for PA |
| Safety and efficacy | No: PA not a priority |
| Potential for misuse/abuse | No: PA not a priority |
| Cost of drug | Yes: Consider for PA |

## Appendix 1 – Covered Diagnosis Codes

| ICD-10 | ICD-10 Description |
|---|---|
| C83.50 | Lymphoblastic (diffuse) lymphoma, unspecified site |
| C83.51 | Lymphoblastic (diffuse) lymphoma, lymph nodes of head, face, and neck |
| C83.52 | Lymphoblastic (diffuse) lymphoma, intrathoracic lymph nodes |
| C83.53 | Lymphoblastic (diffuse) lymphoma, intra-abdominal lymph nodes |



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| ICD-10 | ICD-10 Description |
|---|---|
| C83.54 | Lymphoblastic (diffuse) lymphoma, lymph nodes of axilla and upper limb |
| C83.55 | Lymphoblastic (diffuse) lymphoma, lymph nodes of inguinal region and lower limb |
| C83.56 | Lymphoblastic (diffuse) lymphoma, intrapelvic lymph nodes |
| C83.57 | Lymphoblastic (diffuse) lymphoma, spleen |
| C83.58 | Lymphoblastic (diffuse) lymphoma, lymph nodes of multiple sites |
| C83.59 | Lymphoblastic (diffuse) lymphoma, extranodal and solid organ sites |
| C84.90 | Mature T/NK-cell lymphomas, unspecified, unspecified site |
| C84.91 | Mature T/NK-cell lymphomas, unspecified, lymph nodes of head, face, and neck |
| C84.92 | Mature T/NK-cell lymphomas, unspecified, intrathoracic lymph nodes |
| C84.93 | Mature T/NK-cell lymphomas, unspecified, intra-abdominal lymph nodes |
| C84.94 | Mature T/NK-cell lymphomas, unspecified, lymph nodes of axilla and upper limb |
| C84.95 | Mature T/NK-cell lymphomas, unspecified, lymph nodes of inguinal region and lower limb |
| C84.96 | Mature T/NK-cell lymphomas, unspecified, intrapelvic lymph nodes |
| C84.97 | Mature T/NK-cell lymphomas, unspecified, spleen |
| C84.98 | Mature T/NK-cell lymphomas, unspecified, lymph nodes of multiple sites |
| C84.99 | Mature T/NK-cell lymphomas, unspecified, extranodal and solid organ sites |
| C84.Z0 | Other mature T/NK-cell lymphomas, unspecified site |
| C84.Z1 | Other mature T/NK-cell lymphomas, lymph nodes of head, face, and neck |
| C84.Z2 | Other mature T/NK-cell lymphomas, intrathoracic lymph nodes |
| C84.Z3 | Other mature T/NK-cell lymphomas, intra-abdominal lymph nodes |
| C84.Z4 | Other mature T/NK-cell lymphomas, lymph nodes of axilla and upper limb |
| C84.Z5 | Other mature T/NK-cell lymphomas, lymph nodes of inguinal region and lower limb |
| C84.Z6 | Other mature T/NK-cell lymphomas, intrapelvic lymph nodes |
| C84.Z7 | Other mature T/NK-cell lymphomas, spleen |
| C84.Z8 | Other mature T/NK-cell lymphomas, lymph nodes of multiple sites |
| C84.Z9 | Other mature T/NK-cell lymphomas, extranodal and solid organ sites |
| C86.00 | Extranodal NK/T-cell lymphoma, nasal type not having achieved remission |
| C91.00 | Acute lymphoblastic leukemia not having achieved remission |
| C91.01 | Acute lymphoblastic leukemia, in remission |
| C91.02 | Acute lymphoblastic leukemia, in relapse |



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## Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

| Medicare Part B Administrative Contractor (MAC) Jurisdictions | | |
|---|---|---|
| **Jurisdictio** | **Applicable State/US Territory** | **Contractor** |
| E (1) | CA, HI, NV, AS, GU, CNMI | Noridian Healthcare Solutions, LLC |
| F (2 & 3) | AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ | Noridian Healthcare Solutions, LLC |
| 5 | KS, NE, IA, MO | Wisconsin Physicians Service Insurance Corp (WPS) |
| 6 | MN, WI, IL | National Government Services, Inc. (NGS) |
| H (4 & 7) | LA, AR, MS, TX, OK, CO, NM | Novitas Solutions, Inc. |
| 8 | MI, IN | Wisconsin Physicians Service Insurance Corp (WPS) |
| N (9) | FL, PR, VI | First Coast Service Options, Inc. |
| J (10) | TN, GA, AL | Palmetto GBA |
| M (11) | NC, SC, WV, VA (excluding below) | Palmetto GBA |
| L (12) | DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA) | Novitas Solutions, Inc. |
| K (13 & 14) | NY, CT, MA, RI, VT, ME, NH | National Government Services, Inc. (NGS) |
| 15 | KY, OH | CGS Administrators, LLC |



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