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

Document Number: IC-0612

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I. Length of Authorization

Coverage will be provided for 6 months and may be renewed.

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]

Coverage 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**
- 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 – Grade 1: Systemic intervention not indicated – Grade 2: Oral intervention indicated – Grade 3: Bronchospasm; hospitalization indicated for clinical sequelae; IV intervention indicated – Grade 4: Life-threatening consequences; urgent intervention indicated – Grade 5: Death **Anaphylaxis** – Grade 1 or 2: N/A – Grade 3: Symptomatic bronchospasm, with or without urticaria; parenteral intervention indicated; allergy-related edema/angioedema; hypotension – Grade 4: Life-threatening consequences; urgent intervention indicated – Grade 5: Death

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

IV. Renewal Criteria [1]

Coverage 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)

- 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

- 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).
• Rylaze 25 mg/m^2 administered intramuscularly every 48 hours; OR
• 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

VII. References

1. Rylaze [package insert]. Palo Alto, CA; Jazz Pharmaceuticals, Inc.; April 2024. Accessed November 2024.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Asparaginase Erwinia chrysanthemi (recombinant)-rywn. National Comprehensive Cancer Network, 2024. 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 2024.

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: https://ctep.cancer.gov/protocoldevelopment/electronic_applications/ctc.htm#ctc_50.

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
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

ICD-10	ICD-10 Description
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
C86.0	Extranodal NK/T-cell lymphoma, nasal type
C91.00	Acute lymphoblastic leukemia not having achieved remission
C91.01	Acute lymphoblastic leukemia, in remission
C91.02	Acute lymphoblastic leukemia, in relapse

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		
Jurisdiction	**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