TWO IM DOSING OPTIONS
MONDAY, WEDNESDAY, FRIDAY
OR EVERY 48 HOURS

RYLAZE®
asparaginase erwinia chrysanthemi (recombinant)-rywn for injection 10mg/0.5mL per vial

RYLAZE BILLING & CODING GUIDE

TABLE OF CONTENTS

For questions or support, contact your Jazz Pharmaceuticals, Inc. Oncology Business Manager using the information below, or click here.

Name: _____ **Cell:** _____

Email: _____

Indication

RYLAZE is indicated as a component of a multi-agent chemotherapeutic regimen given by intramuscular injection 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.

IMPORTANT SAFETY INFORMATION

Contraindications

RYLAZE is contraindicated in patients with: history of serious hypersensitivity reactions to *Erwinia asparaginase*, including anaphylaxis; history of serious pancreatitis during previous asparaginase therapy; history of serious thrombosis during previous asparaginase therapy; history of serious hemorrhagic events during previous asparaginase therapy; or severe hepatic impairment.

E. coli=Escherichia coli; IM=intramuscular/intramuscularly.

Please see additional Important Safety Information throughout and full Prescribing Information.

Introduction

This guide provides an overview of billing, coding, and coverage information related to RYLAZE (asparaginase erwinia chrysanthemi (recombinant)-rywn) injection, for intramuscular use—**the only FDA-approved *Erwinia* asparaginase for the treatment of ALL/LBL.**[1] Healthcare providers can use this guide to determine for themselves the appropriate claims to file for RYLAZE-related services. Jazz Pharmaceuticals does not guarantee payment or coverage for any product or service. Information specific to billing and coding should be verified by the provider for each patient prior to treatment. Providers should contact payers directly for any revised or additional requirements, information, or guidance. It is the provider's responsibility to determine the appropriate healthcare setting, and to submit true and correct claims for the products and services rendered.

RYLAZE billing and coding requirements will vary based on many factors, including the site of service where the drug is administered, the type of insurance the patient has, and the benefit under which RYLAZE is covered.

SITE OF SERVICE

RYLAZE may be administered in hospitals, infusion centers, and other healthcare facilities where medical support is available to appropriately manage anaphylactic reactions. For most payers, the site of service will affect the billing and coding requirements. This guide focuses on billing, coding, and coverage for RYLAZE when administered in hospital outpatient departments and other healthcare facilities where medical support is available to appropriately manage anaphylactic reactions.

COVERAGE GUIDANCE

Hospitals, infusion centers, and other healthcare facilities:

- For patients enrolled in Medicaid, a Medicare Advantage plan, or a commercial health plan, coverage of RYLAZE will vary by payer and may also be subject to utilization restrictions
- For Medicare patients, RYLAZE will be covered under Medicare Part B when used for an FDA-approved indication. There are no precertification requirements for RYLAZE under traditional fee-for-service

BENEFIT CATEGORY

Most payers cover physician-administered products such as RYLAZE under a medical benefit rather than a pharmacy benefit. For Medicare, while RYLAZE will typically be covered under Part B, private payers and Medicaid, including managed Medicaid, may require that physicians obtain RYLAZE through a specialty pharmacy. Specialty pharmacies may bill the payer under the medical or pharmacy benefit, depending on what that payer requires.

ALL=acute lymphoblastic leukemia; FDA=Food and Drug Administration; LBL=lymphoblastic lymphoma.

IMPORTANT SAFETY INFORMATION (cont.)

Warnings and Precautions

Hypersensitivity Reactions

Hypersensitivity reactions after the use of RYLAZE occurred in 29% of patients in clinical trials, and it was severe in 6% of patients. Anaphylaxis was observed in 2% of patients after intramuscular administration. Discontinuation of RYLAZE due to hypersensitivity reactions occurred in 5% of patients. Hypersensitivity reactions were higher in patients who received intravenous asparaginase erwinia chrysanthemi (recombinant)-rywn. The intravenous route of administration is not approved.

In patients administered RYLAZE intramuscularly in clinical trials, the median number of doses of RYLAZE that patients received prior to the onset of the first hypersensitivity reaction was 12 doses (range: 1-64 doses). The most commonly observed reaction was rash (19%), and 1 patient (1%) experienced a severe rash.

Please see additional Important Safety Information throughout and full Prescribing Information.

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Ordering Information

Specialty Distributors

RYLAZE is available for purchase from the authorized Specialty Distributors listed below. Verify that your facility has an account with the Specialty Distributor before ordering. If not, they should contact the Specialty Distributor. The facility should also contact the Specialty Distributor with questions regarding product returns, specific pricing, and payment terms.

cencora (formerly AmerisourceBergen)

ASD Healthcare	Oncology Supply
Phone/Fax: (800) 746-6273/(800) 547-9413 **Online:** https://www.asdhealthcare.com/home	**Phone/Fax:** (800) 633-7555/(800) 248-8205 **Online:** https://www.oncologysupply.com

CardinalHealth™

Cardinal Specialty Pharmaceutical Distribution (SPD)
Phone/Fax: (877) 453-3972/(877) 274-9897 **Online:** Order Express (Hospitals) https://orderexpress.cardinalhealth.com **Specialty Online (Clinics):** https://specialtyonline.cardinalhealth.com

McKESSON

McKesson Plasma and Biologics (MPB)	McKesson Specialty Health (MSH)
Phone/Fax: (877) 625-2566/(888) 752-7626 **Online:** https://connect.mckesson.com	**Phone/Fax:** (800) 482-6700/(800) 289-9285 **Online:** https://MSCS.McKesson.com

The information above is subject to change at Jazz's discretion, is for informational purposes only, and is not intended to supersede or revise any agreements with Group Purchasing Organizations.

Please see Important Safety Information throughout and full Prescribing Information.

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Dosage and Administration

Recommended Dosage[1]

There are 2 RYLAZE regimens that can be used to replace a long-acting asparaginase product. The recommended dosages of RYLAZE are:

MON MORNING	WED MORNING	FRI AFTERNOON
IM 25 mg/m^2	IM 25 mg/m^2	IM 50 mg/m^2
within 67 hours of FRI dose	48 hours after MON dose	within 53-58 hours of WED dose

OR

EVERY 48 HOURS
IM 25 mg/m^2

Table 1 in the full prescribing information shows the number of RYLAZE dosages recommended for the intended duration of treatment for replacement of 1 dose of calaspargase pegol products (3 weeks of asparaginase coverage) or 1 dose of pegaspargase products (2 weeks of asparaginase coverage). See the full prescribing information for the long-acting asparaginase product to determine the total duration of administration of RYLAZE as replacement therapy.

Recommended Premedication[1]

Premedicate patients with acetaminophen, an H-1 receptor blocker (such as diphenhydramine), and an H-2 receptor blocker (such as famotidine) 30-60 minutes prior to administration of RYLAZE to decrease the risk and severity of hypersensitivity reactions.

Recommended Monitoring and Dosage Modifications for Adverse Reactions[1]

Monitor patient's bilirubin, transaminases, glucose, and clinical examinations prior to treatment every 2-3 weeks and as indicated clinically. If results are abnormal, monitor patients until recovery from the cycle of therapy. See page 3 of the full Prescribing Information for the recommended dose modifications for the following adverse reactions: hypersensitivity reactions, pancreatitis, thrombosis, hemorrhage, and hepatotoxicity.

Preparation and Administration Instructions[1]

Ensure that medical support is available to appropriately manage anaphylactic reactions when administering RYLAZE.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. If particulate matter, cloudiness, or discoloration are present, discard the vial.

- Use aseptic technique
- Determine the dose, total volume of RYLAZE solution required, and the number of RYLAZE vials needed based on the individual patient's BSA. More than one vial may be needed for a full dose
- Withdraw the indicated injection volume of RYLAZE into the syringe for injection
  - Do not shake the vial
  - Limit the volume of RYLAZE at a single injection site to 2 mL
  - If the volume to be administered is greater than 2 mL, divide the doses equally into multiple syringes, one for each injection site
  - Discard the remaining unused RYLAZE in the single-dose vial

IMPORTANT SAFETY INFORMATION (cont.)

Warnings and Precautions (cont.)

Hypersensitivity Reactions (cont.)

Hypersensitivity reactions observed with L-asparaginase class products include angioedema, urticaria, lip swelling, eye swelling, rash or erythema, blood pressure decreased, bronchospasm, dyspnea, and pruritus.

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Dosage and Administration (cont.)

Preparation and Administration Instructions (cont.)[1]

- Administer RYLAZE by intramuscular injection
  - Rotate injection sites
  - Do not inject RYLAZE into scar tissue or areas that are reddened, inflamed, or swollen
- If the prepared dose is not used immediately, store the syringe(s) at room temperature 15°C to 25°C (59°F to 77°F) for up to 8 hours or refrigerated at 2°C to 8°C (36°F to 46°F) for up to 24 hours. The syringe does not need to be protected from light during storage

How Supplied/Storage and Handling[1]

RYLAZE injection is supplied as a sterile, clear to opalescent, colorless to slightly yellow, preservative-free solution in single-dose vials.

Each single-dose vial (NDC 68727-900-01) contains 10 mg/0.5 mL asparaginase erwinia chrysanthemi (recombinant)-rywn. Each carton of RYLAZE (NDC 68727-900-03) contains 3 single-dose vials.

Store RYLAZE vials refrigerated at 2°C to 8°C (36°F to 46°F) in the original carton to protect from light. Do not shake or freeze.

NDC=National Drug Code.

IMPORTANT SAFETY INFORMATION (cont.)

Warnings and Precautions (cont.)

Hypersensitivity Reactions (cont.)

Premedicate patients prior to administration of RYLAZE as recommended. Because of the risk of serious allergic reactions (e.g., life-threatening anaphylaxis), administer RYLAZE in a setting with resuscitation equipment and other agents necessary to treat anaphylaxis (e.g., epinephrine, oxygen, intravenous steroids, antihistamines). Discontinue RYLAZE in patients with serious hypersensitivity reactions.

Pancreatitis

Pancreatitis, including elevated amylase or lipase, was reported in 20% of patients in clinical trials of RYLAZE and was severe in 8%. Symptomatic pancreatitis occurred in 7% of patients, and it was severe in 6% of patients. Elevated amylase or lipase without symptomatic pancreatitis was observed in 13% of patients treated with RYLAZE. Hemorrhagic or necrotizing pancreatitis have been reported with L-asparaginase class products.

Inform patients of the signs and symptoms of pancreatitis, which, if left untreated, could be fatal. Evaluate patients with symptoms compatible with pancreatitis to establish a diagnosis. Assess serum amylase and lipase levels in patients with any signs or symptoms of pancreatitis. Discontinue RYLAZE in patients with severe or hemorrhagic pancreatitis. In the case of mild pancreatitis, withhold RYLAZE until the signs and symptoms subside and amylase and/or lipase levels return to 1.5 times the ULN. After resolution of mild pancreatitis, treatment with RYLAZE may be resumed.

Thrombosis

Serious thrombotic events, including sagittal sinus thrombosis and pulmonary embolism, have been reported in 1% of patients following treatment with RYLAZE. Discontinue RYLAZE for a thrombotic event, and administer appropriate antithrombotic therapy. Consider resumption of treatment with RYLAZE only if the patient had an uncomplicated thrombosis.

Hemorrhage

Bleeding was reported in 25% of patients treated with RYLAZE, and it was severe in 2%. Most commonly observed reactions were bruising (12%) and nose bleed (9%).

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Sample Coding

This section provides sample codes for hospitals, infusion centers, and other healthcare facilities where medical support is available to appropriately manage anaphylactic reactions for ALL or LBL. Note that many of the codes are the same for all sites of care.

ICD-10-CM diagnosis codes and ICD-10-PCS codes[2,3]	
C91.00	ALL not having achieved remission: ALL with failed remission, ALL NOS
C91.01	ALL, in remission
C91.02	ALL, in relapse
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
3E03305	Introduction of other antineoplastic into peripheral vein, percutaneous approach
3E04305	Introduction of other antineoplastic into central vein, percutaneous approach

Revenue codes[4]	
0636	Pharmacy: Drugs requiring detailed coding
0250	Pharmacy: General
0331	Radiology therapeutic and/or chemotherapy administration: Chemotherapy administration, injection

MS-DRG codes[5]	
834	Acute leukemia without major O.R. procedure with MCC
835	Acute leukemia without major O.R. procedure with CC
836	Acute leukemia without major O.R. procedure without CC/MCC

CC=comorbid conditions; ICD-10-CM=International Classification of Diseases, Tenth Revision, Clinical Modification; ICD-10-PCS=International Classification of Diseases, Tenth Revision, Procedure Coding System; MCC=major complications or comorbidities; MS-DRG=Medicare severity diagnosis-related group; NOS=not otherwise specified; O.R.=operating room.

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Sample Coding (cont.)

Permanent J-code for RYLAZE[6,a]	Description[1]	HCPCS code dosage (billing units)	Example
J9021	IM injection: 25 mg/m^2	0.1 mg = 1 unit	4 mg = 40 units

[a]The HCPCS Level II code J9021 is effective for Medicare Part B patients as of January 1, 2022.[6] Please check with commercial and Medicaid resources for the effective date.

JW modifier: Providers and suppliers are required to report the JW modifier on Part B drug claims for discarded drugs or biologicals. Also, providers and suppliers must document the amount of discarded drugs or biologicals in Medicare beneficiaries' medical records.

NDC[1]		
10-digit	11-digit	Description
68727-900-01	68727-0900-01	Single-dose vial of RYLAZE
68727-900-03	68727-0900-03	Carton containing 3 single-dose vials of RYLAZE

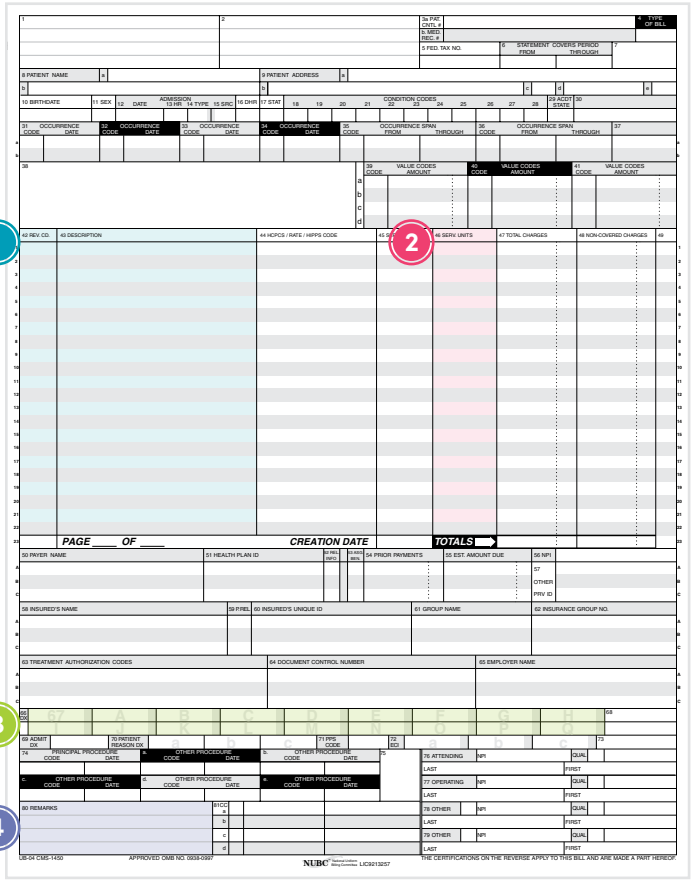
Payers may require a 10-digit or 11-digit NDC. Both are provided for your convenience. These are sample codes based on publicly available information and are informational only and not a guarantee or promise of coverage. Appropriate codes can vary by patient, setting of care, and payer. Correct coding is the responsibility of the provider submitting the claim for the item or service. Please check with the payer to verify codes and special billing requirements.

CMS=Centers for Medicare & Medicaid Services; HCPCS=Healthcare Common Procedure Coding System; IM=intramuscular.

Sample Medicare Claim Forms

CMS-1450 Form (Hospital Outpatient)

This sample claim form is provided only as an example. The healthcare provider is responsible for determining appropriate codes for an individual patient for related and/or separate procedures and for completing the appropriate forms.



1 **Fields 42 and 43**

Enter the appropriate revenue code (Field 42) and description (Field 43) corresponding to HCPCS code (Field 44).

2 **Field 46**

Enter the number of units billed that corresponds to the vial size used. Contact your Medicare contractor and/or all other contracted/noncontracted payer(s) for any questions regarding filling guidelines for coverage, coding, and payment.

3 **Field 67**

Enter the diagnosis code.

4 **Field 80**

Product information: Billing with a specific HCPCS code allows for faster payment through electronic billing. Manual billing may still be required in certain circumstances.

In those cases, it may be necessary to provide the following product information for payment: NDC, quantity of the drugs administered (expressed in unit of measure applicable to the drug or biological) and the date the drug was administered to the patient.

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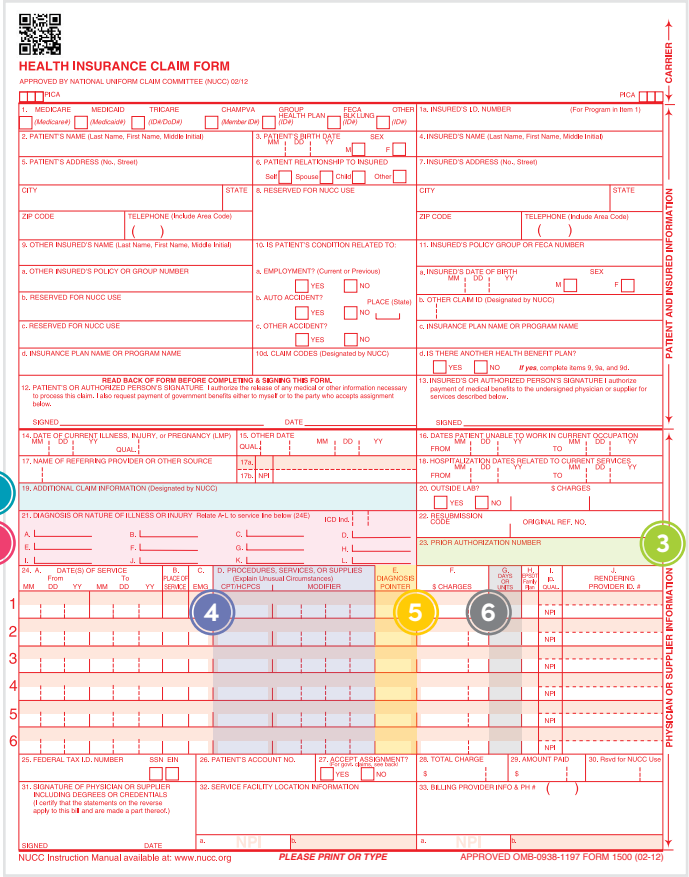
Sample Medicare Claim Forms (cont.)

CMS-1500 Form (Other Healthcare Facilities)

This sample claim form is provided only as an example. The healthcare provider is responsible for determining appropriate codes for an individual patient for related and/or separate procedures and for completing the appropriate forms. Guidance is provided below for how to incorporate the miscellaneous J-codes (J3490, J3590, J9999).

This sample claim form assumes a patient received the recommended dosage of RYLAZE: 25 mg/m^2 administered intramuscularly on Monday morning and Wednesday morning, and 50 mg/m^2 administered intramuscularly on Friday afternoon; or 25 mg/m^2 administered intramuscularly every 48 hours.[1,a]



1 Field 19

Billing with a specific HCPCS code allows for faster payment through electronic billing. Manual billing by the payer may still be required in certain circumstances. In those cases, it may be necessary to provide the following information for payment: specify drug information, ie, drug name, NDC,[b] dosage, strength, and route of administration.

2 Field 21

Enter the appropriate ICD-10-CM diagnosis code corresponding to the patient's diagnosis, such as C91.02.

3 Field 23

If required, report the prior authorization number here.

4 Field 24, Column D

Enter the correct miscellaneous J-code to report the use of RYLAZE. Also include the CPT code representing procedures performed as well as the appropriate modifier (append modifier if needed/appropriate).

5 Field 24, Column E

Specify diagnosis from Box 21 relating to each CPT/HCPCS code listed in Field 24, Column D.

6 Field 24, Column G

For miscellaneous J-code, enter a 1 and provide descriptor information in Box 19.[c]

CPT=Current Procedural Terminology.

[a]Table 1 in the full prescribing information shows the number of RYLAZE dosages recommended for the intended duration of treatment for replacement of 1 dose of calaspargase pegol products (3 weeks of asparaginase coverage) or 1 dose of pegaspargase products (2 weeks of asparaginase coverage). See the full prescribing information for the long-acting asparaginase product to determine the total duration of administration of RYLAZE as replacement therapy.[1]

[b]Please note that for billing purposes, the NDC requires 11 digits (thus a zero has been entered into the sixth digit). This is consistent with the Red Book® and First Databank® listings.

[c]Contact your Medicare contractor and/or all other contracted/non-contracted payer(s) for any questions regarding filing guidelines for coverage, coding, and payment.

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Jazz Is Committed to Removing Barriers to Access and Reimbursement

JazzCares®
Making a difference in Patients' lives, one Patient at a time

JazzCares® supports healthcare providers and office staff with coverage and reimbursement support[a] so appropriate patients can get access to RYLAZE and reduce their out-of-pocket costs.[b]

JazzCares
Assists you with benefits investigations, prior authorizations and appeals,[a] and referrals to other financial assistance options for eligible patients

Savings Card
Eligible, commercially insured patients can pay as little as $10 for their RYLAZE medication, subject to an annual maximum (restrictions apply)[a]

Free Drug Program
Uninsured or underinsured patients who meet certain financial criteria may be eligible to receive RYLAZE at no cost[b]

Your Jazz Oncology Business Manager provides expertise and support

- Assistance with reimbursement-related questions about RYLAZE
- Purchasing, procurement and distribution support, and education on billing and coding

To contact your Oncology Business Manager, click **here** or refer to page 1

For More Information

Visit	Call the	Contact
www.jazzcares.com/hcp/rylaze or www.rylazepro.com	Patient Support Hotline at **(833) 533-5299** Monday–Friday 8:00 AM to 8:00 PM ET	Jazz Pharmaceuticals Medical Information at **(800) 520-5568** or click **here**

[a]Insurance coverage and plans may vary. JazzCares provides general information only and is not a guarantee of any coverage or reimbursement outcome. All treatment decisions rest solely with the treating physician or qualified healthcare professional.
[b]Subject to eligibility requirements and terms and conditions.

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Checklists and Sample Letters

Benefits Verification Checklist

When calling a payer to verify benefits and inquire about prior authorization, the following key questions should be considered.

Verify patient eligibility and benefits with the payer before providing RYLAZE.

- [ ] **What is the patient's copayment, coinsurance, deductible, or out-of-pocket maximum?**
  - Has it been met? If not, what amount has been applied to date?
- [ ] **Does the patient have an annual or lifetime benefit maximum?**
  - Has it been met? If not, what amount has been applied to date?
- [ ] **Does the patient have other insurance benefits that will need to be coordinated? Is prior authorization required? If so, what are the submission requirements for RYLAZE?**
  - HCPCS code to report RYLAZE
  - Number of units
  - Where and how to submit prior authorizations
  - Prior authorization process
  - Required documentation (eg, forms, Prescribing Information, and Letter of Medical Necessity)
  - Is there a medical policy in place for ALL or LBL and/or RYLAZE?
  - How long will it take?
- [ ] **Check criteria for reauthorization and obtain appropriate documentation.**

Checklists and Sample Letters (cont.)

Claims Filing Checklist

The following tips may assist you with successfully filing claims for an intramuscular therapy.

- [ ] **Use appropriate codes to report the patient's condition, the drugs the patient received, and the services you have provided.**
  - HCPCS code
  - CPT code
  - ICD-10-CM code
  - ICD-10-PCS code
  - Document waste per payer protocol, if necessary
- [ ] **Include additional information requested by the payer in Box 19 of the CMS-1500 form or in Box 80 of the CMS-1450.**
  - RYLAZE
  - Dosage
  - NDC number
  - Route of administration
  - Unit description (as required by the specific payer for a code that is not otherwise classified)
- [ ] **Attach additional information to the claim, if necessary.**
  - Letter of Medical Necessity
  - Prescribing Information
  - Patient notes
- [ ] **Review claim for accuracy, including patient identification numbers, coding, and number of units.**
- [ ] **File claim as soon as possible and within timely payer filing limits.**
- [ ] **Reconcile claim reports promptly and thoroughly to ensure claims have been appropriately processed and paid.**
- [ ] **Verify that payment amounts correspond with your public-payer allowables and your private-payer contracts.**

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Checklists and Sample Letters (cont.)

Letter of Medical Necessity Checklist

This section provides information and sample letter components that can help ensure your medical-necessity communications are as complete as possible. These samples describe the type of information usually required. You can refer to the checklist below as you develop and complete your own letters.

Items that may be needed to support the development of your Letter of Medical Necessity:

Patient information

- ☑ Patient name
- ☑ Patient date of birth
- ☑ Insurance ID
- ☑ Insurance group number
- ☑ Case ID (if applicable)

Clinical rationale

- ☑ Patient diagnosis
- ☑ Comprehensive list of previous treatment therapies used
- ☑ Confirmation that the patient has experienced hypersensitivity reaction with previous treatments
- ☑ Rationale for selecting RYLAZE
- ☑ Test results and chart notes
- ☑ Hospital admission and/or emergency room notes

Additional supporting documentation may vary between health plans, but may include:

- ☑ Prescribing Information
- ☑ Documentation required for prior authorization, if any
- ☑ Relevant peer-reviewed articles

Checklists and Sample Letters (cont.)

Sample Letter of Medical Necessity

This is an example of what payers may require in a Letter of Medical Necessity.

Be sure to understand the specific payer requirements for your patient.

[Date]
[Payer name]
[Payer street address]
[Payer city, state]
[ZIP code]

Patient name: [Patient full name]
Date of birth: [Patient birth date]
Member ID: [Patient member ID number]
Policy or group number: [Patient policy or group number]
Case ID number: [Case ID number (if applicable)]

To Whom It May Concern,

Patient's clinical/medical history:

- Patient's age
- Patient's diagnosis (eg, ICD-10-CM code)
- Date of diagnosis
- Patient's first visit, date of referral
- Previous treatments including drug names, duration of treatment(s), responses to those treatments
- Complications associated with the patient's ALL/LBL

Treatment plan:

- Include plan of treatment (eg, dosage, frequency of therapy, length of treatment)
- Clinical rationale for the RYLAZE prescription

Enclosures:

- Prescribing Information
- Clinical notes/medical records
- Test results
- Relevant peer-reviewed articles

Sincerely,

_____

[Physician name and signature]
[Physician address]
[Physician phone number]

Checklists and Sample Letters (cont.)

Letter of Appeal Checklist

This section provides information and examples that can help ensure your communications with health plans regarding an appeal are as complete as possible. These samples provide the type of information that will usually be required. Refer to this checklist as you develop and complete your own letters. One sample appeals letter is provided on the next page. Incorrect or incomplete submissions may delay the review process or result in an automatic denial of the request.

Below is a checklist of items that may be needed to support the development of your Letter of Appeal:

Patient information

- ☑ Patient name
- ☑ Patient date of birth
- ☑ Insurance ID
- ☑ Insurance group number
- ☑ Case ID (if applicable)

Clinical rationale

- ☑ Patient diagnosis
- ☑ Comprehensive list of previous treatment therapies used
- ☑ Confirmation that the patient has experienced hypersensitivity reaction with previous treatments
- ☑ Rationale for selecting RYLAZE
- ☑ Test results and chart notes
- ☑ Hospital admission and/or emergency room notes

Additional supporting documentation may vary between health plans, but may include:

- ☑ Prescribing Information
- ☑ Relevant peer-reviewed articles
- ☑ A copy of previous denial letters (only for 2nd- and 3rd-level appeals)

Checklists and Sample Letters (cont.)

Sample Letter of Appeal – Step Edit

To Whom It May Concern,

We have read and acknowledged your policy for the responsible management of drugs in the acute lymphoblastic leukemia (ALL) or lymphoblastic lymphoma (LBL) category. We are writing to request that you reconsider your denial of coverage for RYLAZE. This letter is being submitted on behalf of the above referenced patient for the treatment of ALL/LBL (dose, frequency).

The reason given for the denial was [state reason from insurer's letter]. A copy of the most recent denial letter is included along with medical notes in response to the denial. After reviewing the denial letter, we continue to feel that RYLAZE (dose, frequency) is the appropriate therapy. The relevant clinical history is summarized below.

(If patient is already taking RYLAZE, consider including information outlining the disease severity at the time of RYLAZE initiation. Medical records may need to be pulled from past dates to capture information relevant to RYLAZE treatment.)

This plan currently lists [required step-edit therapies] to be attempted prior to treatment with RYLAZE. These step-edit therapies are not viable for this patient. We are requesting that the step-edit therapy requirement be bypassed.

Document the patient's history, diagnosis, current condition, and symptoms. For example, confirm the patient's

_____ Diagnosis of ALL/LBL (eg, ICD-10-CM code)

_____ Age (if relevant)

_____ Previous treatments including drug names, duration of treatment(s), responses to those treatments

_____ Rationale and clinical support for why other treatments are not appropriate for this patient

Previous therapies:	**Reason for discontinuation:**	**Duration of therapy:**
_____	_____	_____
_____	_____	_____

(Provide rationale for prescribing RYLAZE, which may include that the patient experienced hypersensitivity reaction. Provide clinical support for your recommendation. This can be clinical trial data from the RYLAZE Prescribing Information.)

The ordering physician is [physician name, NPI #]. The prior authorization decision may be faxed to [fax #] or mailed to [physician business office address]. Please also send a copy of the coverage determination decision to [patient name].

Sincerely,

_____ _____

[Physician name and signature]
[Name of practice]
[Phone number]
Encl:

[Patient name and signature]

NPI=National Provider Identifier.

Please see Important Safety Information throughout and full Prescribing Information.

RYLAZE®
asparaginase erwinia chrysanthemi (recombinant)-rywn for injection 10mg/0.5mL per vial

IMPORTANT SAFETY INFORMATION (cont.)

Warnings and Precautions (cont.)

Hemorrhage (cont.)

In patients treated with L-asparaginase class products, hemorrhage may be associated with increased prothrombin time (PT), increased partial thromboplastin time (PTT), and hypofibrinogenemia. Consider appropriate replacement therapy in patients with severe or symptomatic coagulopathy.

Hepatotoxicity, including Hepatic Veno-Occlusive Disease

Elevated bilirubin and/or transaminases occurred in 75% of patients treated with RYLAZE in clinical trials, and 26% had Grade ≥3 elevations. Elevated bilirubin occurred in 28% of patients treated with RYLAZE in clinical trials, and 2% had Grade ≥3 elevations. Elevated transaminases occurred in 73% of patients treated with RYLAZE in clinical trials, and 25% had Grade ≥3 elevations.

Hepatotoxicity, including severe, life-threatening, and potential fatal cases of hepatic veno-occlusive disease (VOD), have been observed in patients treated with asparaginase class products in combination with standard chemotherapy, including during the induction phase of multiphase chemotherapy. Do not administer RYLAZE to patients with severe hepatic impairment. Inform patients of the signs and symptoms of hepatotoxicity.

Evaluate bilirubin and transaminases prior to each cycle of RYLAZE and at least weekly during cycles of treatment that include RYLAZE, through four weeks after the last dose of RYLAZE. Monitor frequently for signs and symptoms of hepatic VOD, which may include rapid weight gain, fluid retention with ascites, hepatomegaly (which may be painful), and rapid increase of bilirubin. For patients who develop abnormal liver tests after RYLAZE, more frequent monitoring for liver test abnormalities and clinical signs and symptoms of VOD is recommended. In the event of serious liver toxicity, including VOD, discontinue treatment with RYLAZE and provide supportive care.

Adverse Reactions

The most common adverse reactions (incidence >20%) with RYLAZE are abnormal liver test, nausea, musculoskeletal pain, infection, fatigue, headache, febrile neutropenia, pyrexia, hemorrhage, stomatitis, abdominal pain, decreased appetite, drug hypersensitivity, hyperglycemia, diarrhea, pancreatitis, and hypokalemia.

Use in Specific Populations

Pregnancy and Lactation

RYLAZE can cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential to use effective non-hormonal contraceptive methods during treatment with RYLAZE and for 3 months after the last dose. Advise women not to breastfeed during treatment with RYLAZE and for 1 week after the last dose.

Please see full Prescribing Information.

For more information on RYLAZE, visit www.rylazepro.com.

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Insurance coverage and plans may vary. This is general information only and is not a guarantee of any coverage or reimbursement outcome. All treatment decisions rest solely with the treating physician or qualified healthcare professional.

References: 1. RYLAZE [package insert]. Palo Alto, CA: Jazz Pharmaceuticals, Inc. **2.** ICD-10-CM tabular list of diseases and injuries. Centers for Medicare & Medicaid Services website. https://www.cms.gov/files/zip/2024-code-tables-tabular-and-index-updated-02/01/2024.zip. Updated February 1, 2024. Accessed April 30, 2024. **3.** ICD-10 Procedure Coding System (ICD-10-PCS) 2024 code tables and index. Centers for Medicare & Medicaid Services website. https://www.cms.gov/files/zip/2024-icd-10-pcs-code-tables-and-index-updated-12/19/2023.zip. Updated December 19, 2023. Accessed April 30, 2024. **4.** Revenue codes. Noridian Healthcare Solutions website. https://med.noridianmedicare.com/web/jea/topics/claim-submission/revenue-codes. Updated March 18, 2024. Accessed April 30, 2024. **5.** ICD-10-CM/PCS MS-DRG v39.0 definitions manual. Centers for Medicare & Medicaid Services website. https://www.cms.gov/icd10m/version39-fullcode-cms/fullcode_cms/P0320.html. Updated March 8, 2021. Accessed April 30, 2024. **6.** Centers for Medicare & Medicaid Services (CMS) Healthcare Common Procedure Coding System (HCPCS) application summaries and coding decisions third quarter 2021 coding cycle for drug and biological products. Centers for Medicare & Medicaid Services website. https://www.cms.gov/files/document/2021-hcpcs-application-summary-quarter-3-2021-drugs-and-biologics-updated-10012021.pdf. Accessed April 30, 2024.

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