

Rely on ^{Pr}Rylaze[®]

The **FIRST** *recombinant* asparaginase in Canada and the **ONLY** approved non-*E. coli* asparaginase for the treatment of ALL/LBL.

Rylaze (crisantaspase recombinant) is indicated as a component of a multi-agent chemotherapeutic regimen for the treatment of:¹

- Acute lymphoblastic leukemia (ALL) and lymphoblastic lymphoma (LBL) in adult and pediatric patients 1 year or older who have developed hypersensitivity to *E. coli*-derived asparaginase.



Rely on "Rylaze"

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Complete

Consistent

Care

Home

PATIENT OUTCOMES

COMPLETE ASPARAGINASE TREATMENT SIGNIFICANTLY INCREASES PATIENT OUTCOMES

Impact of Asparaginase Discontinuation on Outcome in AYAs and adults with BCR-ABL-negative ALL on a paediatric-inspired protocol^{1,2,3}

Survival probability in 85 BCR-ABL-negative ALL patients aged 18-60 years from 2006 until 2008 on a modified DFCI 91-01 protocol

Patients who received at least 80% of the planned asparaginase dosing had a significantly higher 3-year OS (p=0.002) and RFS (p=0.002), and a lower cumulative risk of relapse (p=0.001), compared to those who received < 80% of the planned dosing due to intolerance.

Patient outcomes

HYPERSENSITIVITY REACTIONS

HYPERSENSITIVITY REACTIONS CAN COMPROMISE PATIENT OUTCOMES^{1,4}

Hypersensitivity reactions (HSRs) from *E. coli*-derived asparaginase can lead to treatment interruptions, which can increase relapse when patients don't complete their full course of therapy.

Up to **30%** of patients receiving *E. coli*-derived asparaginase experience clinical hypersensitivity.

It is the most common asparaginase-associated toxicity requiring treatment discontinuation.

Treatment interruption increases the chance of relapse.

Switch to an asparaginase with no expected immunologic cross-reactivity to *E. coli* asparaginase to reduce the risk of relapse.^{1,4}

Hypersensitivity reactions

COMPLETE TREATMENT

ADVANCING TREATMENT THROUGH RECOMBINANT TECHNOLOGY BRINGS CONFIDENCE IN A RELIABLE NON-*E. coli*-DERIVED ASPARAGINASE⁵

A reliable, high-volume and sustainable supply of high-quality non-*E. coli*-derived asparaginase to help complete your patient's treatment plan.

Sustainable supply
High yields using 30 times fewer fermentation batches than traditional asparaginase manufacturing.

Highly purified
Consistent quality with no filtration requirements. Using low particulate filling components ensures a low risk of having impurities.

Higher-concentration, ready-to-use vials
Higher-concentration formulation means less waste and more convenience with no reconstitution and lower injection volumes.

Complete treatment

EXPANDED MANUFACTURING PROCESS

COMPARISON OF RECOMBINANT AND TRADITIONAL MANUFACTURING PROCESSES

Optimal growth conditions in the recombinant manufacturing process help maximize cell growth and increase yield.

Recombinant manufacturing process

- 1 x 1,000 L fermentation
- Filling of drug product "ready-to-use" solution in low particulate filling components
- Product is ready to use

Traditional manufacturing process

- 30 x 750 L fermentation
- Formulation, filling, and lyophilization
- Product must be reconstituted at clinic

Expanded manufacturing process

FIRST AND ONLY

THE FIRST RECOMBINANT ASPARAGINASE IN CANADA AND THE ONLY NON-*E. coli* ASPARAGINASE APPROVED FOR THE TREATMENT OF ALL/LBL^{1,4}

Asparaginase

Disrupts essential enzymatic pathways, slowing leukemic cells and leading to cell death.

Recombinant technology

- DNA is introduced in suitable organisms for protein production.
- Enables high yield, consistent quality and higher concentrations.

First & only

DEMONSTRATED EFFICACY

RELIABLE EFFICACY THROUGH SUSTAINED, CONSISTENT ASPARAGINASE ACTIVITY THROUGHOUT THE ENTIRE COURSE OF TREATMENT^{1,3,5,6,8}

Rylaze demonstrated efficacy through a clinical trial with endpoints of > 90% of patients achieving NSAA ≥ 0.1 U/mL at both 48 and 72 hours.

Proportion of patients with NSAA ≥ 0.1 U/mL at both 48 and 72 hours

Observed Clinical Data
Based on PopTb modeling and simulations

Serum asparaginase activity levels are the accepted surrogate measure for asparaginase efficacy.^{1,3}

Demonstrated efficacy

SAFETY PROFILE

RELIABLE AND CONSISTENT SAFETY PROFILE^{1,4}

Rylaze is expected to have no immunologic cross-reactivity to *E. coli*, and presents a safety profile that is consistent with other asparaginase treatments.

Non-hematologic adverse reactions (≥ 10%) in patients receiving Rylaze as a component of multi-agent chemotherapy (Study J2P466-2007)^{1,4}

System organ class	Adverse reaction	Rylaze (asparaginase recombinant) 25 mg/m ² (n=107)	Control 3 (n=107)
Blood and lymphatic system disorders	Fatigue	14 (13%)	14 (13%)
Cardiac disorders	Sinus tachycardia	4 (4%)	1 (1%)
	Nausea	18 (17%)	1 (1%)
	Headache	12 (11%)	2 (2%)
	Stomatitis	14 (13%)	2 (2%)
	Diarrhoeal pain	12 (11%)	1 (1%)
Gastrointestinal disorders	Diarrhoea	12 (11%)	1 (1%)
	Constipation	7 (7%)	1 (1%)
	Fatigue	4 (4%)	4 (4%)
General disorders and administration site conditions	Fatigue	11 (10%)	0
	Pain	10 (9%)	0
Infection and infestations	Septic	5 (5%)	6 (6%)
History of poisoning and procedural complications	Constipation	7 (7%)	0

10% of Rylaze patients discontinued treatment due to an adverse event, which included hypersensitivity (2%) and pancreatitis (3%).

Safety profile from the clinical trial was consistent with those of other asparaginases.

Safety profile

OPTIMIZED DOSING

OPTIMIZED MONDAY-WEDNESDAY-FRIDAY DOSING TO SUSTAIN EFFECTIVE ASPARAGINASE ACTIVITY LEVELS OVER THE WEEKEND^{1,8}

The recommended dosage of Rylaze is 25 mg/m² on Monday and Wednesday and 50 mg/m² on Friday.

- Administered by intramuscular injection
- For a total of six doses to replace each planned dose of asparaginase
- Available in a ready-to-use liquid formulation with no reconstitution requirements
- The dose is not administered in units as per other asparaginase preparations

Use aseptic technique when administering Rylaze:

- Determine the dose, the total volume of Rylaze required, and the number of Rylaze vials needed.
- Withdraw the required injection volume into the syringe.
- Limit the volume of Rylaze of a single injection site to 2 mL.
- Use multiple injection sites if more than 2 mL is required.
- Discard any remaining unused Rylaze in the single-dose vial.
- Administer Rylaze within four hours of syringe preparation.
- Rotate injection sites.
- Do not inject into scar tissue or areas that are reddened, inflamed, or swollen.

Other important administration information:

- Administer Rylaze in a setting with resuscitation equipment and other agents necessary to treat anaphylaxis.
- Do not shake the vial.
- Visually inspect and before use. Discard old if you see any fine particles, cloudiness, or discoloration.

Optimized dosing

ADULT DOSING CHART

HOW TO CALCULATE FOR DOSING AND ORDERING¹

To calculate dose volume for **25 mg/m² on Monday and Wednesday, and 50 mg/m² on Friday:**

- Each single-dose vial of Rylaze contains 10 mg/0.5 mL (20 mg/mL).
- Use the chart to determine the injection volume based on patient's body surface area (BSA).
- Calculate the total volume of Rylaze solution required for each dose: Volume (mL) = BSA (m²) × Individual dose (mg/m²) × Concentration (20 mg/mL)

BSA (m ²)	Monday/Wednesday dose 25 mg/m ²		Friday dose 50 mg/m ²	
	Volume (mL)	Number of vials	Volume (mL)	Number of vials
0.5	0.63	2	1.25	3
1.0	1.25	3	2.50	5
1.5	1.88	4	3.75	8
2.0	2.50	5	5.00	10
2.5	3.13	7	6.25	13
3.0	3.75	8	7.5	15

Adult dosing chart

PATIENT PROFILES

RELIABLE TREATMENT FOR ALL/LBL PATIENTS

The **FIRST** recombinant asparaginase in Canada and the **ONLY** non-*E. coli* asparaginase approved for the treatment of ALL/LBL.

Anthony, 18

- Diagnosed with ALL at 18 years old
- Being treated with the modified DFCI 91-01 protocol
- Experienced a reaction to long-acting *E. coli*-derived asparaginase during induction
- Remaining scheduled asparaginase doses 10

Consider Rylaze for ALL/LBL patients 1 year or older who have developed hypersensitivity to *E. coli*-derived asparaginase.

CARE PROVIDER PROFILES

HOW CAN RYLAZE HELP YOU PROVIDE COMPLETE, CONSISTENT CARE?

Dr. Thomas, 46, Hematologist*

Looking for:

- Highly purified asparaginase activity levels in > 90% of patients
- Options to complete asparaginase treatment through sustainable supply
- Consistent safety profile

Fatima, 41, Pharmacist*

Looking for:

- Reliable, sustainable supply
- Ready-to-use formulation

RESOURCES

REACH OUT FOR MORE!

To receive Rylaze product information, including supply and other updates.

To schedule an in-person or virtual meeting.

For information on how to order Rylaze.

Have questions? Contact your Jazz Pharmaceuticals representative for more information.

Alberta, British Columbia, and Saskatchewan: Scott Beattie, scott.beattie@jazzpharma.com or 416-524-9930 (toll-free)

Ontario West, Ontario, and Manitoba: Lisa Miller, lisa.miller@jazzpharma.com or 416-524-9930 (toll-free)

Ontario East and Atlantic Canada: Sarah Mullins, sarah.mullins@jazzpharma.com or 416-524-9930 (toll-free)

Quebec: Anna Bois, anna.bois@jazzpharma.com or 514-941-1881 (toll-free)

Resources

SUMMARY

RELY ON Rylaze^{1,4}

To help you deliver

Now reimbursed in Canada^{1,5,6}

Complete

Advancing asparaginase treatment with recombinant technology and sustainable supply.

- High-volume production
- Consistent quality
- Higher concentration in a ready-to-use vial

Consistent

Consistent efficacy with > 90% of patients sustaining therapeutic activity levels at both 48 and 72 hours.

Safety profile consistent with other asparaginase therapies

Care

Committed to patient care, caregiver reassurance, and HCP confidence.

Summary

SAFETY INFORMATION

SAFETY INFORMATION¹

Indications and clinical use

Rylaze (asparaginase recombinant) 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 year or older who have developed hypersensitivity to *E. coli*-derived asparaginase.

Efficacy and safety have not been established in geriatric patients (≥ 65 years).

Contraindications:

Patients with a history of:

- Serious hypersensitivity reactions to Erwinia asparaginase, including anaphylaxis.
- Serious pancreatitis during previous asparaginase therapy
- Serious hemorrhagic events during previous asparaginase therapy

Patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medical ingredient, or component of the container.

Warnings and precautions:

- Endocrine and metabolism
- Hepatitis
- Immune
- Reproductive health, female and male potential
- Driving and operating machinery
- Pregnancy
- Breastfeeding

For more information:

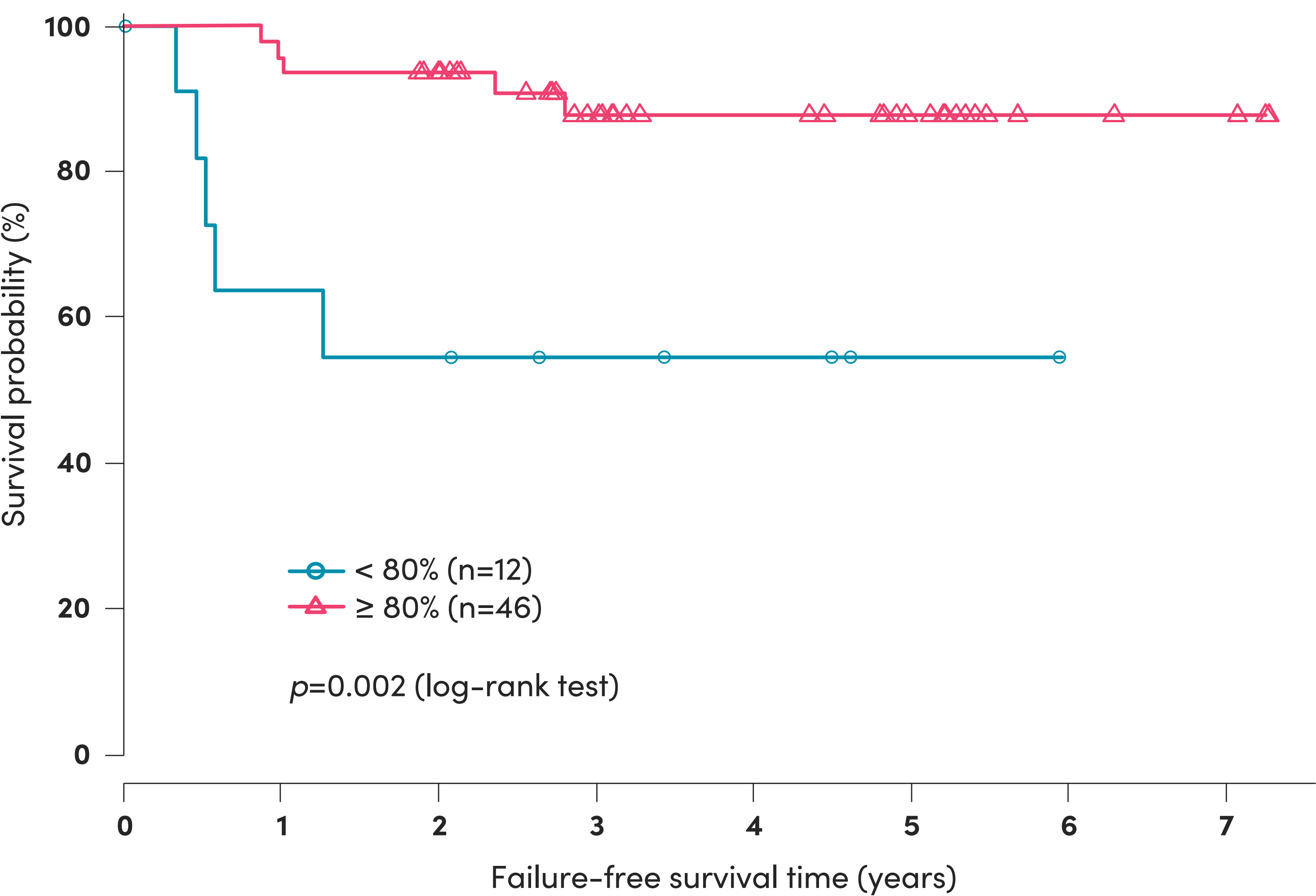
Please consult the Product Monograph at <https://pml.jazzpharma.com/> or Rylaze.ca/PML-en.pdf for important information relating to adverse reactions, drug interactions, and dosing that has not been discussed in this page. The Product Monograph is also available by calling us at 1-800-525-5946.

Safety information

COMPLETE ASPARAGINASE TREATMENT SIGNIFICANTLY INCREASES PATIENT OUTCOMES

Impact of Asparaginase Discontinuation on Outcome in AYAs and adults with *BCR-ABL*-negative ALL on a paediatric-inspired protocol^{*,†,2}

Survival probability in 85 *BCR-ABL*-negative ALL patients aged 18–60 years from 2000 until 2006 on a modified DFCI 91-01 protocol



Patients who received at least 80% of the planned asparaginase dosing had a **significantly higher 3-year OS ($p=0.003$)** and **RFS ($p=0.002$)**, and a **lower cumulative risk of relapse ($p=0.01$)**, compared to those who received < 80% of the planned dosing due to intolerance

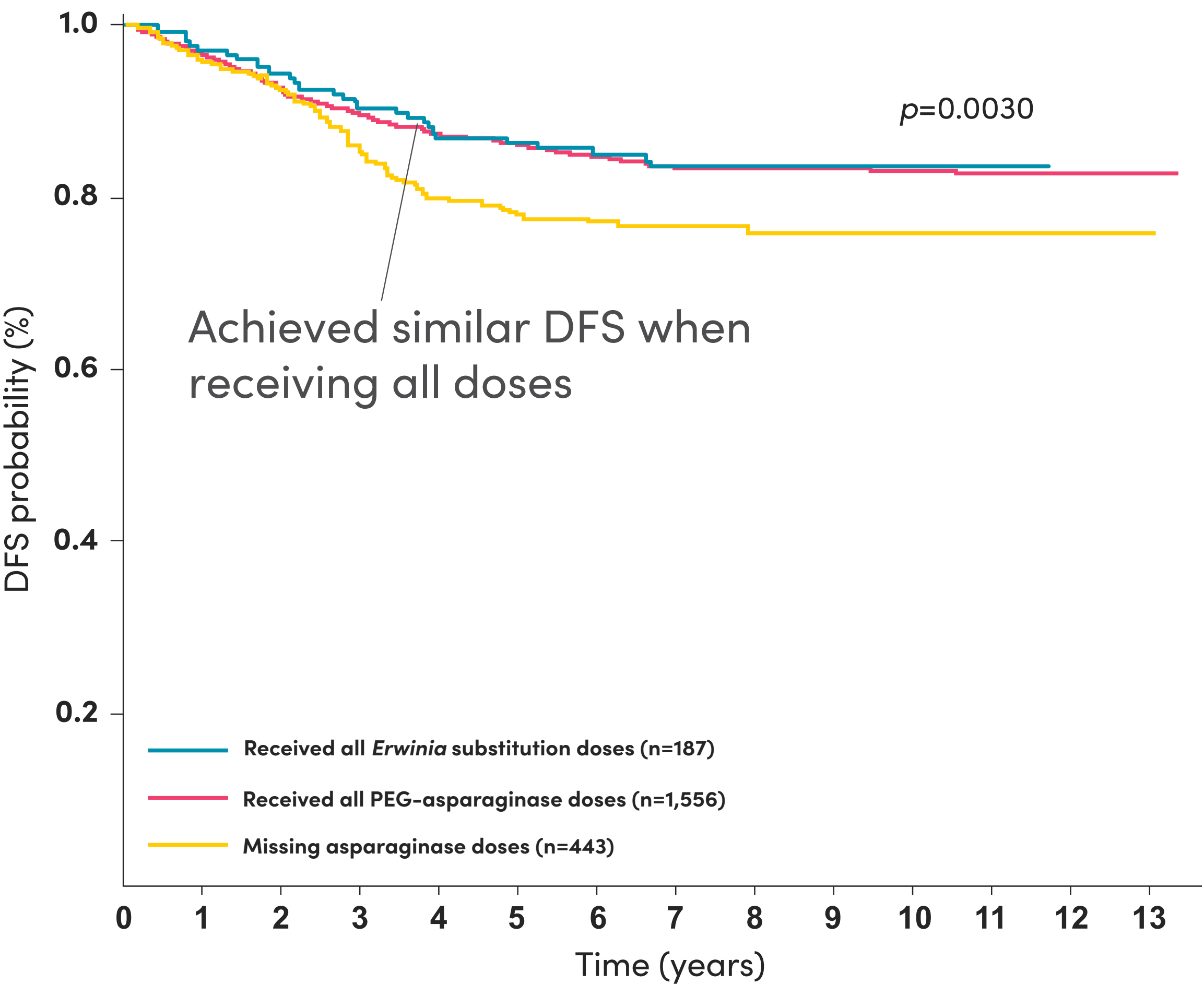
Storring et al. 2009.²

AYA: adolescents and young adults; ALL: acute lymphoblastic leukemia; DFCI: Dana-Farber Cancer Institute; OS: overall survival; RFS: relapse-free survival
*Between 2000 and 2006, 85 adult *BCR-ABL*-negative ALL patients between 18 and 60 years of age were treated using a modified pediatric regimen. Treatment included high doses of asparaginase delivered weekly for 30 weeks during intensification.
†RFS was defined as the time from first complete remission after induction until either disease relapse or death from any cause; only patients achieving complete remission with DFCI induction were analysed for RFS.

COMPLETE ASPARAGINASE TREATMENT SIGNIFICANTLY INCREASES PATIENT OUTCOMES

Impact of Asparaginase Discontinuation on Outcome of Childhood ALL:
A Report from the Children’s Oncology Group^{*,†,3}

DFS probability in high-risk B-ALL patients aged 1–31 years of age from COG stratified by asparaginase received



Number at risk:														
<i>Erwinia</i>	187	176	169	159	147	140	130	97	61	36	19	5	0	0
Not all doses	443	422	400	351	320	294	268	218	157	118	77	51	19	1
All doses	1,556	1,487	1,410	1,322	1,225	1,131	1,002	771	584	430	259	143	48	13

50% (HR: 1.5, 95% CI: [1.1–1.9], $p=0.002$) increased risk of an event when missing asparaginase doses

21.3% of patients experienced relapse when failing to receive all prescribed asparaginase doses



Children’s Oncology Group study



8-year comprehensive study including 8,300 patients

ALL: acute lymphoblastic leukemia; DFS: disease-free survival; B-ALL: B-cell acute lymphoblastic leukemia; COG: Children’s Oncology Group; PEG-asparaginase: polyethylene glycol asparaginase; HR: hazard ratio; CI: confidence interval; NCI: National Cancer Institute; SR: standard risk; WBC: white blood cell

^{*}A comprehensive 8-year (2004–2011) COG study including more than 8,300 patients. The study included newly diagnosed B-ALL patients (1–31 years of age) who were enrolled in two trials. This included 5,195 patients within the COG study AALL0331 (NCI SR B-ALL, age > 1 and < 10 years, initial WBC count < 50,000/ μ L, 2005–2010) and 3,001 patients within AALL0232 (NCI high-risk B-ALL, aged 10–30 years or initial WBC count $\geq$ 50,000/ μ L and any age, 2004–2011; or NCI SR with testicular disease or some patients with steroid pretreatment). This landmark survival analysis was for the 2,186 NCI high-risk patients who started maintenance.

[†]DFS was defined as time from maintenance initiation to relapse, death, development of a second malignant neoplasm, or last follow-up.

Adapted from Gupta et al.²

HYPERSENSITIVITY REACTIONS CAN COMPROMISE PATIENT OUTCOMES^{3,4}

Hypersensitivity reactions (HSRs) from *E. coli*-derived asparaginase can lead to treatment interruptions, which can increase relapse when patients don't complete their full course of therapy.

Up to
30%

of patients receiving
E. coli-derived asparaginase
experience clinical hypersensitivity.



It is the most common
asparaginase-associated toxicity
requiring treatment discontinuation.


21.3%

Treatment interruption
increases the chance of relapse.

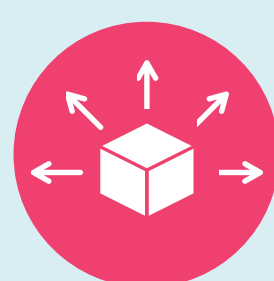
**Switch to an asparaginase with no expected
immunologic cross-reactivity to *E. coli* asparaginase
to reduce the risk of relapse.^{3,5}**

ADVANCING TREATMENT THROUGH RECOMBINANT TECHNOLOGY BRINGS CONFIDENCE IN A RELIABLE NON-*E. COLI*-DERIVED ASPARAGINASE⁶



A reliable, high-volume and sustainable supply of high-quality non-*E.coli*-derived asparaginase to help complete your patient's treatment plan.⁷

Recombinant manufacturing process



Sustainable supply

High yields using 30 times fewer fermentation batches than traditional asparaginase manufacturing.



Highly purified

Consistent quality with no filtration requirements. Using low particulate filling components ensures a low risk of having impurities.

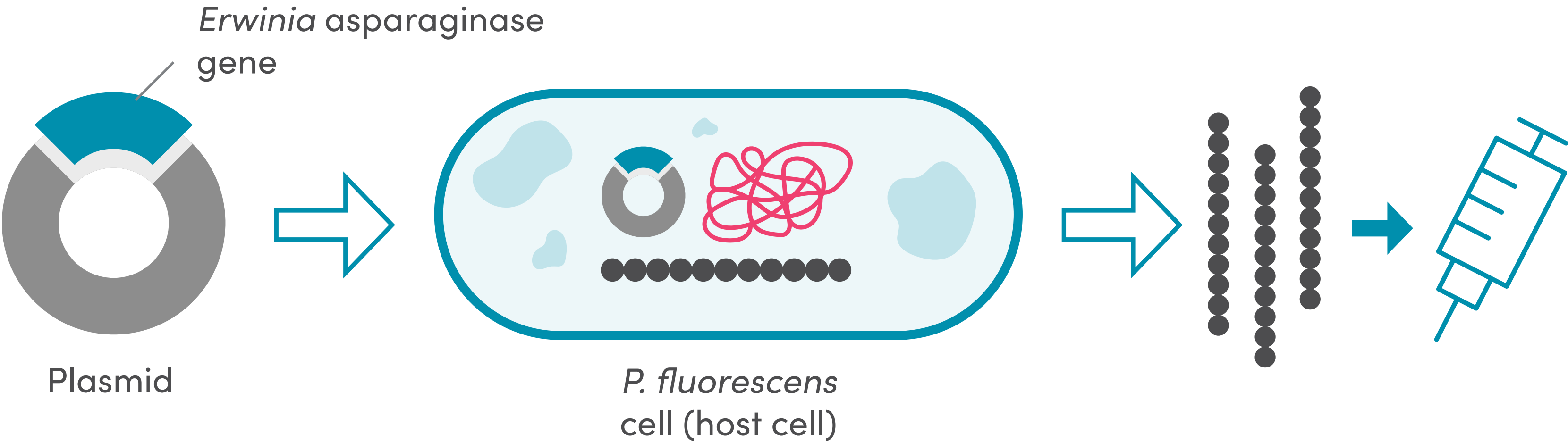


Higher-concentration, ready-to-use vials

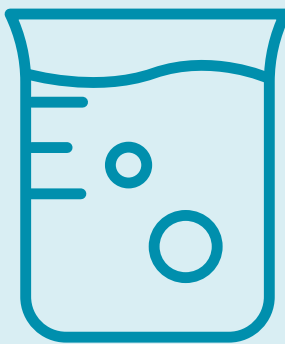
Higher-concentration formulation means less waste and more convenience with no reconstitution and lower injection volumes.

COMPARISON OF RECOMBINANT AND TRADITIONAL MANUFACTURING PROCESS

Optimal growth conditions in the recombinant manufacturing process help maximize cell growth and increase yield



Recombinant manufacturing process

1 x  1,000 L fermentation

Filling of drug product “ready-to-use” solution in low particulate filling components

Product is ready to use

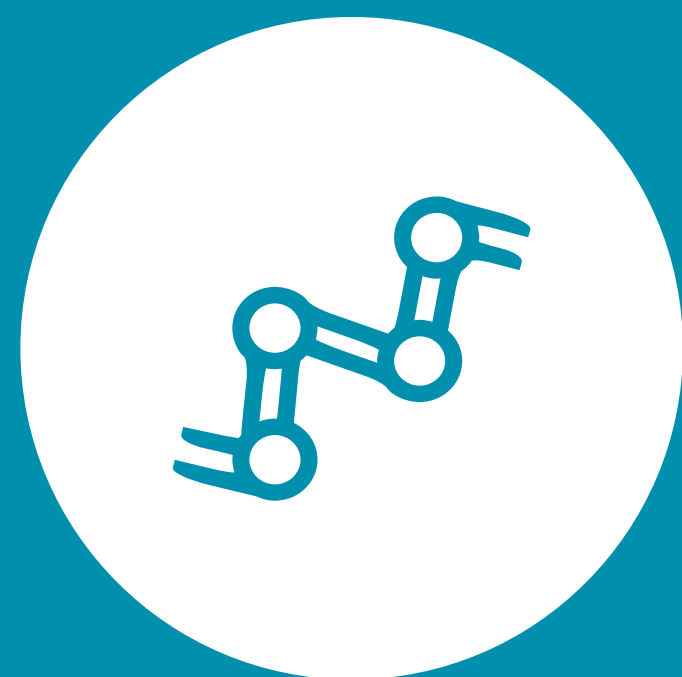
Traditional manufacturing process

30 x  750 L fermentation

Formulation, filling, and lyophilization

Product must be reconstituted at clinic

THE FIRST RECOMBINANT ASPARAGINASE IN CANADA AND THE ONLY NON-*E. COLI* ASPARAGINASE APPROVED FOR THE TREATMENT OF ALL/LBL^{1,6}



Asparaginase

Depletes serum asparagine, starving leukemic cells and leading to cell death.



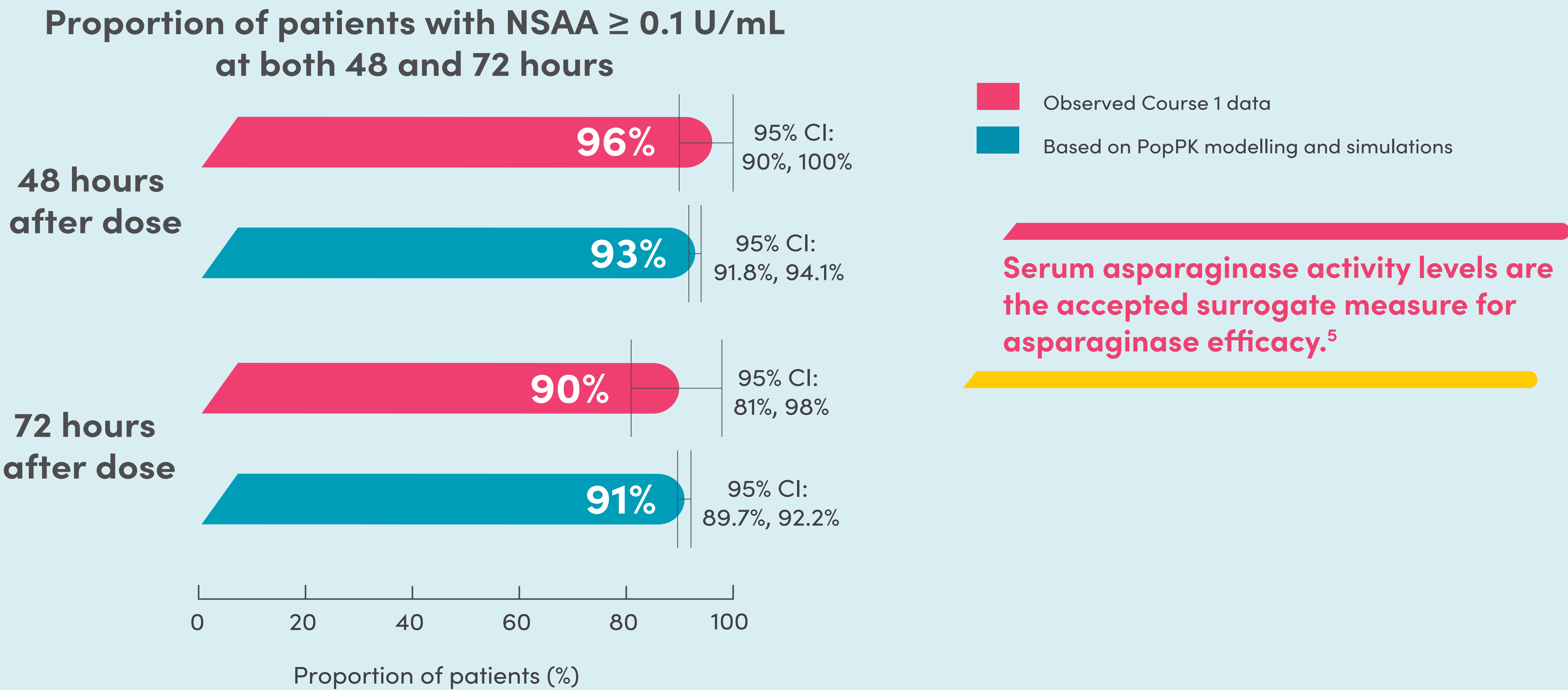
Recombinant technology

- DNA is introduced in suitable organisms for protein production.
- Enables high yield, consistent quality, and higher concentrations.

ALL: acute lymphoblastic leukemia; LBL: lymphoblastic lymphoma

RELIABLE EFFICACY THROUGH SUSTAINED, CONSISTENT ASPARAGINASE ACTIVITY THROUGHOUT THE ENTIRE COURSE OF TREATMENT^{*,†,1,5,8}

Rylaze demonstrated efficacy through a clinical trial with endpoints of > 90% of patients achieving NSAA ≥ 0.1 U/mL at both 48 and 72 hours



NSAA: nadir serum asparaginase activity; U: unit; CI: confidence interval; PopPK: population pharmacokinetic; ALL: acute lymphoblastic leukemia; LBL: lymphoblastic lymphoma
*Results from modelling and simulations in patients who received a dose of 25 mg/m² intramuscularly on a Monday and Wednesday and 50 mg/m² on a Friday during Course 1.
†Study JZP458-201: An open-label, multi-cohort, multicentre safety and clinical pharmacology trial that treated 102 adults and pediatric patients with ALL or LBL who developed hypersensitivity to *E. coli*-derived asparaginases. Cohort 1a was administered Rylaze 25 mg/m² on a Monday, Wednesday, and Friday schedule over two weeks. Cohort 1b was administered Rylaze 37.5 mg/m² on a Monday, Wednesday, and Friday schedule over two weeks. Cohort 1c was administered Rylaze 25 mg/m² on Monday and Wednesday and 50 mg/m² on Friday over two weeks.

RELIABLE AND CONSISTENT SAFETY PROFILE^{1,4}

Rylaze is expected to have no immunologic cross-reactivity to *E. coli*, and presents a safety profile that is consistent with other asparaginase treatments

Non-hematologic adverse reactions (≥ 10%) in patients receiving Rylaze as a component of multi-agent chemotherapy (Study JZP458-201)*†

System organ class	Adverse reaction	Rylaze (intramuscular 25/25/50 mg/m ²) (N=51)	
		All grades	Grade ≥ 3
Blood and lymphatic system disorders	Febrile neutropenia	14 (28)	14 (28)
Cardiac disorders	Sinus tachycardia	8 (16)	1 (2)
Gastrointestinal disorders	Nausea	18 (35)	3 (6)
	Vomiting	17 (33)	2 (4)
	Stomatitis	14 (28)	2 (4)
	Abdominal pain	13 (26)	1 (2)
	Diarrhea	12 (24)	1 (2)
	Constipation	7 (14)	1 (2)
	Pancreatitis	6 (12)	4 (8)
General disorders and administration-site conditions	Fatigue	11 (22)	0
	Pyrexia	10 (20)	0
Infections and infestations	Sepsis	5 (10)	5 (10)
Injury, poisoning, and procedural complications	Contusion	7 (14)	0

Safety profile from the clinical trial was consistent with those of other asparaginases.

10% of Rylaze patients discontinued treatment due to an adverse event, which included hypersensitivity (2%) and pancreatitis (8%).

RELIABLE AND CONSISTENT SAFETY PROFILE^{1,3} (CONT'D)

Rylaze is expected to have no immunologic cross-reactivity to *E. coli*, and presents a safety profile that is consistent with other asparaginase treatments

Non-hematologic adverse reactions (≥ 10%) in patients receiving Rylaze as a component of multi-agent chemotherapy (Study JZP458-201)^{*†}

System organ class	Adverse reaction	Rylaze (intramuscular 25/25/50 mg/m ²) (N=51)	
Investigations	Transaminase increased	11 (22)	4 (8)
	Weight decreased	7 (14)	2 (4)
Metabolism and nutrition disorders	Decreased appetite	14 (28)	3 (6)
	Hypokalemia	11 (22)	4 (8)
	Dehydration	6 (12)	3 (6)
	Hyperglycemia	6 (12)	2 (4)
	Hypertriglyceridemia	6 (12)	1 (2)
Musculoskeletal and connective tissue disorders	Pain in extremity	8 (16)	1 (2)
	Back pain	6 (12)	1 (2)
Nervous system disorders	Headache	11 (22)	0
Psychiatric disorders	Anxiety	5 (10)	1 (2)
Respiratory, thoracic, and mediastinal disorders	Cough	7 (14)	0
	Epistaxis	5 (10)	2 (4)
	Oropharyngeal pain	5 (10)	0
Skin and subcutaneous tissue disorders	Dry skin	5 (10)	0
Vascular disorders	Hypertension	7 (14)	0

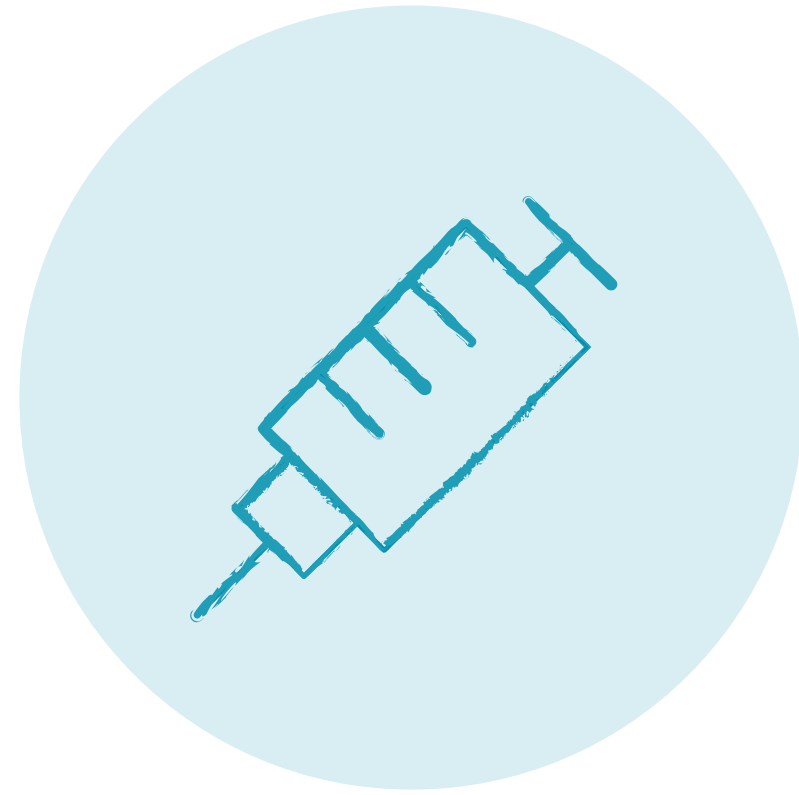
Safety profile from the clinical trial was consistent with those of other asparaginases.

10% of Rylaze patients discontinued treatment due to an adverse event, which included hypersensitivity (2%) and pancreatitis (8%).

^{*}Hematologic adverse reactions are not included in the table. Rylaze was administered intramuscularly at a dosage of 25 mg/m² on Monday and Wednesday and 50 mg/m² on Friday. Rylaze was administered as a component of multi-agent chemotherapy. The analysis data cut-off date was July 19, 2021.
[†]Adverse drug reaction “Abdominal pain” is a combined term for “Abdominal pain” and “Abdominal pain upper”; “Bilirubin increased” is a combined term for “Blood bilirubin increased” and “Bilirubin conjugated increased”; “Fatigue” is a combined term for “Fatigue” and “Asthenia”; “Pancreatitis” is a combined term for “Pancreatitis” and “Pancreatitis acute”; “Transaminase increased” is a combined term for “Transaminase increased,” “Alanine aminotransferase increased,” and “Aspartate aminotransferase increased.”

Adapted from the Rylaze Product Monograph.¹

OPTIMIZED **MONDAY-WEDNESDAY-FRIDAY** DOSING TO SUSTAIN EFFECTIVE ASPARAGINASE ACTIVITY LEVELS OVER THE WEEKEND^{1,6}



The recommended dosage of Rylaze is 25 mg/m² on Monday and Wednesday and 50 mg/m² on Friday:

- Administered by intramuscular injection.
- For a total of six doses to replace each planned dose of pegaspargase.
- Available in a ready-to-use liquid formulation with no reconstitution requirements.
- The dose is not administered in units as per other asparaginase preparations.



Use aseptic technique when administering Rylaze:

- Determine the dose, the total volume of Rylaze required, and the number of Rylaze vials needed.
- Withdraw the required injection volume into the syringe.
- Limit the volume of Rylaze at a single injection site to 2 mL.
 - Use multiple injection sites if more than 2 mL is required.
- Discard any remaining unused Rylaze in the single-dose vial.
- Administer Rylaze within four hours of syringe preparation.
 - Rotate injection sites.
 - Do not inject into scar tissue or areas that are reddened, inflamed, or swollen.



Other important administration information:

- Administer Rylaze in a setting with resuscitation equipment and other agents necessary to treat anaphylaxis.
- Do not shake the vial.
- Visually inspect vial before use. Discard vial if you see any fine particles, cloudiness, or discolouration.

HOW TO CALCULATE FOR DOSING AND ORDERING¹

To calculate dose volume for 25 mg/m² on Monday and Wednesday, and 50 mg/m² on Friday:

- Each single-dose vial of Rylaze contains 10 mg/0.5 mL (20 mg/mL).
- Use the chart to determine the injection volume based on patient’s body surface area (BSA).
 - Calculate the total volume of Rylaze solution required for each dose:
Volume (mL) = BSA (m²) x Individual dose (mg/m²) ÷ Concentration (20 mg/mL)

BSA (m ²)	Monday/Wednesday dose 25 mg/m ²		Friday dose 50 mg/m ²	
	Volume (mL)	Number of vials	Volume (mL)	Number of vials
0.5	0.63	2	1.25	3
1.0	1.25	3	2.50	5
1.5	1.88	4	3.75	8
2.0	2.50	5	5.00	10
2.5	3.13	7	6.25	13
3.0	3.75	8	7.50	15

RELIABLE TREATMENT FOR ALL/LBL PATIENTS

The **FIRST *recombinant*** asparaginase in Canada and the **ONLY non-*E. coli*** asparaginase approved for the treatment of ALL/LBL

Anthony, 18*

- Diagnosed with ALL at 18 years old
- Being treated with the modified DFCI 91-01 protocol
- Experienced a reaction to long-acting *E. coli*-derived asparaginase during induction
- Remaining scheduled pegaspargase doses: 10



Consider Rylaze for ALL/LBL patients 1 year or older who have developed hypersensitivity to *E. coli*-derived asparaginase.

Rosa, 40*

- Diagnosed with ALL at 40 years old
- Being treated with CALGB10403 protocol
- Experienced a reaction to long-acting *E. coli*-derived asparaginase during consolidation
- Remaining scheduled pegaspargase doses: 5



Elizabeth, 64*

- Diagnosed with ALL at 64 years old
- treated with the modified DFCI 91-01 protocol
- Reacted on dose 2 of intensification
- Remaining scheduled pegaspargase doses: 4



ALL: acute lymphoblastic leukemia; LBL: lymphoblastic lymphoma; CALGB: Cancer and Leukemia Group B; DFCI: Dana-Farber Cancer Institute

*Profiles based on fictitious patients in alignment with the approved indication for Rylaze.

HOW CAN RYLAZE HELP YOU PROVIDE COMPLETE, CONSISTENT CARE?



**Dr. Thomas, 46,
Hematologist***

- Looking for:
- Heightened asparaginase activity levels in > 90% of patients
 - Option to complete asparaginase treatment through sustainable supply
 - Consistent safety profile



**Fatima, 41,
Pharmacist***

- Looking for:
- Reliable, sustainable supply
 - Ready-to-use formulation

Ashley, 55, Family member*

- Looking for:
- Reassurance of complete asparaginase treatment if her loved one experiences a reaction
 - Convenience of weekend-free dosing



Sarah, 35, Nurse*

- Looking for:
- A partnership that can help elevate care for ALL patients
 - Consistent and manageable safety profile

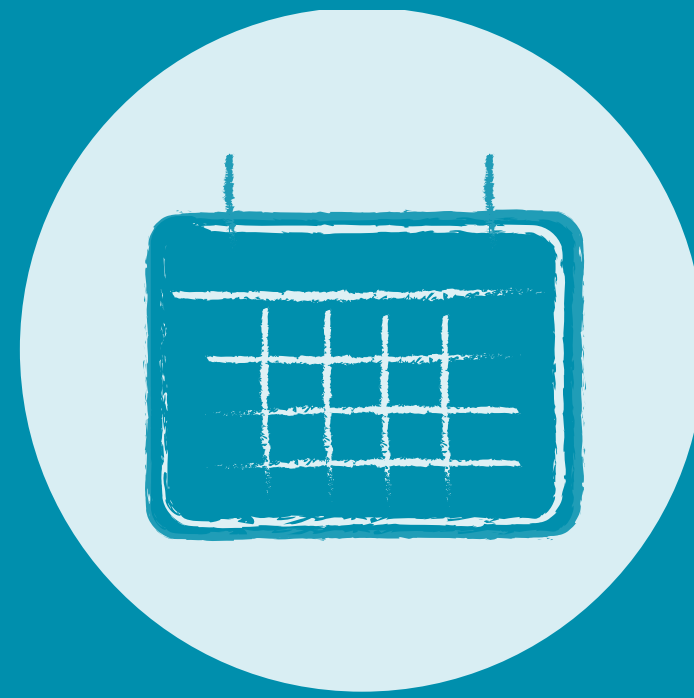


ALL: acute lymphoblastic leukemia
*Fictitious healthcare professionals and caregivers.

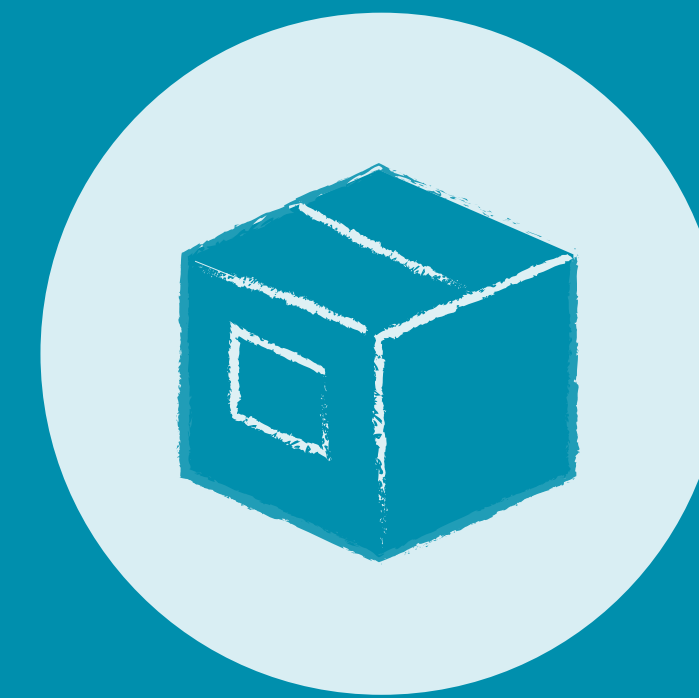
REACH OUT FOR MORE!



To receive Rylaze product information, including supply and other updates



To schedule an in-person or virtual meeting



For information on how to order Rylaze

Have questions?

Contact your Jazz Pharmaceuticals representative for more information.

Alberta, British Columbia, and Saskatchewan:

Scott Bellerby, scott.bellerby@jazzpharma.com
or 368-999-9491 (mobile)

Ontario West, Ottawa, and Manitoba:

Lisa Miller, lisa.miller@jazzpharma.com
or 905-599-5472 (mobile)

Ontario East and Atlantic Canada:

Sean Mullins, sean.mullins@jazzpharma.com
or 416-524-9930 (mobile)

Quebec:

Annie Bois, annie.bois@jazzpharma.com
or 514-941-3861 (mobile)

RELY ON Rylaze^{1,6}

To help you deliver



Now reimbursed
in Canada!^{9,10}



Complete

Advancing asparaginase treatment with recombinant technology and sustainable supply:

- High-volume production
- Consistent quality
- Higher concentration in a ready-to-use vial⁶



Consistent

- **Consistent efficacy** with > 90% of patients sustaining therapeutic activity levels at both 48 and 72 hours¹
- **Safety profile** consistent with other asparaginase therapies¹



Care

Committed to patient care, caregiver reassurance, and HCP confidence

The **FIRST** *recombinant* asparaginase in Canada and the **ONLY** non-*E. coli* asparaginase approved for the treatment of ALL/LBL.

ALL: acute lymphoblastic leukemia; LBL: lymphoblastic lymphoma;
HCP: healthcare professional



Indications and clinical use:

Rylaze (crisantaspase recombinant) 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 year or older who have developed hypersensitivity to *E. coli*-derived asparaginase.

Efficacy and safety have not been established in geriatric patients (≥ 65 years).

Contraindications:

Patients with a history of:

- Serious hypersensitivity reactions to *Erwinia* asparaginase, including anaphylaxis
- Serious pancreatitis during previous asparaginase therapy
- Serious thrombosis during previous asparaginase therapy
- Serious hemorrhagic events during previous asparaginase therapy

Patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container.

Warnings and precautions:

- Endocrine and metabolism
- Hematologic
- Hepatic
- Pancreatic
- Immune
- Reproductive health: female and male potential
- Driving and operating machinery
- Pregnancy
- Breastfeeding

For more information:

Please consult the Product Monograph at <https://pp.jazzpharma.com/pi/Rylaze.ca.PM-en.pdf> for important information relating to adverse reactions, drug interactions, and dosing that has not been discussed in this piece. The Product Monograph is also available by calling us at 1-800-520-5568.

References: 1. Rylaze Product Monograph. Jazz Pharmaceuticals Canada Inc. September 2, 2022. 2. Storrington JM et al. Treatment of adults with BCR-ABL negative acute lymphoblastic leukaemia with a modified paediatric regimen. *Br J Haematol*. 2009;146(1):76–85. 3. Gupta S et al. Impact of asparaginase discontinuation on outcome in childhood acute lymphoblastic leukemia: a report from the Children's Oncology Group. *J Clin Oncol*. 2020;38(17):1897–1905. 4. Hijiya N et al. Asparaginase-associated toxicity in children with acute lymphoblastic leukemia. *Leuk Lymphoma*. 2016;57(4):748–757. 5. van der Sluis et al. Consensus expert recommendations for identification and management of asparaginase hypersensitivity and silent inactivation. *Hematologica*. 2016;100(3):279–285. 6. Maese L et al. Can recombinant technology address asparaginase *Erwinia chrysanthemi* shortages? *Pediatr Blood Cancer*. 2021;68(10):e29169. 7. Jazz Pharmaceuticals [internet]. Dublin: PR Newswire; 2021 June 30. Jazz Pharmaceuticals Announces U.S. FDA Approval of Rylaze™ (asparaginase erwinia chrysanthemi (recombinant)-rywn) for the Treatment of Acute Lymphoblastic Leukemia or Lymphoblastic Lymphoma [cited 2023 Aug 16]; [about 7 screens]. Available from: <https://investor.jazzpharma.com/news-releases/news-release-details/jazz-pharmaceuticals-announces-us-fda-approval-rylaze> 8. Maese L et al. Recombinant *Erwinia* Asparaginase (JZP458) in Acute Lymphoblastic Leukemia: Results from the Phase 2/3 AALL1931 Study. *Blood*. 2022; Sep 15;blood.2022016923.doi: 10.1182/blood.2022016923. 9. Rylaze (crisantaspase recombinant). pan-Canadian Pharmaceutical Alliance. Available from: <https://www.pcpacanada.ca/negotiation/22356>. Last accessed June 13, 2024. 10. Liste des médicaments (1^{er} février 2024). Régie de l'assurance maladie du Québec. Available from: https://www.ramq.gouv.qc.ca/sites/default/files/documents/non_indexes/liste_med_etab_2024-02-01_fr.pdf. Last accessed: June 13, 2024.