

Help your patients with ALL maintain uninterrupted asparaginase treatment

Dosing schedules vary across asparaginase regimens

Asparaginase*	Week 1	Week 2	Week 3	Week 4
Pegaspargase ¹⁰				
Calaspargase pegol-mknl ¹¹				
Asparaginase erwinia chrysanthemi (recombinant)-rywn ¹²				

Syringes and intravenous bags represent typical dosing schedules for the different asparaginase products.

 = 1 dose (dosed at 2000 IU/m² or 2500 IU/m² depending on age and product; average of 3750 IU dose or one vial.)

 = 1 dose (dosed at 25 mg/m² every 48 hours; average of 2 IM injections per dose.)

*Asparaginase is used as part of a multicomponent chemotherapeutic regimen for the treatment of ALL.

References: 1. Vogel WH. Infusion reactions: diagnosis, assessment, and management. *Clin J Oncol Nurs*. 2010;14(2):E10-E21. 2. Marini BL et al. A single-center multidisciplinary approach to managing the global Erwinia asparaginase shortage. *Leuk Lymphoma*. 2019;60(12):2854-2868. 3. Asselin B. Immunology of infusion reactions in the treatment of patients with acute lymphoblastic leukemia. *Future Oncol*. 2016;12(13):1609-1621. 4. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines[®]) for Acute Lymphoblastic Leukemia V.1.2021. © National Comprehensive Cancer Network, Inc. 2021. All rights reserved. Accessed August 12, 2021. To view the most recent and complete version of the guideline, go online to NCCN.org. 5. Common Terminology Criteria for Adverse Events (CTCAE). Version 4.03. June 14, 2010. Available at: https://evs.nci.nih.gov/ftp1/CTCAE/CTCAE_4.03/CTCAE_4.03_2010-06-14_QuickReference_8.5x11.pdf. Accessed August 30, 2021. 6. Burke MJ, et al. Differentiating hypersensitivity versus infusion-related reactions in pediatric patients receiving intravenous asparaginase therapy for acute lymphoblastic leukemia. *Leuk Lymphoma*. 2017;58(3):540-551. 7. Cooper SL, et al. Universal premedication and therapeutic drug monitoring for asparaginase-based therapy prevents infusion-associated acute adverse events and drug substitutions. *Pediatr Blood Cancer*. 2019;66(8):e27797. 8. Egler RA, Ahuja SP, Matloub Y. L-asparaginase in the treatment of patients with acute lymphoblastic leukemia. *J Pharmacol Pharmacother*. 2016;7(2):62-71. 9. Stock W, et al. Prevention and management of asparaginase/pegasparaginase-associated toxicities in adults and older adolescents: recommendations of an expert panel. *Leuk Lymphoma*. 2011;52(12):2237-2253. 10. ONCASPAR [package insert]. Gaithersburg, MD: Sigma-Tau Pharmaceuticals, Inc; 1994. 11. ASPARLAS [package insert]. Boston, MA: Servier Pharmaceuticals LLC; 2018. 12. RYLAZE [package insert]. Palo Alto, CA: Jazz Pharmaceuticals, Inc; 2021.

Oncology nurses play a critical role in the successful completion of chemotherapy used to treat acute lymphoblastic leukemia (ALL)

Learn about strategies that can assist in the proper management and assessment of asparaginase-related reactions



Proper identification, grading, and documentation of reactions to asparaginase is critical in the treatment of ALL.¹

- Asparaginase therapy is a crucial part of a multi-agent chemotherapy regimen, providing significantly improved outcomes in the treatment of ALL.²
- Patients may experience allergic, infusion-related, or hyperammonemia reactions to asparaginase treatment, all of which have different clinical implications.³
- Due to potentially overlapping clinical signs and symptoms of asparaginase reactions, confusion in proper identification may lead to unwarranted discontinuation of asparaginase therapy.³

NCCN's 2021 Guidelines for ALL Recommend Using CTCAE version 4.03 for Asparaginase Toxicity Management^{3,4*,5,6}

	Allergic Reaction/ Hypersensitivity	Infusion-related Reaction/ Non-antibody-mediated	
Adverse Event Grade	<p>Grade 1 Transient flushing or rash, drug fever <38°C (<100.4°F); intervention not indicated</p> <p>Grade 2 Intervention or infusion interruption indicated; responds promptly to symptomatic treatment (e.g., antihistamines, NSAIDs, narcotics); prophylactic medications indicated for ≤24 hr</p>	<p>Grade 3 Prolonged (e.g., not rapidly responsive to symptomatic medication and/or brief interruption of infusion); recurrence of symptoms following initial improvement; hospitalization indicated for clinical sequelae (e.g., renal impairment, pulmonary infiltrates)</p> <p>Grade 4 Life-threatening consequences; urgent intervention indicated</p>	<p>Grades 1-4</p> <ul style="list-style-type: none"> Mild reaction with no interruption indicated Infusion interruption with response to symptomatic treatment Prolonged symptoms despite adequate intervention Recurrence of symptoms following initial improvement Hospitalization required due to clinical sequelae Life-threatening consequences and urgent intervention indicated
Action	<p>May continue pegylated-asparaginase</p> <p>Consider: for anti-allergy premedication</p> <ul style="list-style-type: none"> Hydrocortisone Diphenhydramine Acetaminophen Famotidine 	<p>Discontinue pegylated-asparaginase product permanently</p>	<p>Re-challenge in mild-to-moderate cases, with offending pegylated-asparaginase product once symptoms have been successfully managed</p> <ul style="list-style-type: none"> Slow infusion rate Premedication with antihistamines and immune suppressants

ALL=acute lymphoblastic leukemia; CTCAE=Common Terminology Criteria for Adverse Events; NCCN=National Comprehensive Cancer Network.

CTCAE version 4.03 is recommended by the NCCN for grading asparaginase-associated reactions.² It is based on symptom severity rather than institution-specific treatment protocols or the subjective judgment of the practitioner administering the infusion.^{4*}

*NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

Accurate and detailed documentation may improve the assessment and grading of asparaginase-associated reactions.²

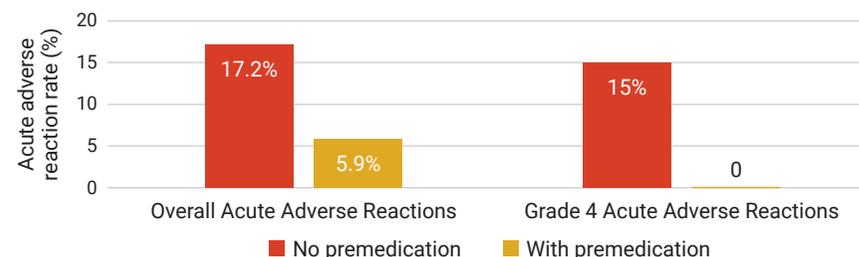
Suggested Documentation Checklist for Nursing Staff²

- Time during infusion reaction occurred
- Reaction details, vital signs, O₂ saturation/requirement, and symptoms
- Medications administered and order of administration
- Response to medications
- Rechallenge details – when restarted, rate, and if reaction re-occurred (include reaction details and interventions)

Therapeutic drug monitoring (TDM) and premedication may help patients with ALL maintain uninterrupted asparaginase treatment^{2,7}

- TDM can be used to help differentiate between allergic and infusion-related reactions⁶ with serum asparaginase activity ≥0.1IU/mL accepted as the standard marker for adequate asparagine depletion⁸
- The use of premedication—with hydrocortisone, diphenhydramine, famotidine, ± acetaminophen—is one of the measures recommended by the NCCN to potentially reduce the incidence of clinical reactions and improve tolerance of asparaginase therapy^{4*,7,9}

Premedication reduced the incidence of asparaginase-related acute adverse reactions^{7†}



[†]In a single academic center, retrospective chart review of clinically apparent reactions to asparaginase before and after the implementation of a universal premedication protocol prior to pegylated asparaginase dosing. Adverse reactions were coded according to the CTCAE, version 4.03. The study included 177 patients with a mean age of 9.1 years, who were treated with at least one dose of pegylated asparaginase. Of these patients, 109 patients were treated prior to the implementation of the universal premedication policy, and 55 were treated following implementation. An additional 13 patients received pegylated asparaginase both without and with premedication.⁷

For more information on how to help your patients stay on treatment for ALL, visit



www.staythecourseforall.com