A Guide for Nurses:

- ☐ How asparaginase works
- ☐ About ASPARLAS® and ONCASPAR®
- ☐ Dosing, preparation, administration, and handling
- ☐ Management of allergic and nonallergic reactions to ASPARLAS or ONCASPAR
- ☐ Patient counseling

ASPARLAS®
(calaspargase pegol-mknl)
750 units/mL injection

oncaspar®
pegaspargase

To learn more about ASPARLAS and ONCASPAR, scan here

AsparlasHCP.com

OncasparHCP.com

How does asparaginase work?

Asparaginase is an enzyme that catalyzes the conversion of asparagine into aspartic acid and ammonia, thereby depleting asparagine from plasma[1-3]

Although normal cells can make asparagine via asparagine synthetase, leukemic cells cannot and must rely on an extracellular asparagine supply[3-5]

The depletion of extracellular plasma asparagine by asparaginase leads to leukemic cell death[1,2,5]

Why is asparaginase important?

Asparaginase has been used for over 50 years as part of chemotherapeutic regimens to treat acute lymphoblastic leukemia (ALL)[6,7] and has been shown to contribute to significantly improved outcomes in patients with ALL.[4,6-9]

What is PEGylation?

PEGylation is the process of linking polyethylene glycol (PEG) polymer chains to a molecule,[10] which serves to[7,10,11]:

- Decrease immunogenicity
- Shield asparaginase from neutralizing antibodies
- Increase the half-life by slowing the rate of degradation or elimination

IMPORTANT SAFETY INFORMATION

Contraindications for ASPARLAS and ONCASPAR

- History of serious hypersensitivity reactions to ASPARLAS (calaspargase pegol-mknl) or ONCASPAR (pegaspargase) or to any of the excipients.
- History of serious thrombosis with prior L-asparaginase therapy.
- History of serious pancreatitis, including pancreatitis related to prior L-asparaginase therapy.
- History of serious hemorrhagic events with prior L-asparaginase therapy.
- Severe hepatic impairment.

What are ASPARLAS® and ONCASPAR®?

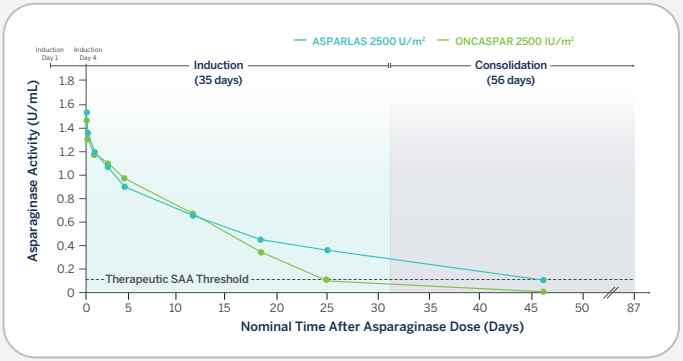
ASPARLAS (calaspargase pegol-mknl) and ONCASPAR (pegaspargase) are PEGylated asparaginases.[1,2]

ASPARLAS is indicated as a component of a multi-agent chemotherapeutic regimen for the treatment of ALL in pediatric and young adult patients age 1 month to 21 years.[1]

ONCASPAR is indicated as a component of a multi-agent chemotherapeutic regimen for the treatment of pediatric and adult patients with first-line ALL or ALL and hypersensitivity to native forms of asparaginase.[2]

ASPARLAS and ONCASPAR are PEGylated for sustained asparaginase activity.[1,2]

Mean plasma asparaginase activity after a single induction dose of ASPARLAS or ONCASPAR in the COG AALL07P4 study[12]



- ASPARLAS has been shown to have therapeutic activity for at least 25 days in the plasma[13]
- ONCASPAR has been shown to have therapeutic activity for at least 18 days in the plasma[13]

Study design: The COG AALL07P4 study was an open-label, randomized trial designed to assess the pharmacokinetic and pharmacodynamic comparability of ASPARLAS and ONCASPAR when administered intravenously during induction and consolidation therapy in 165 evaluable newly diagnosed patients with National Cancer Institute–designated high-risk B-cell ALL receiving an otherwise identical COG augmented Berlin-Frankfurt-Münster–based chemotherapy regimen.[13]

Please see Important Safety Information throughout and accompanying ASPARLAS and ONCASPAR Full Prescribing Information.

How do ASPARLAS® and ONCASPAR® compare in indication, availability, dosing, half-life, and shelf life?

	ASPARLAS (calaspargase pegol-mknl)[1,14]	ONCASPAR (pegaspargase)[2,15]
Indication	ASPARLAS is indicated as a component of a multi-agent chemotherapeutic regimen for the treatment of ALL in **pediatric and young adult patients age 1 month to 21 years**	ONCASPAR is indicated as a component of a multi-agent chemotherapeutic regimen for the treatment of **pediatric and adult patients** with first-line ALL or ALL and hypersensitivity to native forms of asparaginase.
Dosing and administration schedule	The recommended dose of ASPARLAS is **2500 U/m² IV no more frequently than every 21 days**	For patients aged ≤21 years, the recommended dose of ONCASPAR is **2500 IU/m² IM or IV no more frequently than every 14 days*** For patients aged >21 years, the recommended dose of ONCASPAR is **2000 IU/m² IM or IV no more frequently than every 14 days***
Half-life (days, mean)	**~16 days IV administration**	• **5.3 days IV administration** • **5.8 days IM administration**
Shelf life	**36 months**	**8 months**

*To address challenges in ONCASPAR production, distribution, and inventory management and to ensure that patients have access to PEGylated asparaginase, as of December 1, 2022, ONCASPAR was made available only for patients less than 1 month (31 days) or 21.5 years old or older.

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions for ASPARLAS and ONCASPAR

Anaphylaxis and Serious Hypersensitivity Reactions: Anaphylaxis and serious hypersensitivity reactions can occur with ASPARLAS or ONCASPAR. Grade 3 and 4 hypersensitivity reactions including anaphylaxis have been reported in clinical trials with ASPARLAS and ONCASPAR. The risk of serious hypersensitivity reactions is higher in patients with known hypersensitivity to *(E.) coli* derived L-asparaginase formulations. Premedicate patients 30-60 minutes prior to administration of ASPARLAS or ONCASPAR. Observe patients for 1 hour after administration in a clinical setting with resuscitation equipment and other agents necessary to treat anaphylaxis. Discontinue ASPARLAS or ONCASPAR in patients with serious hypersensitivity reactions.

Thrombosis: Serious thrombotic events, including sagittal sinus thrombosis, were seen in clinical trials with ASPARLAS and ONCASPAR. Discontinue ASPARLAS or ONCASPAR in patients with serious thrombotic events.

Please see Important Safety Information throughout and accompanying ASPARLAS and ONCASPAR Full Prescribing Information.

What is the dosing for ASPARLAS® and ONCASPAR®?

ASPARLAS Dosing[1]

The recommended dose of ASPARLAS is 2500 U/m^2 given intravenously no more frequently than every 21 days in patients aged 1 month to 21 years

ONCASPAR Dosing[2]

For patients aged ≤21 years, the recommended dose of ONCASPAR is 2500 IU/m^2 IM or IV no more frequently than every 14 days*

The recommended dose of ONCASPAR for patients aged >21 years is 2000 IU/m^2 IM or IV no more frequently than every 14 days*

How should ASPARLAS and ONCASPAR be stored, handled, and administered?

Storage and handling[1,2]

Store ASPARLAS and ONCASPAR 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 product

Unopened vials may be stored at room temperature (15°C to 25°C [59°F to 77°F]) for no more than 48 hours

Do not administer if ASPARLAS or ONCASPAR has been shaken or vigorously agitated, frozen, or stored at room temperature for more than 48 hours

Please refer to Sections 2.4 and 16 of the accompanying ASPARLAS and ONCASPAR Full Prescribing Information for complete preparation, administration and handling information.

What is the recommended premedication regimen?

To reduce the risk and severity of both infusion and hypersensitivity reactions, premedicate patients 30 to 60 minutes prior to the administration of ASPARLAS or ONCASPAR with[1,2]:

- Acetaminophen
- An H1-receptor blocker (such as diphenhydramine)
- An H2-receptor blocker (such as famotidine)

ASPARLAS administration

ASPARLAS IV Administration[1]

ASPARLAS should be given over a period of 1 hour in 100 mL of 0.9% sodium chloride or 5% dextrose injection through an infusion line that is already running

Do not infuse other drugs through the same IV line during administration of ASPARLAS

ONCASPAR administration

ONCASPAR IV Administration[2]

When ONCASPAR is administered intravenously, it should be given over a period of 1 to 2 hours in 100 mL of 0.9% sodium chloride or 5% dextrose injection through an infusion line that is already running

Do not infuse other drugs through the same IV line during administration of ONCASPAR

ONCASPAR IM Administration[2]

When ONCASPAR is administered intramuscularly, the volume at a single injection site should be limited to 2 mL. If the volume to be administered is >2 mL, multiple injection sites should be used

*To address challenges in ONCASPAR production, distribution, and inventory management and to ensure that patients have access to PEGylated asparaginase, as of December 1, 2022, ONCASPAR was made available only for patients less than 1 month (31 days) or 21.5 years old or older.

What were the most common adverse reactions with ASPARLAS® and ONCASPAR® in clinical studies?

ASPARLAS (calaspargase pegol-mknl) and ONCASPAR (pegaspargase) have comparable safety profiles.[1,16]

Adverse events during induction phase and postinduction phase among randomly assigned patients in the DFCI 11-001 study

There was 1 fatal adverse reaction (multi-organ failure in the setting of chronic pancreatitis associated with a pancreatic pseudocyst). Not all Grade 1 and 2 adverse reactions were collected prospectively.[1]

	ASPARLAS 2500 U/m^2 (n=118)	ONCASPAR 2500 IU/m^2 (n=119)
Adverse Reaction[a]	Grades ≥3[b]	
Elevated transaminase	52%	66%
Bilirubin increased	20%	25%
Pancreatitis	18%	24%
Abnormal clotting studies	14%	21%
Diarrhea	9%	5%
Hypersensitivity	8%	7%
Embolic and thrombotic events	8%	8%
Sepsis	5%	6%
Dyspnea	4%	1%
Hemorrhages	4%	4%
Fungal infection	3%	3%
Pneumonia	3%	7%
Arrhythmia	2%	1%
Cardiac failure	2%	1%

[a]Grouped terms: **Elevated transaminase:** Alanine aminotransferase increased, aspartate aminotransferase increased, transaminases increased; **Bilirubin increased:** Bilirubin conjugated increased, blood bilirubin increased; **Pancreatitis:** Amylase increased, lipase increased, pancreatic necrosis, pancreatitis, pancreatitis relapsing; **Abnormal clotting studies:** Activated partial thromboplastin time prolonged, blood fibrinogen decreased; **Diarrhea:** Colitis, diarrhea, enterocolitis, neutropenic colitis; **Hypersensitivity:** Anaphylactic reaction, drug hypersensitivity, hypersensitivity; **Embolic and thrombotic events (SMQ):** Device-related thrombosis, disseminated intravascular coagulation, embolism, intracardiac thrombus, intracranial venous sinus thrombosis, pulmonary embolism, superior sagittal sinus thrombosis, thrombosis in device, venous thrombosis, venous thrombosis limb; **Sepsis:** Bacterial sepsis, sepsis; **Dyspnea:** Hypoxia, respiratory failure; **Hemorrhages (SMQ) (excludes laboratory terms):** Disseminated intravascular coagulation, epistaxis, hematoma, hemorrhage intracranial, melena, esophageal ulcer hemorrhage, small intestinal hemorrhage, upper gastrointestinal hemorrhage; **Fungal infection:** Fungal infection, hepatic infection fungal, respiratory tract infection fungal, splenic infection fungal, systemic candida; **Pneumonia:** Lung infection, pneumonia, pneumonitis; **Arrhythmia:** Atrioventricular block complete, sinus tachycardia, ventricular arrhythmia; **Cardiac failure:** Ejection fraction decreased, left ventricular dysfunction.[1]

[b]Grading is based on the Common Terminology Criteria for Adverse Events v4.0.[1]

Please see Important Safety Information throughout and accompanying ASPARLAS and ONCASPAR Full Prescribing Information.

What measures can be taken to prevent or limit the severity of hypersensitivity and infusion reactions?

Premedicating with acetaminophen, an H1-receptor blocker (such as diphenhydramine), and an H2-receptor blocker (such as famotidine) 30-60 minutes prior to administration of ASPARLAS or ONCASPAR[1,2]

ASPARLAS and ONCASPAR administration considerations[1,2]:

- After dilution with either 0.9% sodium chloride or 5% dextrose, administer immediately into a running infusion of the respective diluent
- Administer the dose over a period of 1 hour for ASPARLAS and 1-2 hours for ONCASPAR

Administration adjustments for infusion and/or hypersensitivity reactions to ASPARLAS and ONCASPAR[1,2]:

- Grade 1:
  - Reduce the infusion rate by 50%
- Grade 2:
  - Interrupt the infusion
  - Treat the symptoms
  - When symptoms resolve, resume the infusions and reduce the infusion rate by 50%

- Routine premedication has been avoided in the past for fear of "masking" allergic reactions[17]
- However, given the difficulty in differentiating between allergic reactions and nonallergic infusion reactions and the availability of therapeutic drug monitoring (TDM), the **NCCN Clinical Guidelines in Oncology (NCCN Guidelines®) recommend consideration of universal premedication and TDM**, which can reduce[17]
  - The incidence and severity of adverse events
  - The need for substitution of asparaginase therapies

If a patient experiences an infusion reaction or hypersensitivity reaction to ASPARLAS® or ONCASPAR®, what actions should be taken?

Reaction	Action[1,2]
Grade 1	Reduce infusion rate by 50%
Grade 2	Interrupt infusion of ASPARLAS (calaspargase pegol-mknl) or ONCASPAR (pegaspargase) and treat symptoms. When symptoms resolve, resume infusion and reduce infusion rate by 50%
Grade 3 to 4	Discontinue ASPARLAS or ONCASPAR permanently

For what other adverse reactions should treatment be modified?

Treatment should also be modified if pancreatitis, thrombosis, hemorrhage, or hepatotoxicity occur.[1,2] **Always refer to the accompanying Full Prescribing Information for ASPARLAS and ONCASPAR for further details on managing adverse events and dosing.**

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions for ASPARLAS and ONCASPAR (cont'd)

Pancreatitis: Pancreatitis can occur and has been reported in clinical trials with ASPARLAS and ONCASPAR. Fatal outcomes have been reported. Inform patients of the signs and symptoms of pancreatitis, which, if left untreated, could be fatal. Assess serum amylase and/or lipase levels to identify early signs of pancreatic inflammation. Discontinue ASPARLAS or ONCASPAR in patients where pancreatitis is suspected. If pancreatitis is confirmed, do not resume ASPARLAS or ONCASPAR.

What are the differences between allergic and nonallergic reactions?

Some patients treated with asparaginase may have the following responses.

Nonallergic Reactions

Infusion-Related Reaction
• Non-antibody–mediated (mechanisms may include direct cytokine release, activation of the complement system, or sharp elevations in ammonia levels*)[4,18] • Often occurs at the beginning of an infusion and can occur with the first dose[18] • Risk may diminish with exposure[18]
If an infusion reaction is misdiagnosed as an allergic reaction, it can lead to unnecessary switching from or discontinuation of asparaginase treatment.[4,19]

Allergic Reactions

Clinical Hypersensitivity	Silent Inactivation (Subclinical Hypersensitivity)
• Antibody-mediated; antibodies inactivate asparaginase, reducing asparaginase activity[4,18,20] • Typically occurs after second asparaginase dose or later, as sensitization is required[4,18]	• Patients develop anti-asparaginase antibodies without clinical signs of hypersensitivity[4] • Typically occurs after second asparaginase dose or later, as sensitization is required[4,18]
Nonallergic reactions usually cannot be distinguished from allergic reactions based on clinical symptoms or grade[4,17,21]	**If unrecognized, patients are often continued on the same asparaginase formulation with decreased therapeutic effect[4]**

*Symptoms of hyperammonemia, which results from a rapid rise in serum ammonia levels, include nausea, vomiting, dizziness, headache, and rash and may appear similar to symptoms of an allergic reaction. If hyperammonemia is suspected, monitoring of serum ammonia levels is recommended.[4]

What is Therapeutic Drug Monitoring (TDM), and when is it useful?

- TDM is a test that measures serum asparaginase activity levels, helping clinicians distinguish between true allergic reactions and nonallergic infusion reactions to determine when switching asparaginase formulations may be warranted[4,7]
- TDM helps to establish whether a patient has silent inactivation[4]
- If anti-allergy premedication is used prior to asparaginase administration, consideration should be given to TDM using commercially available asparaginase activity assays, since premedication may "mask" the systemic allergic reactions that can indicate the development of neutralizing antibodies[22,23]

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions for ASPARLAS and ONCASPAR (cont'd)

Glucose Intolerance: Glucose intolerance can occur and was seen in patients receiving ONCASPAR. In some cases, it can be irreversible. Monitor serum glucose in patients receiving ASPARLAS or ONCASPAR.

Hemorrhage: Increased prothrombin time (PT), increased partial thromboplastin time (PTT), and hypofibrinogenemia can occur. Evaluate patients with signs and symptoms of hemorrhage with coagulation parameters including PT, PTT, and fibrinogen. Consider appropriate replacement therapy in patients with severe or symptomatic coagulopathy. Discontinue ASPARLAS or ONCASPAR for severe or life-threatening hemorrhage.

How does the CTCAE v5.0 adverse event criteria help grade asparaginase-related reactions?

IMMUNE SYSTEM DISORDERS[24]

CTCAE TERM	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
ANAPHYLAXIS			Symptomatic bronchospasm, with or without urticaria; parenteral intervention indicated: allergy-related edema/angioedema; hypotension	Life-threatening consequences; urgent intervention indicated	Death
Definition: A disorder characterized by an acute inflammatory reaction resulting from the release of histamine and histamine-like substances from mast cells, causing a hypersensitivity immune response. Clinically, it presents with breathing difficulty, dizziness, hypotension, cyanosis, and loss of consciousness and may lead to death.					
ALLERGIC REACTION	**Navigational Note:** If related to infusion, use injury, poisoning, and procedural complications; infusion-related reaction. Do not report both.				

INJURY, POISONING, AND PROCEDURAL COMPLICATIONS[24]

CTCAE TERM	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
INFUSION-RELATED REACTION	Mild transient reactions; infusion interruption not indicated; intervention not indicated	Therapy or infusion interruption indicated but responds promptly to symptomatic treatment (eg, antihistamines, NSAIDs, narcotics, IV fluids); prophylactic medications indicated for ≤24 hours	Prolonged (eg, not rapidly responsive to symptomatic medications and/or brief interruption of infusion): recurrence of symptoms following initial improvement; hospitalization indicated for clinical sequelae	Life-threatening consequences; urgent intervention indicated	Death
Definition: A disorder characterized by adverse reaction to the infusion of pharmacological or biological substances.					

CTCAE, Common Terminology Criteria for Adverse Events.

If a patient experiences a reaction to ASPARLAS® or ONCASPAR®, should the patient be rechallenged?

Reaction	Action
Grade 1 and 2 Rash, flushing, urticaria, and fever ≥38°C (≥100.4°F) without bronchospasm, hypotension, edema, or need for parenteral intervention[22,24]	The asparaginase that caused the reaction may be continued, with consideration for anti-allergy premedication (such as hydrocortisone, famotidine, diphenhydramine, cetirizine, and acetaminophen)[22]
Grade 3 and 4 Including anaphylaxis or other allergic reactions of grade 3 or 4 severity[1,2]	Discontinue the causative agent permanently[1,2]

The recommended action for Grade 1 and 2 reactions comes from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Acute Lymphoblastic Leukemia V.2.2024.

Please see Important Safety Information throughout and accompanying ASPARLAS and ONCASPAR Full Prescribing Information.

What counsel should be given to patients who are taking ASPARLAS® or ONCASPAR®?

The ASPARLAS (calaspargase pegol-mknl) and ONCASPAR (pegaspargase) package inserts suggest the following; however, you should always use your medical judgment when counseling patients.[1,2]

- Inform patients of the possibility of serious allergic reactions, including anaphylaxis, and advise them to seek immediate medical care for any swelling or difficulty breathing
- Instruct patients on the signs and symptoms of pancreatitis and to seek immediate medical attention for severe abdominal pain
- Instruct patients on the risk of hyperglycemia and glucose intolerance and to immediately report excessive thirst or an increase in the volume or frequency of urination
- Instruct patients on the risk of thrombosis and to seek immediate medical attention for severe headache, arm or leg swelling, shortness of breath, or chest pain
- Advise patients to report any unusual bleeding or bruising
- Instruct patients to immediately report jaundice, rapid weight gain, abdominal swelling, or right upper abdominal pain or tenderness for hepatotoxicity, including veno-occlusive disease (VOD)
- Advise female patients of reproductive potential to use effective nonhormonal contraceptive methods while receiving ASPARLAS or ONCASPAR and for 3 months after the last dose since ASPARLAS and ONCASPAR can render hormonal contraceptives ineffective. Advise patients to notify their healthcare provider immediately in the event of a pregnancy or suspected pregnancy during ASPARLAS or ONCASPAR treatment
- Advise lactating women not to breastfeed during treatment with ASPARLAS or ONCASPAR and for 1 month after the last dose of ONCASPAR or for at least 3 months after the last dose of ASPARLAS

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions for ASPARLAS and ONCASPAR (cont'd)

Hepatotoxicity: Hepatotoxicity, including severe, life-threatening, and potentially fatal cases of hepatic veno-occlusive disease (VOD), have been observed in patients treated with ASPARLAS or ONCASPAR in combination with standard chemotherapy, including during the induction phase of multiphase chemotherapy. Do not administer ASPARLAS or ONCASPAR to patients with severe hepatic impairment. Evaluate bilirubin and transaminases prior to each dose of ASPARLAS or ONCASPAR and at least weekly, during cycles of treatment that include ASPARLAS or ONCASPAR, through 6 weeks after the last dose of ASPARLAS or ONCASPAR. 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 ASPARLAS or ONCASPAR, 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 ASPARLAS or ONCASPAR and provide supportive care.

Adverse Reactions for ASPARLAS

The most common grade 3 and above adverse reactions (incidence ≥10%) for patients receiving ASPARLAS with multiagent chemotherapy observed in the DFCI clinical trial were elevated transaminase (52%), increased bilirubin (20%), pancreatitis (18%) and abnormal clotting studies (14%). There was 1 fatal adverse reaction (multi-organ failure in the setting of chronic pancreatitis associated with a pancreatic pseudocyst). Not all grade 1 and 2 adverse reactions were collected prospectively.

Adverse Reactions for ONCASPAR

The most common grade 3 and 4 adverse reactions with ONCASPAR (>5%) included hypoalbuminemia, elevated transaminase, febrile neutropenia, hypertriglyceridemia, hyperglycemia, bilirubin increased, pancreatitis, abnormal clotting studies, embolic and thrombotic events, hypersensitivity, sepsis, and infections.

Please see the accompanying Full Prescribing Information for ASPARLAS and ONCASPAR.

References: 1. Asparlas. Package insert. Servier Pharmaceuticals LLC; 2023. **2.** Oncaspar. Package insert. Servier Pharmaceuticals LLC; 2024. **3.** Kumar K, Kaur J, Walia S, Pathak T, Aggarwal D. L-asparaginase: an effective agent in the treatment of acute lymphoblastic leukemia. *Leuk Lymphoma*. 2014;55(2):256-262. **4.** Burke MJ, Rheingold SR. Differentiating hypersensitivity versus infusion-related reactions in pediatric patients receiving intravenous asparaginase therapy for acute lymphoblastic leukemia. *Leuk Lymphoma*. 2017;58(3):540-551. **5.** Asselin B, Rizzari C. Asparaginase pharmacokinetics and implications of therapeutic drug monitoring. *Leuk Lymphoma*. 2015;56(8):2273-2280. **6.** 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. **7.** Marini BL, Perissinotti AJ, Bixby DL, Brown J, Burke PW. Catalyzing improvements in ALL therapy with asparaginase. *Blood Rev*. 2017;31(5):328-338. **8.** Gupta S, Wang C, Raetz EA, 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. **9.** Silverman LB, Gelber RD, Dalton VK, et al. Improved outcome for children with acute lymphoblastic leukemia: results of Dana-Farber Consortium Protocol 91-01. *Blood*. 2001;97(5):1211-1218. **10.** Milla P, Dosio F, Cattel L. PEGylation of proteins and liposomes: a powerful and flexible strategy to improve the drug delivery. *Curr Drug Metab*. 2012;13(1):105-119. **11.** Veronese FM, Mero A. The impact of PEGylation on biological therapies. *BioDrugs*. 2008;22(5):315-329. **12.** Data on file. Servier Pharmaceuticals LLC. **13.** Angiolillo AL, Schore RJ, Devidas M, et al. Pharmacokinetic and pharmacodynamic properties of calaspargase pegol *Escherichia coli* L-asparaginase in the treatment of patients with acute lymphoblastic leukemia: results from Children's Oncology Group study AALL07P4. *J Clin Oncol*. 2014;32(34):3874-3882. **14.** US Food and Drug Administration. BLA 761102: ASPARLAS biologics license application approval [letter]. December 20, 2018. **15.** Faschinger AM, Sessler N. Development of a lyophilized formulation of pegaspargase and comparability versus liquid pegaspargase. *Adv Ther*. 2019;36(8):2106-2121. **16.** Vrooman LM, Blonquist TM, Stevenson KE, et al. Efficacy and toxicity of pegaspargase and calaspargase pegol in childhood acute lymphoblastic leukemia: results of DFCI 11-001. *J Clin Oncol*. 2021;39(31):3496-3505. doi:10.1200/JCO.20.03692 **17.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Pediatric Acute Lymphoblastic Leukemia V.1.2025. © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed November 6, 2024. To view the most recent and complete version of the guideline, go online to NCCN.org. **18.** Asselin B. Immunology of infusion reactions in the treatment of patients with acute lymphoblastic leukemia. *Future Oncol*. 2016;12(13):1609-1621. **19.** Demoly P, Adkinson NF, Brockow K, et al. International Consensus on drug allergy. *Allergy*. 2014;69(4):420-437. **20.** Tong WH, Pieters R, Kaspers GJ, et al. A prospective study on drug monitoring of PEGasparaginase and Erwinia asparaginase and asparaginase antibodies in pediatric acute lymphoblastic leukemia. *Blood*. 2014;123(13):2026-2033. **21.** Kloos RQH, Pieters R, Escherich G, van der Sluis IM. Allergic-like reactions to asparaginase: atypical allergies without asparaginase inactivation. *Pediatr Blood Cancer*. 2016;63(11):1928-1934. **22.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Acute Lymphoblastic Leukemia V.2.2024. © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed November 6, 2024. To view the most recent and complete version of the guideline, go online to NCCN.org. 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. **23.** Bleyer A, Asselin BL, Koontz SE, Hunger SP. Clinical application of asparaginase activity levels following treatment with pegaspargase. *Pediatr Blood Cancer*. 2015;62(6):1102-1105. **24.** US Department of Health and Human Services. Common Terminology Criteria for Adverse Events (CTCAE). Version 5.0. November 17, 2017. Accessed November 6, 2024. https://ctep.cancer.gov/protocolDevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_8.5x11.pdf

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