Drug Monograph

A - Drug Name

calaspargase pegol

COMMON TRADE NAME(S): Asparlas®

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B - Mechanism of Action and Pharmacokinetics

Calaspargase pegol contains an E.coli-derived L-asparaginase conjugated with monomethoxy polyethylene glycol via a succinimidyl carbonate linker that improves stability. L-asparagine reduces circulating levels of asparagine, which is essential for leukemic cells that are unable to synthesize asparagine, by catalyzing the conversion of L-asparagine to aspartic acid and ammonia. Therefore, the mechanism of action of calaspargase pegol is based on the depletion of plasma L-asparagine. This results in the inhibition of protein synthesis, DNA synthesis, and RNA synthesis of leukemic cells and subsequently in apoptosis.

Absorption	T max	1.17 h
Elimination	Elimination is time-dependent. Asparaginase activity typically showed first a linear elimination, followed by a faster decline in asparaginase activity levels (non-linear). Elimination pathways of calaspargase pegol is unknown.	
	Half-life	16.1 days

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C - Indications and Status

Health Canada Approvals:

- Acute lymphoblastic leukemia (ALL)

Refer to the product monograph for a full list and details of approved indications.

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D - Adverse Effects

Emetogenic Potential: Minimal

Extravasation Potential: None

The following adverse events occurred in ≥ 5% of newly-diagnosed ALL or lymphoblastic lymphoma patients aged 1 to 21 years receiving calaspargase pegol as part of a Dana Farber Cancer Institute (DFCI) ALL Consortium backbone therapy in a randomized, open-label trial. Severe or life-threatening adverse effects may also be included from other sources and post-marketing.

ORGAN SITE	SIDE EFFECT* (%)	ONSET**
Cardiovascular	Hypertension (5%)	E
	Thromboembolism (12%) (including CNS; may be severe)	E
Gastrointestinal	Colitis (7%) (neutropenic) (severe)	E
	Mucositis (25%) (severe)	E
Hematological	Disseminated intravascular coagulation (<5%)	E
	Fibrinogen decreased (22%)	E
	INR / prothrombin time increased (12%)	E
	Myelosuppression ± infection, bleeding (34%) (severe)	E
Hepatobiliary	↓ albumin (81%) (27% severe)	E
	↑ Amylase / lipase (18%) (15% severe)	E
	Hepatotoxicity (<5%)	E
	↑ LFTs (79%) (49% severe)	E
	Pancreatitis (12%) (10% severe)	E
	Veno-occlusive disease (rare)	E

Hypersensitivity	Hypersensitivity (9%) (5% severe)	I
Metabolic / Endocrine	Abnormal electrolyte(s) (46%) (↓ K, ↓ Na) (43% severe)	E
	Hyperglycemia (34%) (24% severe)	E
	Hypoglycemia (31%)	E
	↑ Triglycerides (28%) (21% severe)	E
Nervous System	Confusion (<5%)	E
	Encephalopathy (7%)	E
	Posterior reversible encephalopathy syndrome (PRES) (<5%)	E
	Seizure (5%)	E
Renal	Renal failure (<5%)	E

* "*Incidence*" may refer to an absolute value or the higher value from a reported range.
"*Rare*" may refer to events with < 1% incidence, reported in post-marketing, phase 1 studies, isolated data or anecdotal reports.

** I = *immediate* (onset in hours to days) E = *early* (days to weeks)
D = *delayed* (weeks to months) L = *late* (months to years)

The most common side effects for calaspargase pegol include ↓ albumin, ↑ LFTs, abnormal electrolyte(s), hyperglycemia, myelosuppression ± infection, bleeding, hypoglycemia, ↑ triglycerides, mucositis, fibrinogen decreased and ↑ amylase / lipase.

Glucose intolerance has occurred in patients receiving asparaginase products and may be irreversible.

Anti-drug antibodies (ADA) were detected during clinical trials. The presence of ADA correlated with hypersensitivity reactions. There is insufficient information to determine whether antibodies are associated with loss of asparaginase activity.

Serious **infections**, including fatal cases of sepsis, have been reported.

Asparaginase products may worsen pre-existing liver impairment. There is an increased risk of **hepatic effects** (e.g. ↑ LFTs) in patients >18 years of age using asparaginase products.

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E - Dosing

Refer to protocol by which the patient is being treated.

Screen for hepatitis B virus in all cancer patients starting systemic treatment. Refer to the hepatitis B virus screening and management guideline.

Different asparaginase products are **not interchangeable** and dosing schedules are different. For example, giving calaspargase pegol at the same dose and frequency as pegaspargase may result in higher asparaginase activity exposures, which may increase toxicities.

Pre-medications (prophylaxis for infusion reactions)

To be given 30-60 minutes prior to calaspargase pegol administration:

- Acetaminophen
- H-1 receptor blocker (e.g. diphenhydramine)
- H-2 receptor blocker (e.g. famotidine)
- Optional: steroids may also be considered.

Adults:

Intravenous: 2500 units/m² q21 days

Dosage with Toxicity:

Toxicity	Severity	Action
Thrombosis	Uncomplicated DVT	Hold. Treat with appropriate antithrombotic therapy. Consider restart when symptoms resolve, while continuing antithrombotic therapy.
	Severe or life-threatening	Discontinue. Treat with appropriate antithrombotic therapy.
Hemorrhage	Grade 3 or 4	Hold. Evaluate for coagulopathy and consider clotting factor replacement as needed. If bleeding is controlled, restart with the next scheduled dose.
Pancreatitis	lipase or amylase >3 x ULN	Hold until enzyme levels stabilize or decline.
	Grade 3 or 4	Discontinue if clinical pancreatitis is confirmed.
↑ bilirubin	>3 to 10 x ULN	Hold. Restart when bilirubin ≤1.5 x ULN.
	>10 x ULN	Discontinue.

Management of Infusion-related reactions:

Also refer to the CCO guideline for detailed description of Management of Cancer Medication-Related Infusion Reactions.

Grade	Management	Re-challenge
1	• Reduce the infusion rate by 50%	• No specific recommendations available.
2	• Stop the infusion. • Manage the symptoms. **Restart:** • After symptom resolution, restart by reducing the infusion rate by 50%.	
3 or 4	• Stop treatment. • Aggressively manage symptoms.	• Permanently discontinue. (Do not re-challenge.)

Dosage with Hepatic Impairment:

Calaspargase pegol is **contraindicated** in patients with severe hepatic impairment.

The effects of hepatic impairment on the pharmacokinetics (PK) of calaspargase pegol are unknown.

Dosage with Renal Impairment:

The effects of renal impairment on the PK of calaspargase pegol are unknown.

Dosage in the elderly:

No data available.

Children:

Calaspargase pegol has been shown in clinical trials to be safe and effective in children ≥1 year of age

Refer to product monograph for additional information.

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F - Administration Guidelines

Different asparaginase products are **not interchangeable** and dosing schedules are different. For example, giving calaspargase pegol at the same dose and frequency as pegaspargase may result in higher asparaginase activity exposures, which may increase toxicities.

- Calaspargase pegol is for **intravenous infusion** only.
- Dilute in 100 mL of NS or D5W prior to administration.
- After dilution, administer immediately into a running infusion of NS or D5W.
- Administer IV over 1 to 2 hours. Observe patient during and for at least 60 minutes after the infusion.
- Do not administer other drugs through the same IV line during calaspargase pegol infusion.
- Store unopened vials refrigerated at 2-8°C in the original carton to protect from light. Do not shake or freeze.

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G - Special Precautions

Contraindications:

- Patients who are anaphylactic or have severe hypersensitivity to asparaginase (including pegylated L-asparaginase), to this drug or any of its components
- Patients who experience serious thrombosis, serious pancreatitis, or serious hemorrhagic events during previous L-asparaginase treatment
- Patients with severe hepatic impairment

Other Warnings/Precautions:

- Live vaccines should not be given during treatment and for at least 3 months after the end of treatment.
- Exercise caution when driving or operating potentially dangerous machinery as calaspargase pegol may cause seizures, drowsiness, or confusion.

Other Drug Properties:

- Carcinogenicity: Unknown

Pregnancy and Lactation:

- Genotoxicity: Unknown
- Fetotoxicity: Documented in animals
- Pregnancy:
  Calaspargase pegol is not recommended for use in pregnancy. Adequate contraception should be used by patients and their partners during treatment, and for at least **3 months** after the last dose.
- Excretion into breast milk: Unknown
  Breastfeeding is not recommended during treatment and for **3 months** after the last dose.
- Fertility effects: Unknown

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H - Interactions

No formal drug interaction studies have been conducted with calaspargase pegol.

A decrease in serum proteins caused by asparaginase products may increase the toxicity of other medications that are protein bound.

The following drug interactions have been observed with **various** asparaginase products.

AGENT	EFFECT	MECHANISM	MANAGEMENT
Methotrexate (when given before asparaginase)	↑ effect of both drugs	Synergistic effect	Caution
Methotrexate (when given after asparaginase)	↓ effect of both drugs	Antagonistic effect	Caution
Cytarabine (when given before asparaginase)	↑ effect of asparaginase	Synergistic effect	Caution
Cytarabine (when given after asparaginase)	↓ effect of asparaginase	Antagonistic effect	Caution
Antineoplastic agents that are substrates for CYPs		Interference with metabolism and clearance of these substrates	Caution
Neurotoxic products (e.g. vincristine, methotrexate)	↑ risk of CNS toxicity	Additive	Monitor
Hepatotoxic drugs or drugs metabolized by the liver	↑ risk of hepatotoxicity	Additive	Monitor liver function; use with caution, especially in patients with pre-existing hepatic impairment
Glucocorticoids (e.g. prednisolone, dexamethasone)	↑ glucocorticoid exposure	Decreased glucocorticoid elimination	Monitor for glucocorticoid adverse effects
Glucocorticoids (e.g. prednisolone, dexamethasone)	↑ risk of glucocorticoid-induced osteonecrosis in children > 10 years of age, higher incidence in girls	Unknown	Monitor

Drugs affecting coagulation (e.g. glucocorticoids, methotrexate, daunorubicin, warfarin, heparin, ASA, Dipyridamole, NSAIDs)	↑ tendency to bleeding and/or thrombosis	Alter coagulation parameters	Caution. Monitor coagulation parameters, adjust procoagulant/anticoagulant dose if needed, and manage bleeding/thrombotic risk.
Oral contraceptives	May ↓ efficacy of oral contraceptives	Hepatic clearance of oral contraceptives may be reduced	Avoid concomitant use. Use alternative methods of contraception.
Live vaccines	↑ risk of severe infections	Additive immunosuppressive effects of asparaginase, chemotherapy, and underlying condition	Avoid. Live vaccines should not be given during treatment and for at least 3 months after the end of treatment
Highly protein-bound drugs	↑ risk of toxicity from these drugs	Decreased serum proteins	Caution
Immunosuppressants	↑ risk of immunosuppression	Additive	Caution
Thyroid function tests	Test results can be affected	↓ synthesis of thyroxine-binding globulin in liver	Delay measurement until 4 weeks after end of asparaginase therapy

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I - Recommended Clinical Monitoring

Treating physicians may decide to monitor more or less frequently for individual patients but should always consider recommendations from the product monograph.

Refer to the hepatitis B virus screening and management guideline for monitoring during and after treatment.

Recommended Clinical Monitoring

Monitor Type	Monitor Frequency
Liver function tests, serum albumin	Baseline, before each dose, and as clinically indicated
Serum amylase, lipase levels	Baseline, before each dose, and as clinically indicated
Clotting profile (PT, aPTT, fibrinogen, ATIII)	Baseline, before each dose, and as clinically indicated
Blood and urine glucose levels	Baseline, before each dose, and as clinically indicated
CBC	Baseline and as clinically indicated
Uric acid levels, especially during induction	Baseline and as clinically indicated
Ammonia levels, in the presence of symptoms of hyperammonemia (e.g. nausea, vomiting, lethargy, irritation)	Baseline and as clinically indicated
Trough asparaginase activity levels	Before the dose (refer to local protocol)
Clinical toxicity assessment for hypersensitivity, tumour lysis syndrome, infection, bleeding, thrombosis, pancreatitis, GI and neurologic effects	At each visit

Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

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J - Supplementary Public Funding

High Cost Therapy Funding Program

- Calaspargase Pegol (Inpatient) - Relapsed or Refractory Acute Lymphoblastic Leukemia, Lymphoblastic Lymphoma or Mixed_Biphenotypic Leukemia
- Calaspargase Pegol (Inpatient) - Newly Diagnosed Acute Lymphoblastic Leukemia, Lymphoblastic Lymphoma or Mixed_Biphenotypic Leukemia

New Drug Funding Program (NDFP Website)

- Calaspargase Pegol (Outpatient) - Relapsed or Refractory Acute Lymphoblastic Leukemia, Lymphoblastic Lymphoma or Mixed_Biphenotypic Leukemia
- Calaspargase Pegol (Outpatient) - Newly Diagnosed Acute Lymphoblastic Leukemia, Lymphoblastic Lymphoma or Mixed_Biphenotypic Leukemia

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K - References

CADTH. CADTH Reimbursement Recommendation: Calaspargase Pegol (Asparlas). Canadian Journal of Health Technologies. January 2024.

CADTH. CADTH Reimbursement Review: Calaspargase Pegol (Asparlas). Canadian Journal of Health Technologies. April 2024

National Cancer Institute. NCI Drug Dictionary. Accessed on November 2024. Available from: https://www.cancer.gov/publications/dictionaries/cancer-drug.

Prescribing Information: ASPARLAS® (calaspargase pegol-mknl) injection. Servier Pharmaceuticals LLC. December 2023

Product monograph. Asparlas (Calaspargase pegol). Servier Canada Inc. March 8, 2024.

Product monograph. ERWINASE® (Erwinia L-asparaginase). Jazz Pharmaceuticals France SAS. August 30, 2016.

Product monograph. KIDROLASE® (L-asparaginase). Jazz Pharmaceuticals France SAS. August 12, 2019.

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 Nov 1;39(31):3496-3505.

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L - Disclaimer

Refer to the New Drug Funding Program or Ontario Public Drug Programs websites for the most up-to-date public funding information.

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