Asparaginase

Pronunciation: as-PAR-a-jin-ase
Class: Enzyme, Antineoplastic agent

Trade Names

Elspar
- Injection, lyophilized powder for solution 10,000 units (Escherichia coli –derived)

Erwinaze
- Injection, lyophilized powder for solution 10,000 units (Erwinia chrysanthemi –derived)

Kidrolase (Canada)

Pharmacology

Asparaginase ultimately reduces the levels of asparagine. Some leukemic cells are unable to synthesize asparagine because of a lack of asparagine synthetase; therefore, depletion of asparagine selectively kills the malignant cells.

Pharmacokinetics

Absorption

IM
T_{max} is 14 to 24 h.

Distribution

CSF levels were less than 1%.

Elimination

IV
Half-life is 8 to 30 h.

IM
Half-life is 34 to 49 h.

Indications and Usage

Elspar

For the treatment of patients with acute lymphoblastic leukemia (ALL) as a component of a multiagent chemotherapeutic regimen.

Erwinaze
For the treatment of patients with ALL who have developed hypersensitivity to E. coli –derived asparaginase as a component of a multiagent chemotherapeutic regimen.

Contraindications

Serious allergic reactions to asparaginase, other E. coli –derived L-asparaginases (Elspar only), or E. chrysanthemi –derived asparaginase (Erwinase only); serious thrombosis, pancreatitis, and serious hemorrhagic events with prior L-asparaginase therapy.

Dosage and Administration

Acute lymphoblastic leukemia
Adults Elspar
IM or IV 6,000 units/m^2 three times weekly.

Erwinaze To substitute for a dose of pegaspargase
IM 25,000 units/m^2 three times a week for 6 doses for each planned dose of pegaspargase.

To substitute for a dose of native E. coli asparaginase
IM 25,000 units/m^2 for each scheduled dose of native E. coli asparaginase within a treatment.

Children Elspar Younger than 16 y
IM 6,000 units/m^2 three times a week for a total of 9 doses.

Erwinaze 2 to 18 y of age To substitute for a dose of pegaspargase
IM 25,000 units/m^2 three times a week for 6 doses for each planned dose of pegaspargase.

To substitute for a dose of native E. coli asparaginase
IM 25,000 units/m^2 for each scheduled dose of native E. coli asparaginase within a treatment.

General Advice

Elspar

- Use reconstituted solution within 8 h and only if clear. A small number of gelatinous fiber-like particles may develop upon standing. Filtration through a 5 micron filter during administration will remove the particles with no loss of potency.

Erwinaze

- Withdraw dose from the vial into a polypropylene syringe within 15 min of reconstitution. Administer IM within 4 h of reconstitution.

IM

- The volume at a single injection site should be limited to 2 mL. If a volume greater than 2 mL is to be administered, use 2 injection sites.

IV

- Administer Elspar over a period of not less than 30 min through the side arm of an infusion of sodium chloride injection or dextrose 5% injection.

Storage/Stability

Store unreconstituted vials between 36° and 46°F. Protect Erwinaze from light. Store unused Elspar reconstituted

solution between 36° and 46°F; discard after 8 h, or sooner if cloudy. Do not freeze or refrigerate reconstituted Erwinaze solution; discard after 4 hours. Discard unused portion.

Drug Interactions

Vaccines, live
The risk of live vaccine–induced adverse reactions may be increased by coadministration of asparaginase. Use of live vaccines in patients receiving asparaginase should be deferred.

Adverse Reactions

Cardiovascular

Sagittal sinus thrombosis, thrombosis.

CNS

CNS hemorrhages, CNS thrombosis, coma, hallucinations, headache, seizures.

GI

Abdominal pain, diarrhea, nausea, vomiting.

Hematologic

Coagulopathy, decreased fibrinogen, decreased protein C, decreased protein S and antithrombin III, increased PT, increased PTT.

Hepatic

Elevated transaminases, hepatotoxicity (some fatal), hyperbilirubinemia, liver function abnormalities.

Hypersensitivity

Anaphylaxis, serious allergic reactions, urticaria.

Metabolic

Glucose intolerance (some irreversible), hyperammonemia, hypercholesterolemia, hyperglycemia, hyperlipidemia, hypertriglyceridemia.

Miscellaneous

Azotemia, fever, pancreatitis (fulminant or fatal).

Precautions

Monitor

Monitor coagulation parameters and serum glucose and evaluate hepatic enzymes and bilirubin at baseline and periodically during and after treatment. Observe patient for 1 h after administration of asparaginase in a setting with necessary agents to treat anaphylaxis (eg, antihistamines, epinephrine, IV steroids, oxygen).

Pregnancy

Category C .

Lactation

Undetermined.

Hypersensitivity

Serious allergic reactions may occur. This risk is higher in patients with prior exposure to asparaginase or other E. coli –derived L-asparaginase (Elspar).

Coagulopathy

Hypofibrinogenemia, increased PTT, and increased PT can occur. CNS hemorrhages have been observed with Elspar . Decreased protein C activity, protein S activity, and antithrombin III have also occurred with Erwinaze .

Glucose intolerance

May occur during treatment and is irreversible in some cases.

Hepatic effects

Fulminant hepatic failure, hepatotoxicity and abnormal liver function, including elevations of AST, ALT, alkaline phosphatase, bilirubin (direct and indirect), and depression of serum albumin and plasma fibrinogen may occur. Fatty changes in the liver may occur.

Immunogenicity

Development of binding and/or neutralizing antibodies to asparaginase may occur.

Pancreatitis

Pancreatitis, in some cases fulminant or fatal, may occur.

Thrombosis

Serious thrombotic events, including sagittal sinus thrombosis, may occur.

Patient Information

- Advise patients, families, or caregivers to immediately report any of the following to the health care provider: rash; hives; acute difficulty in breathing or shortness of breath; new onset of chest pain; severe headache; swelling of the face, arms, or legs; seizures; changes in mental status; severe abdominal pain.
- Advise patients to inform their health care provider if they experience excessive thirst or an increase in the volume or frequency of urination.
- Instruct diabetic patients to monitor blood glucose more frequently when drug is started or dose is changed, and to inform health care provider of significant changes in readings.