L-asparginase

Class: Miscellaneous

Indications:

Acute lymphoblastic leukemia (ALL): Treatment (in combination with other chemotherapy) of ALL

Available dosage form in the hospital:10000 U VIAL

Trade name : Elspar

Doses: **Note:** Dose, frequency, number of doses, and start date may vary by protocol and treatment phase.

-**Acute lymphoblastic leukemia (ALL):** Manufacturer's U.S. labeling: I.V., I.M.: 6000 units/m^2/dose 3 times weekly

-*Hyper-CVAD regimen (unlabeled dosing):* I.V. 20,000 units weekly for 4 doses (starting on day 2) during either months 7 and 19 or months 7 and 11 of intensification phase

-*Larson regimen (unlabeled dosing):* SubQ: 6000 units/m^2/dose on days 5, 8, 11, 15, 18, and 22 (induction phase) and on days 15, 18, 22, and 25 (early intensification phase)

-*Linker regimen (unlabeled dosing):* I.M.:

-Remission induction: 6000 units/m^2/dose on days 17-28; if bone marrow on day 28 is positive for residual leukemia: 6000 units/m^2/dose on days 29-35

-Consolidation (Treatment A; cycles 1, 3, 5, and 7): 12,000 units/m^2/dose on days 2, 4, 7, 9, 11, and 14

-**Lymphoblastic lymphoma (unlabeled use):** Hyper-CVAD regimen: I.V.: 20,000 units weekly for 4 doses (starting on day 2) for 2 cycles (months 7 and 11) during maintenance phase.

Geriatric
Refer to adult dosing.

Renal Impairment:
No dosage adjustment provided in manufacturer's labeling.

Hepatic Impairment:
No dosage adjustment provided in manufacturer's labeling.

Dosing: Obesity
ASCO Guidelines for appropriate chemotherapy dosing in obese adults with cancer: Utilize patient's actual body weight (full weight) for calculation of body surface area- or weight-based dosing, particularly when the intent of therapy is curative; manage regimen-related toxicities in the same manner as for nonobese patients; if a dose reduction is utilized due to toxicity, consider resumption of full weight-based dosing with subsequent cycles, especially if cause of toxicity (eg, hepatic or renal impairment) is resolved (Griggs, 2012).

Dosing: Adjustment for Toxicity
-Allergic reaction/hypersensitivity: Discontinue for severe reactions.

-Neurotoxicity (posterior reversible encephalopathy syndrome; PRES): Interrupt therapy for suspected PRES; control blood pressure and closely monitor for seizure activity.
-Pancreatitis: Discontinue permanently (per manufacturer).
-Thrombotic event: Discontinue for serious reactions.

Common side effect :

Central nervous system: Fatigue, fever, chills, depression, agitation, seizure (10% to 60%), somnolence, stupor, confusion, coma (25%)

Endocrine & metabolic: Hyperglycemia/glucose intolerance (10%)

Gastrointestinal: Nausea, vomiting (50% to 60%), anorexia, abdominal cramps (70%), acute pancreatitis (15%, may be severe in some patients)

Hematologic: Hypofibrinogenemia and depression of clotting factors V and VIII, variable decrease in factors VII and IX, severe protein C deficiency and decrease in antithrombin III (may be dose limiting or fatal)

Hepatic: Transaminases, bilirubin, and alkaline phosphatase increased (transient)

Hypersensitivity: Acute allergic reactions (fever, rash, urticaria, arthralgia, hypotension, angioedema, bronchospasm, anaphylaxis (15% to 35%); may be dose limiting in some patients, may be fatal)

Renal: Azotemia (66%)

Endocrine & metabolic: Hyperuricemia

Gastrointestinal: Stomatitis

Miscellaneous: Allergic reaction (including anaphylaxis), antibody formation/immunogenicity (~25%)

Pregnancy category : C