New Zealand Datasheet

Name of Medicine

Erwinase®

Erwinia L-asparaginase

Presentation

Crisantaspase (Asparaginase from *Erwinia chrysanthemi*; Erwinia L-asparaginase), 10,000 Units/vial as a freeze-dried powder for reconstitution.

Uses

Actions

Neoplastic cells associated with Acute Lymphoblastic Leukaemia (ALL), Acute Myeloid Leukaemia (AML) and Lymphoblastic Lymphosarcoma (LSA) are asparagine-dependent. Reduction of plasma asparagine levels achieved by administration of L-asparaginase produces an anti-neoplastic effect. The animal studies carried out with Erwinase provide only an approximate indication of the human dose required when comparisons are made on a mg/kg basis. However, clinical studies have used doses in the range 500 to 60,000 Units/m2/day. The upper dose level is made possible by the intrinsically low toxicity of the Erwinia enzyme.

Pharmacokinetics

Peak levels of Erwinase are achieved in blood in 1 to 2 hours. The fall in enzyme levels follows first order kinetics with half-life of 7 to 13 hours.

Indications

Erwinase is used in combination with other antineoplastic agents to treat acute lymphoblastic leukaemia. It may also be used in other neoplastic conditions where depletion of asparagine might be expected to have a useful effect. Patients receiving treatment with L-asparaginase from *Escherichia coli,* and who develop hypersensitivity to that enzyme may be able to continue treatment with Erwinase as the enzymes are immunologically distinct.

Dosage and Administration

Erwinase solution can be given by intravenous injection or infusion or by intramuscular or subcutaneous injection.

For all patients the usual dose is 6,000 Units/m2body surface area (200 Units/kg of body weight), three times a week for three weeks.

Therapy may be further intensified according to protocol.

Reference to current Medical Research Council protocols on leukaemia therapy should be made for information on dose, route and frequency of treatment.

Contraindications

Previous allergic reaction to Erwinia asparaginase.

Warnings and Precautions

Asparaginase is a bacterial protein and repeated use can, therefore, lead to

sensitisation reactions.

Erwinase should preferably be given without interruption. If, however, an interruption cannot be avoided, treatment should be resumed with a low dose, 10 Units/kg/day, and increased to the full dose over five days if tolerated. Anaphylaxis is rare but facilities should be made available for its management during administration.

Use in Pregnancy and Lactation
Asparaginase should not be given women who are, or are likely to become pregnant.

Effects on Ability to Drive and Use Machines
None known.

Adverse Effects
Neurotoxicity, life-threatening sepsis and severe hypersensitivity have been described in patients treated with L-asparaginases. Other effects reported with both enzymes include fever; nausea; vomiting; CNS depression; hypersensitivity and various plasma biochemical changes including increased BSP retention and elevation of bilirubin, SGOT, alkaline phosphatase and cholesterol levels; decreases in fibrinogen and some clotting factors. For these reasons, careful monitoring is therefore necessary and urine should be tested for glucose to exclude hyperglycaemia.

Undesirable effects are generally reversible and are less common with Erwinia L-asparaginase than with *E.coli* asparaginase.

Interactions
Asparaginase must not be mixed with any other drugs prior to administration.

Overdosage
No specific measures are recommended.

Pharmaceutical Precautions
Store between 2°C and 8°C.

Medicine Classification
Prescription Medicine

Package Quantities
20 x 1ml single dose glass vials (20 Dose units)

Further Information

List of Excipients
Sodium Chloride BP
Dextrose Monohydrate BP

Incompatibilities
See "Interaction with other medicaments and other forms of interaction".

Shelf-life
Shelf-life of product as packed for sale: 3 years.

Shelf-life following reconstitution according to directions: 15 minutes in the original container, 8 hours in a glass or polypropylene syringe. (See "Instructions for use/handling")

Nature and contents of container

Type 1 clear neutral glass vials of 3ml nominal capacity, closed with 13mm halobutyl freeze-drying stoppers and aluminium overseals, containing a white lyophilised solid.

Instructions for use/handling

The contents of each vial should be reconstituted in 1ml to 2ml of Sodium Chloride for Injection BP and dissolved by gentle mixing.

The solution should be administered within 15 minutes of reconstitution. If a delay of more than 15 minutes between reconstitution and administration is unavoidable, the solution should be withdrawn into a glass or polypropylene syringe for the period of the delay. The solution should be used within 8 hours.

Erwinase is not a cytotoxic drug (such as vincristine or methotrexate) and does not require the special precautions needed for manipulating such agents. It should be handled in the same way as other therapeutic enzymes such as hyaluronidase.

Pre-clinical safety data

No further relevant data.

Name and Address

New Zealand Medical & Scientific Ltd
PO Box 24-138,
Royal Oak
Auckland,
New Zealand
Tel (09) 634 1036, Fax (09) 634 5146

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