

ERWINASE[®]
(*Erwinia L-asparaginase*)

1. Name of Medicinal Product

ERWINASE[®]

2. Qualitative and Quantitative Composition

Crisantaspase (Asparaginase from *Erwinia chrysanthemi*; *Erwinia L-asparaginase*),
10,000 Units/vial.

3. Pharmaceutical Form

Freeze-dried powder for reconstitution.

4. Clinical Particulars

4.1 Therapeutic indications

Erwinase is used in combination with other anti-neoplastic 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.

4.2 Posology and method of administration

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

For all patients the usual dose is 6,000 Units/m² body 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.

4.3 Contra-indications

Previous allergic reaction to *Erwinia asparaginase*.

4.4 Special warnings and precautions for use

Warnings: Anaphylactic reactions have been observed after the use of Erwinase.

Special precautions for use: 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.

4.5 Interactions with other medicaments and other forms of interaction

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

4.6 Pregnancy and lactation

Asparaginase should not be given to women who are, or are likely to become, pregnant.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable 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; acute pancreatitis 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.

4.9 Overdose

No specific measures are recommended.

5. Pharmacological Properties

5.1 Pharmacodynamic properties

Neoplastic cells associated with Acute Lymphoblastic Leukaemia (ALL), Acute Myeloid Leukaemia (AML) and Lymphoblastic Lymphosarcoma (LSA) are asparagine-dependant. 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 Erwinase enzyme.

5.2 Pharmacokinetic properties

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

5.3 Pre-clinical safety data

No further relevant data.

6. Pharmaceutical Particulars

6.1 List of excipients

Sodium Chloride BP

Dextrose Monohydrate BP

6.2 Incompatibilities

See section 4.5 "Interactions with other medicaments and other forms of interaction".

6.3 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 section 6.6 "Instructions for use/handling").

6.4 Special precautions for storage

Store between +2°C and +8°C.

6.5 Nature and contents of container

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

6.6 Instructions for use/handling

The contents of each vial should be reconstituted in 1 ml to 2 ml 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.

7. Name and Address of the Marketing Authorisation Holder

Health Protection Agency
Centre for Emergency Preparedness and Response
Porton Down, Salisbury, SP4 0JG
United Kingdom

8. Marketing Authorisation Number

PL 20170/0001

9. Date of First Authorisation

19 July 1985

10. Date of Revision of the SPC

November 2005

Local representative:

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