Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Protamine Sulphate LEO 10 mg/ml solution for injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Protamine sulphate 10 mg/ml.

For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Solution for injection.
Clear, colourless liquid.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

As a heparin antagonist to neutralise the haemorrhagic effects of heparin.
To counteract overdosage with tinzaparin.

4.2 Posology and method of adminstration

No more than 50mg of Protamine Sulphate should be administered in a 10 minute period and the rate of administration should not exceed 5mg/minute.

To neutralise the effects of heparin:
The usual dosage is up to 5ml (50 mg) administered by slow intravenous injection. Dosage depends on patient's blood coagulability. Each 1mg of protamine sulphate is stated to neutralise 100 IU of heparin.
If given after a period of 30 minutes following heparin administration, dosage requirements may be reduced because of heparin metabolism.

To counteract overdosage of tinzaparin:
Limited evidence suggests that a dose of 1mg protamine sulphate per 100 anti-Xa IU tinzaparin neutralises 65-80% of the anti-Xa activity. The protamine sulphate dose should be given intermittently or as a slow continuous intravenous infusion for at least 24 hours to maintain neutralisation of tinzaparin.

4.3 Contraindications

Hypersensitivity to protamine sulphate or the excipients.

4.4 Special warnings and special precautions for use

Excessive dosage may prolong the coagulation time because protamine itself has anticoagulant activity.

The thrombocytopoenia associated with extracorporeal circulation during cardiac surgery may be aggravated by protamine.

This product contains propylhydroxybenzoate (E216) and methylhydroxybenzoate (E218) which may cause allergic reactions (possibly delayed) and exceptionally, bronchospasm. This product contains less than 1 mmol sodium (23 mg) per 5 ml maximum dose, i.e. essentially 'sodium free'.

4.5 Interaction with other medicinal products and other forms of interaction

None known

4.6 Pregnancy and lactation

There is no experience of the use of protamine sulphate in pregnancy or lactation. Therefore, use should be limited to that considered essential by the physician.

4.7 Effects on ability to drive and use machines

Protamine sulphate has no or negligible influence on the ability to drive or use machines.

4.8 Undesirable effects

Protamine Sulphate intravenous injection should be given slowly since rapid injection may cause a fall in blood pressure, bradycardia, dyspnoea or transitory flushing.
Anaphylactic reactions may occur, some due to residual fish antigen.
Refer to section 4.4 for excipient warnings.

4.9 Overdose

There is no experience with this product in overdose.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Protamines are simple low molecular weight proteins, rich in arginine and strongly basic. When administered alone, protamine sulphate has an anticoagulant effect. However, when the strongly basic protamine combines with the strongly acid heparin or Low Molecular Weight Heparin, a stable salt is formed which results in the loss of anticoagulant activity of both drugs.

5.2 Pharmacokinetic properties

The onset of action of protamine sulphate occurs within 30 - 60 seconds following intravenous administration.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Methyl parahydroxybenzoate (E218)
Propyl parahydroxybenzoate (E216)
Sodium dihydrogen phosphate dihydrate
Water for injections

6.2 Incompatibilities

Protamine sulphate has been shown to be incompatible with certain antibiotics, including several cephalosporins and penicillins.

6.3 Shelf Life

3 years.
Single use only. Discard unused portion.

6.4 Special precautions for storage

Store below 25°C.

6.5 Nature and contents of container

5 ml vial made of colourless glass (Type I, Ph. Eur.) and closed with chlorbutyl rubber stoppers.

6.6 Instructions for use and handling

No special instructions.

7 MARKETING AUTHORISATION HOLDER

Leo Laboratories Limited
285 Cashel Road
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8 MARKETING AUTHORISATION NUMBER

PA 46/33/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 1st April 1983

Date of last renewal: 1st April 2003

10 DATE OF REVISION OF THE TEXT

March 2004