

AUSTRALIAN PRODUCT INFORMATION – FISONS PROTAMINE SULFATE INJECTION B.P (PROTAMINE SULFATE)

1 NAME OF THE MEDICINE

Fisons Protamine Sulfate solution for injection.

2 AND 3 QUALITATIVE AND QUANTITATIVE COMPOSITION AND PHARMACEUTICAL FORM

A sterile, pyrogen-free, clear, colourless 1% solution of Protamine Sulfate (Salmine) in Sodium Chloride Intravenous Infusion B.P. (0.9% w/v) adjusted to a pH of 2.5 to 3.5 and supplied in 5mL glass ampoules.

For the full list of excipients, see Section 6.1 List of excipients.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Protamine is a basic protein which combines with heparin to form a stable, inactive complex. It is used to counteract the anticoagulant effect of heparin; before surgery; after renal dialysis; after open-heart surgery; if excessive bleeding occurs and when an overdose has inadvertently been given.

4.2 DOSE AND METHOD OF ADMINISTRATION

Fisons Protamine Sulfate Injection should be administered by slow intravenous injection over a period of about 10 minutes. The dose is dependent on the amount of heparin to be neutralised. 1mg of Fisons Protamine Sulfate will usually neutralise at least 100 international units of mucous heparin or 80 units of lung heparin. Since heparin is being continuously excreted, the dose of Fisons Protamine Sulfate should be reduced if more than 15 minutes have elapsed since the heparin injection. Ideally, the dose required to neutralise the action of heparin should be calculated from the results of determinations of the amount required to produce an acceptable blood clotting time in the patient. In gross excess, protamine itself acts as an anticoagulant.

4.3 CONTRAINDICATIONS

Hypersensitivity to protamine (including protamine contained in insulin NPH [Neutral Protamine Hagedorn]) or to any excipients.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Too rapid administration of protamine sulfate may cause severe hypotension and anaphylactoid reactions. Rapid administration may also influence the severity of symptoms in a sensitized individual. For this reason, protamine sulfate should be administered by slow intravenous injection over a period of about 10 minutes. Facilities for resuscitation and treatment of shock should be available.

Not more than 50mg Fisons Protamine Sulfate (5mL) - 1 ampoule should be given at any one time. Protamine is not suitable for reversing the effect of oral anticoagulants.

Fatal cases of anaphylactic reactions have been reported. Caution should be observed when administering protamine sulfate to patients who may be at increased risk of allergic reaction to protamine. These patients include those who have previously undergone procedures such as coronary angioplasty or cardio-pulmonary by-pass which may include use of protamine, diabetics who have been treated with protamine insulin, patients allergic to fish, and men who have had a vasectomy or are infertile and may have antibodies to protamine.

Patients undergoing prolonged procedures involving repeated doses of protamine should be subject to careful monitoring of clotting parameters. A rebound bleeding effect may occur up to 18 hours post-operatively which responds to further doses of protamine.

To ensure sufficient neutralisation, careful monitoring of clotting parameters is necessary.

Use in the elderly

No data available.

Paediatric use

Safety and efficacy in children have not been established, therefore use in children is not recommended.

Effects on laboratory tests

No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

None known

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

No data available.

Use in pregnancy

Category B2 of Australian Categorisation of Risk of Drug Use in Pregnancy.

There are limited data available from the use of protamine in pregnant women. Therefore, Fisons Protamine Sulfate is not recommended during pregnancy unless the benefit outweighs the risk.

Use in lactation

It is unknown whether Fisons Protamine Sulfate or its metabolites are excreted in human milk. A risk to the breast-fed child cannot be excluded. Therefore, Fisons Protamine sulfate should not be used during breast feeding.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

When used at doses in excess of that required to neutralise the anticoagulant effect of heparin, protamine sulfate exerts its own anticoagulant effect.

Following injection of protamine sulfate the following effects have been observed:

Blood and lymphatic system disorders:

Cases of thrombocytopenia have been reported and in some cases reported with antibody formation.

Cardiac disorders:

Bradycardia, a sudden fall in blood pressure.

Immune system disorders:

Hypersensitivity reactions (including shock) and fatal anaphylaxis have been reported (see Precautions).

Vascular disorders:

Hypotension, acute pulmonary arterial hypertension and systemic hypertension, transitory flushing and a feeling of warmth.

Respiratory, thoracic and mediastinal disorders:

Non cardiogenic pulmonary oedema, sometimes fatal has been reported. Dyspnoea.

Injury, poisoning and procedural complications:

Post procedural haemorrhage has been reported.

Gastrointestinal disorders:

Nausea and vomiting

Musculoskeletal and connective tissue disorder:

Back pain.

General disorders and administration site conditions:

Lassitude

Reporting suspected adverse reactions

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems (Australia) or <https://nzphvc.otago.ac.nz/reporting/> (New Zealand).

4.9 OVERDOSE

Protamine overdose causes a haemorrhagic syndrome because of the anticoagulant activity of protamine.

Symptoms: Overdosage may cause hypotension, bradycardia and dyspnoea with a sensation of warmth, nausea, vomiting, lassitude and transitory flushing.

Treatment: Includes monitoring of coagulation tests, respiratory ventilation and symptomatic treatment. If bleeding is a problem, fresh frozen plasma or fresh whole blood should be given.

For information on the management of overdose, contact the Poisons Information Centre, on 13 11 26 (Australia) or the National Poisons Centre, 0800 POISON or 0800 764 766 (New Zealand).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

No data available.

Clinical trials

No data available.

5.2 PHARMACOKINETIC PROPERTIES

No data available.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No data available.

Carcinogenicity

No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

- Sodium chloride
- Hydrochloric acid
- Sodium hydroxide
- Water for injections

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 25°C.

6.5 NATURE AND CONTENTS OF CONTAINER

10 X 5mL ampoules: 10mg/mL

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

CAS number

9009-65-8

7 MEDICINE SCHEDULE (POISONS STANDARD)

Prescription Medicine (Schedule 4)

8 SPONSOR

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9 DATE OF FIRST APPROVAL

14 May 1991

10 DATE OF REVISION

19 October 2018

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
All	Reformat and editorial changes
4.3	Addition of contraindication
4.4	Addition of precaution
4.6	Update to pregnancy and lactation information
4.8	Addition and update to adverse effects
6.4	Inclusion of registered storage conditions
8	Inclusion of contact number and email