Ballarat Health Services

DRUG GUIDELINE

PROTAMINE

SCOPE (Area): **FOR USE IN:** Intensive Care Unit, ED, Theatre, CVS
EXCLUSIONS: Paediatrics (seek Paediatrician advice), Coronary Care Unit and other Wards
SCOPE (Staff): Medical, Nursing and Pharmacy

BRAND NAMES
No brand name.

PHARMACOLOGY AND PHARMACOKINETICS
Protamine combines with heparin to form a stable inactive complex, reversing the anticoagulant effect of heparin. Following IV administration, neutralisation of heparin occurs within 5 minutes.

INDICATIONS
- **Severe haemorrhage, or high risk of severe haemorrhage in patients who have received an overdose of heparin.**
- **Severe haemorrhage, or high risk of severe haemorrhage in patients who have received an overdose of enoxaparin (Clexane®) –** protamine only partially reverses the anticoagulant effect of low molecular weight heparins.

CONTRAINDICATIONS
- **Hypersensitivity to protamine.**

PRECAUTIONS
- **Rapid IV injection –** has caused acute hypotension, anaphylactic reactions, bradycardia, pulmonary hypertension, dyspnoea, transient flushing and a feeling of warmth. Inject no faster than 5 mg/minute.
- **Excessive dosing of protamine –** when given in excessive amounts (or in the absence of heparin) protamine exerts its own anticoagulant effect.
- **Allergy –** patients with the following have an increased risk of allergy to protamine
  - Those who have previously undergone procedures such as coronary angioplasty or cardio-pulmonary bypass which may include the use of protamine.
  - Diabetics who have been previously treated with protamine insulin.
  - Infertile men or men who have had a vasectomy (may have antibodies to protamine).
  - Allergy to fish – increased risk of allergy to protamine.

PREGNANCY AND BREASTFEEDING
Seek specialist advice before prescribing, information may update regularly.

DRUG INTERACTIONS

- **Nil known.**

DOSAGE AND ADMINISTRATION

Resuscitation facilities must be available. Risk of anaphylaxis with administration.
For administration only

- **in Intensive Care Unit, ED or Theatre**
- **by Registrars or Consultants in Coronary Care Unit or general wards**

The Doctor calculating the protamine dose should be a Registrar or Consultant experienced in the use of protamine.

Review Indications carefully before prescribing. Withdrawal of heparin is usually sufficient to treat minor bleeding as heparin is rapidly eliminated (half-life 30-60 minutes). Blood transfusions may still be needed for severe haemorrhage. Seek Specialist advice if unsure.

Not for rapid IV injection – see Precautions. May be administered via CVC or peripherally.

Maximum dose of protamine is 50 mg at one time.

Protamine has an onset of action of 5 minutes.

Note: Consider the original indication for heparin and that re-heparinisation may be difficult due to circulating protamine, seek Specialist advice. Protamine has no role in warfarin reversal.

Calculation of initial dose for heparin neutralisation:

The first dose of protamine to be given depends on the dose of heparin to be neutralised, its route and method of administration and time since it was given.

Use protamine 50 mg/5 mL ampoules.
Maximum dose: 50 mg (5 mL from ONE ampoule) at one time irrespective of dose calculated.
Maximum rate of injection is 5 mg/minute (50 mg over 10 minutes).

When heparin was administered by IV infusion

Stop heparin infusion.
Protamine 1 mg per 100 units of total heparin given in the previous 2 hours (including any boluses).
Give calculated dose (**maximum 50 mg**) undiluted by slow IV injection over 10 minutes.

When heparin was administered by IV bolus

The protamine dose required decreases with time as heparin is eliminated, the following table provides estimates to assist for protamine dose determination.

Time since last IV heparin **bolus** dose	15 minutes or less	30-60 minutes	2 hours or greater
Protamine dose	1 mg protamine for every 100 units of heparin **Maximum of 50 mg**	0.5 mg protamine for every 100 units of heparin **Maximum of 50 mg**	0.25 mg protamine for every 100 units of heparin **Maximum of 50 mg**

Give calculated dose (**maximum 50 mg**) undiluted by slow IV injection over 10 minutes. Administer by Alaris syringe unit with Guardrails®, or by hand.

Further doses for heparin reversal neutralisation:

Further treatment is guided by monitoring the APTT every 20–30 minutes after protamine administration. Consider using thromboelastgraphy (TEG) if active bleeding. If a further dose is required, half the dose should be given.

Calculation of dose for low molecular weight heparins (e.g. enoxaparin) neutralisation:

Anti-Xa activity is not completely neutralised by protamine (maximum of 60%). Seek Specialist advice if unsure.

Time since last enoxaparin dose	8 hours or less	More than 8 hours and less than 12 hours	12 hours or more
Protamine dose	1 mg protamine for every 1 mg enoxaparin **Maximum of 50 mg**	0.5 mg protamine for every 1 mg enoxaparin **Maximum of 50 mg**	May not be required

Give calculated dose (**maximum 50 mg**) undiluted by slow IV injection over 10 minutes. Administer by Alaris syringe unit with Guardrails®, or by hand.

General Administration Information

- **Routes of administration:**
  - IV injection: Yes, maximum rate 5 mg/min.
  - IV intermittent infusion (15-60 minutes): Yes
  - IV continuous infusion: No
  - IM injection: No
  - Subcut injection: No
- **Infusion pump:** Alaris® syringe unit with Guardrails®.
- **Compatible/incompatible IV drugs/fluids:**

Consult the Australian Injectable Drugs Handbook ('Yellow book') in your ward area. **Assume all unlisted drugs and IV fluids are incompatible – contact Pharmacy for further advice.**

MONITORING (INCLUDING BLOOD TESTS)

- Baseline APTT, and repeated post protamine as described in Dosage and Administration.

NURSING PRACTICE POINTS

- Observe patients for signs of bleeding or allergic reaction.
- Monitor airway for signs of anaphylaxis such as stridor or bronchospasm.
- All injections, infusions and lines are to be labelled as per CPP0022 Labelling of Injectable Medicines and Lines.

ADVERSE EFFECTS

- **Common –** sensation of warmth, flushing, nausea, vomiting and tiredness.
- **Infrequent –** hypotension, bradycardia, dyspnoea (especially if given rapidly), allergy (see below), rebound bleeding with excessive doses.
- **Allergy –** urticaria and severe hypersensitivity reactions including cardiovascular collapse, bronchospasm and death have occurred.

DRUG PRESENTATIONS AND STORAGE

Protamine 50 mg/5 mL ampoules.

Store below 25°C.