Protamine Intravenous for Adults

Who can administer

May be administered by registered competent doctor or nurse/midwife

Important information

- Can cause anaphylactic reactions - resuscitation facilities should be available - see further information
- Very rapid administration of protamine sulphate can lead to **hypotension and anaphylactoid reactions** (ref 1)
- Excessive dosage of protamine sulphate or when given in the absence of heparin or LMWH may induce prolonged coagulation time since protamine sulphate in itself has anticoagulant activity

Available preparations

Protamine sulphate 7,000 anti-heparin units per 5mL ampoule (50mg per 5mL)

Reconstitution

Already in solution

Draw up using a 5 micron filter needle

Infusion fluids

Sodium chloride 0.9% (volume not critical)

Methods of intravenous administration

Slow intravenous injection (max 5mL dose)

- Administer required dose **over approximately 10 minutes - max rate 5mg per minute** (ref 1)
- May cause **severe hypotension** if administered too rapidly

Intermittent intravenous infusion (can be used for all doses)

- Add required dose to infusion fluid (volume not critical), and administer as a continuous infusion, adjusting rate according to aPTT response - **max rate 5mg per minute** (ref 1)

Dose in adults

1. Unfractionated heparin (UFH) neutralisation

- Monitor APTT or use other tests of coagulation before starting Protamine sulphate
- If APTT is not raised, there is no indication to give/continue protamine sulphate
- 1ml (10mg) of Protamine Sulphate will neutralise approximately 1,400 units of heparin
- **Maximum dose is 50mg at any one time (i.e. 7000 units or 5mL)**
- Check APTT 5 to 15 minutes after administration of protamine
- As heparin has a relatively short half-life when given intravenously (30 minutes to 2 hours), the dose of protamine sulphate should be adjusted on the basis of the time elapsed since the intravenous

administration of heparin was discontinued. **The dose of protamine in relation to the administered amount of heparin should be reduced if more than 15 minutes have elapsed since intravenous administration of heparin has stopped.**

2. Low molecular weight heparins (LMWH) neutralisation

- 1mL (10mg) or Protamine Sulphate will **partially** neutralise 1,000 antiXa LMWH (higher doses than those recommended will not produce more effective neutralisation and can result in excessive bleeding due to the anticoagulant effect of protamine in excess
- The degree of neutralisation of LMWH is **product specific (in vitro studies - anti Xa neutralised = 81% for tinzaparin, 46% for enoxaparin)**
- Maximum dose is 50mg (5mL) at any one time (i.e. 7000 units or 5mL)
- **Tinzaparin:** no specific guidance provided by manufacturer
- **Enoxaparin:**
  - The dose of protamine depends on the dose of **enoxaparin** injected; 1 mg protamine neutralizes the anticoagulant effect of 100 units (1 mg) of enoxaparin, if enoxaparin **administered in the previous 8 hours**
  - An infusion of 0.5 mg protamine per 100 units (1 mg) of enoxaparin may be administered if enoxaparin was administered **greater than 8 hours previous to the protamine administration**, or if it has been determined that a second dose of protamine is required
  - **After 12 hours of the enoxaparin injection, protamine administration is rarely required.** However, even with high doses of protamine, the anti-Xa activity of enoxaparin is never completely neutralized (maximum about 60%)

Repeat administration of protamine may be required to neutralise LMWH because:

1. Elimination is determined by the half-life of the particular LMWH used
2. Protamine sulphate is cleared from the blood more rapidly than the LMWHs
3. Absorption of LMWH after subcutaneous administration is prolonged

3. Cardiopulmonary bypass procedures

- Doses guided by blood coagulation studies e.g. APTT, ACT, anti-Xa

Monitoring

- Frequent monitoring of APTT and other coagulation parameters is essential to guide treatment - see under Dose
- Anti Xa level is best for monitoring LMWH but may not always be available on an emergency basis

Further information

- A rebound anticoagulant effect with haemorrhage has been reported occasionally despite adequate heparin inhibition by protamine sulphate
- This occurs more frequently in cases of extra-corporeal circulation in cardiovascular surgery, within 30 minutes to 18 hours after protamine sulphate administration. This rebound bleeding responds to further doses of protamine sulphate
- Excessive dosage may prolong the coagulation time because protamine sulphate in itself has anticoagulant activity
- Hypersensitivity reactions: risk factors include: **allergy to fish, infertility in men, medical history of vasectomy, previous treatment with protamine salts**

Storage

- Store below $25^{0}C$

References

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1: Injectable medicines guide Medusa downloaded 09/02/2026

Therapeutic classification

Antidote