

Protamine

Newborn use only

2021

Alert	<p>Stopping unfractionated heparin (UFH) infusion is adequate in most instances including overdose if no bleeding.</p> <p>Reversal of low molecular weight heparin (e.g. enoxaparin) by protamine is incomplete.</p> <p>Rapid IV injection of protamine can cause anaphylactic reaction and cardiovascular collapse. Facilities for resuscitation and treatment of shock should be available.</p> <p>Protamine acts as an anticoagulant at very high doses.</p> <p>Protamine has variable dose-response and a narrow therapeutic window.</p>										
Indication	Reverses anticoagulant effects of unfractionated and low molecular weight heparin.										
Action	Protamine forms a neutral 1:1 complex and strips heparin from antithrombin III. (1) It inhibits the inactivation of thrombin, factor XII and thrombin-fibrinogen interaction. It reduces prothrombin activator, prolongs prothrombin time, shortens thrombin time, and selectively precipitates fibrinogen. (2, 3)										
Drug type	Antidote to heparin										
Trade name	Protamine sulfate injection BP										
Presentation	Ampoule contains 50 mg/5 mL of protamine sulfate										
Dose	<p>1. Protamine sulfate dose for UFH reversal (4)</p> <table border="1" style="margin-left: 40px;"> <thead> <tr> <th>Time Since Last Heparin Dose</th> <th>Protamine dose per 100 units of heparin received in the last 2 hours</th> </tr> </thead> <tbody> <tr> <td><30 min</td> <td>1 mg</td> </tr> <tr> <td>30-60 min</td> <td>0.5-0.75 mg</td> </tr> <tr> <td>60-120 min</td> <td>0.375-0.5 mg</td> </tr> <tr> <td>>120 min</td> <td>0.25-0.375 mg</td> </tr> </tbody> </table> <p>2. Protamine sulfate dose for reversal of enoxaparin or low molecular weight heparin (LMWH) If within 3 to 4 hr of the administration of LMWH, dose of protamine is 1 mg per 1 mg of enoxaparin given. (5)</p>	Time Since Last Heparin Dose	Protamine dose per 100 units of heparin received in the last 2 hours	<30 min	1 mg	30-60 min	0.5-0.75 mg	60-120 min	0.375-0.5 mg	>120 min	0.25-0.375 mg
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Dose adjustment	<p>Therapeutic hypothermia – No information.</p> <p>ECMO – Refer to local ECMO protocol.</p> <p>Renal impairment – No information.</p> <p>Hepatic impairment – No information.</p>										
Maximum dose	50 mg at any one time (except for reversal of UFH following cardiopulmonary bypass) (4)										
Total cumulative dose											
Route	IV										
Preparation	<p>Usually not required.</p> <p>May be diluted if necessary with sodium chloride 0.9% (6)</p>										
Administration	Slow infusion over 10 minutes (7)										
Monitoring	<p>Blood pressure (for hypotension) and heart rate (bradycardia) (8)</p> <p>Bleeding</p> <p>Monitor activated partial thromboplastin time (APTT) or other appropriate blood clotting parameters</p>										
Contraindications	Hypersensitivity to protamine or to any excipients.										
Precautions	<p>Patients with known hypersensitivity reactions to protamine-containing insulin or previous protamine therapy may be at risk of hypersensitivity reactions</p> <p>Known hypersensitivity reactions to fish (8)</p>										
Drug interactions	None known (6, 8)										
Adverse reactions	Hypotension, bradycardia, pulmonary hypertension, non-cardiogenic pulmonary oedema, transient flushing, anaphylaxis. (7, 8)										
Compatibility	<p>Fluids: Glucose 5%2 , Plasma-Lyte 148 via Y-site , sodium chloride 0.9%</p> <p>Y-site: Some information is available. Consult the pharmacist, pharmacy department or medicines information service for advice.</p>										
Incompatibility	Fluids: No information.										

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	Drugs: Ampicillin, benzylpenicillin, cefazolin, cefotaxime, ceftazidime, ceftriaxone, dexamethasone, folic acid, furosemide, heparin sodium, hydrocortisone sodium succinate, indometacin, insulin (Actrapid), ketorolac, methylprednisolone sodium succinate, pentamidine, phenobarbital, sugammadex (7)
Stability	Diluted solutions should be used immediately and should not be stored as it contains no preservatives.
Storage	Store below 25°C. (8)
Excipients	Sodium chloride, hydrochloric acid, sodium hydroxide, water for injections. (8)
Special comments	The rapid disappearance of protamine from the circulation could contribute to "heparin rebound" after initial adequate reversal of heparin. Repeated doses may be required to neutralise
Evidence	Refer to full version.
Practice points	Refer to full version.
References	Refer to full version.

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