HEPARIN
Newborn use only

2021

Alert	High risk medication in A PINCH Medicines list under New South Wales Clinical Excellence Commission. Also known as unfractionated heparin (UFH). Not equivalent to low molecular weight heparin (LMWH). Use in consultation with haematologist for treatment of thrombosis. Many concentrations of heparin are available. Accidental overdose can occur when multiple concentrations are kept in the unit. In neonatal settings: recommend to store the following preparations only: heparinised saline 50 units/5 mL and heparin sodium injection ampoule 1000 units/1 mL. DBL Heparin sodium injection in ***vials*** **is not recommended** in neonates as it contains benzyl alcohol. However, DBL Heparin sodium injection in ***ampoules*** does **not** contain benzyl alcohol.
Indication	Primary or secondary antithrombotic prophylaxis. Maintenance of arterial and central venous catheter patency.
Action	Heparin binds to antithrombin III (ATIII), potentiating ATIII's activity by at least 1000-fold. ATIII predominantly inactivates factor Xa and thrombin (other proteases/clotting factors to lesser degree), which in turn inhibits conversion of fibrinogen to fibrin. Also possesses anti-complementary activity, inhibiting both the classic and alternative pathways.
Drug type	Anticoagulant
Trade name	Heparin Sodium Injection (Pfizer), DBL Heparin Sodium Injection BP
Presentation	**Antithrombotic prophylaxis** Pfizer Heparin Sodium Injection Ampoule: 5000 units/5 mL DBL Heparin Sodium Injection BP Ampoule: 1000 units/1 mL DBL Heparin Sodium BP Vials – ***Not to be used in neonates as it contains benzyl alcohol.*** **Maintenance of catheter patency** Heparinised saline injection: 50 units/5 mL Also available in premixed infusion bags.
Dose	**Antithrombotic prophylaxis**[1,2,3] Loading dose: 75 (50-100) units/kg over 30 minutes. Initial maintenance dose: 30 (20-40) units/kg/hour as continuous IV infusion. **Adjustment of Heparin dose** Anti-Xa is preferred to assess the effect of heparin and guide dosing (Table 1).

Table 1. Heparin dosing based on anti-Xa levels (therapeutic range 0.3-0.7 unit/mL)(modified from O'Meara et al)[3]

Anti-Xa level (unit/mL)	Dose adjustment
<0.2	Increase infusion by 5 units/kg/hour
0.2-0.29	Increase infusion by 5 units/kg/hour
0.3-0.7	No change
>0.7≤1.0	Decrease infusion by 2 unit/kg/hr
>1	Seek advice from haematologist
Measure anti-Xa levels 6 hours after commencing heparin and then 6 hourly until two consequent values are within therapeutic range. After every heparin adjustment or a blood product administration, the anti-Xa level should be checked again in 6 hours and discuss with haematologist on frequency of further monitoring. PT/INR, PTT, fibrinogen, platelet count, and ATIII levels are measured daily or as advised by the haematologist.	

If anti-Xa levels are not available, APTT can be used to guide heparin dosing (Table 2).

Table 2. Heparin dosing based on APTT levels (therapeutic range 60-85 seconds).[1,4]

APTT (seconds)	Bolus (units/kg)	Hold (min)	Rate change (%)	Time until repeat APTT
<50	50	0	+10	6 h
50-59	0	0	+10	6 h

	<table><tr><td>60-85</td><td>0</td><td>0</td><td>No change</td><td>Next day or as per haematologist advice</td></tr><tr><td>86-95</td><td>0</td><td>0</td><td>-10</td><td>6 h</td></tr><tr><td>96-120</td><td>0</td><td>30</td><td>-10</td><td>6 h</td></tr><tr><td>>120</td><td>0</td><td>60</td><td>-10</td><td>6 h</td></tr><tr><td colspan="5">Obtain blood for APTT 6 hours after administration of loading dose and 6 hours after every change. When APTT values are therapeutic, blood count and APTT daily or as per the advice of haematologist.</td></tr><tr><td colspan="5"></td></tr></table> APTT: Activated partial thromboplastin time **Vascular catheter patency.**[1,2,5-7,18-21] a) Maintenance of patency of peripheral arterial catheters: 0.5 units/mL of IV fluid. b) Maintenance of patency of central vascular catheters: 0.5 units/kg/hour
Dose adjustment	Therapeutic hypothermia – No information. ECMO – Refer to local ECMO protocols for anticoagulation. Renal impairment – Dose adjustment may be required in severe renal impairment. Discuss with haematologist. Hepatic impairment – No dose adjustment is required.[8]
Maximum dose	
Total cumulative dose	
Route	IV
Preparation	**Antithrombotic prophylaxis** The concentrations varying from 100 to 500 units/mL can be used for loading doses and concentrations of 10 to 500 units/mL can be used for continuous IV infusion. **Vascular catheter patency** To prepare 0.5 unit/mL solution, withdraw 5 mL 0.9% sodium chloride from a 100 mL bag, then add 5 mL of 50 units/5 mL (50 units) to make 50 units in 100 mL bag.
Administration	**Systemic antithrombotic therapy** Administer IV loading dose over 30 minutes. Administer maintenance dose as a continuous IV infusion and titrate dose by anti-Xa (or APTT if anti-Xa is not available). **Vascular catheter patency** Arterial lines: Continuous IV infusion of 0.5 units/mL at 0.5-1 mL/hour.
Monitoring	**Antithrombotic prophylaxis** Six hours after initiating therapy, measure anti-Xa (or APTT if anti-Xa is not available), then adjust dose to achieve anti-Xa level of 0.3 to 0.7 unit/mL (equivalent to APTT of 60 to 85 seconds) – Refer to tables 1 and 2 in the dosing section. Platelet count before the commencement and then weekly. Assess for signs of bleeding and thrombosis. **Vascular catheter patency** Standard observations for intravascular catheters.
Contraindications	Known hypersensitivity to heparin, uncontrolled bleeding. Intraventricular haemorrhage, gastrointestinal haemorrhage, thrombocytopenia < 50 x 10^9/L, severe hypertension, Eye, brain or spinal cord surgery- Surgeons to give clearance regarding when to start heparin.[7]
Precautions	Bleeding disorders – Discuss with haematologist. Store heparinised saline ampoules separately from other heparin products and sodium chloride 0.9% ampoules to reduce the risk of selection errors
Drug interactions	Paracetamol, non-steroid anti-inflammatory drugs, alprostadil, thrombolytic agents, vitamin A may increase the risk of bleeding.
Adverse reactions	Haemorrhage and haematoma formation. Heparin-induced thrombocytopenia (HIT). Osteoporosis. Cholestatic liver reaction and elevation of transaminases.

	Hyperaldosteronism can occur after prolonged administration.[8] Treatment of Heparin-Induced Bleeding: (1) cease heparin and (2) if immediate reversal is required, administer protamine sulfate. The required dose of protamine sulfate is based on the amount of UFH received in the previous 2 hours as follows:[1] **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 Maximum dose of 50 mg. Infusion rate of a 10 mg/mL solution should not exceed 5 mg/min. Hypersensitivity reactions to protamine sulfate may occur in patients with known hypersensitivity reactions to fish or those previously exposed to protamine therapy or protamine-containing insulin. For more information, refer to Protamine formulary.
Compatibility	Fluids: Glucose 5%, Sodium chloride 0.9%.[9] Y-site: Aciclovir, ampicillin, atropine, aztreonam, caffeine citrate, calcium chloride, calcium gluconate, cefazolin, cefotaxime, clindamycin, dexamethasone, dexmedetomidine, digoxin, dopamine, ephedrine sulfate, fentanyl, fluconazole, folic acid (sodium salt), furosemide, hydrocortisone sodium succinate, levetiracetam, linezolid, magnesium sulfate, meropenem, metronidazole, midazolam hydrochloride, morphine sulfate, naloxone hydrochloride, noradrenaline, pancuronium bromide, paracetamol, piperacillin/tazobactam, phenobarbital sodium, pipercillin-tazobactam, potassium chloride, rocuronium bromide, suxamethonium, vecuronium, zidovudine.
Incompatibility	Fluids: Fat emulsion Y-site: Benzylpenicillin, ciprofloxacin, cisatracurium, dobutamine, erythromycin, gentamicin, ketamine, tobramycin
Stability	
Storage	Ampoule and vial: Store below 25°C. Bag: Store below 30°C.
Excipients	Pfizer ampoule: Water for injection DBL ampoule: Hydrochloric acid, sodium hydroxide. DBL vial: Benzyl alcohol. Do not give products that contain benzyl alcohol to neonates. Heparinised saline: Hydrochloric acid, sodium chloride, sodium hydroxide.
Special comments	Protamine sulfate is the reversal agent to correct the anticoagulant effect of heparin.
Evidence	Refer to full version.
Practice points	Refer to full version.
References	Refer to full version.

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