

# HEPARIN SODIUM

<b>Indication</b>	<ul style="list-style-type: none"> <li>• Anticoagulant treatment for thrombosis<sup>1</sup> (duration dependent on indication<sup>2</sup>) <ul style="list-style-type: none"> <li>○ Use in consultation with haematologist</li> </ul> </li> </ul>							
<b>INTRAVENOUS</b>	<b>Presentation</b>	<ul style="list-style-type: none"> <li>• Ampoule: 1,000 unit in 1 mL   5,000 unit in 5 mL</li> </ul>						
	<b>Loading dosage<sup>2</sup></b> (if required)	<table border="1"> <thead> <tr> <th>*Current gest age (weeks)</th> <th>Dose</th> </tr> </thead> <tbody> <tr> <td>Less than 35+0</td> <td>50 unit/kg</td> </tr> <tr> <td>35+0 or more</td> <td>75–100 unit/kg</td> </tr> </tbody> </table> <p><i>*Current gestational age is the same as post menstrual age (PMA)</i></p>	*Current gest age (weeks)	Dose	Less than 35+0	50 unit/kg	35+0 or more	75–100 unit/kg
	*Current gest age (weeks)	Dose						
	Less than 35+0	50 unit/kg						
	35+0 or more	75–100 unit/kg						
<b>Maintenance dosage<sup>2</sup></b>	<ul style="list-style-type: none"> <li>• Start at 28 unit/kg/hour, then adjust as per Anti Xa levels <ul style="list-style-type: none"> <li>○ Refer to therapeutic monitoring below</li> </ul> </li> <li>• Maximum dose 40 unit/kg/hour<sup>2</sup></li> </ul>							
<b>Preparation</b>	<ul style="list-style-type: none"> <li>• Select and check appropriate ampoule concentration</li> <li>• Draw up 5,000 unit/kg and make up to 50 mL total volume with 5% glucose or 0.9% sodium chloride <ul style="list-style-type: none"> <li>○ <i>Concentration now equal to 100 unit/kg/mL</i></li> </ul> </li> <li>• Invert syringe at least 6 times to ensure adequate mixing<sup>3</sup></li> <li>• Prime the infusion line with 100 unit/kg/mL solution</li> <li>• IV infusion via medication safety pump</li> </ul>							
<b>Administration</b>	<ul style="list-style-type: none"> <li>○ Loading dose over: 10 minutes<sup>3</sup></li> <li>○ Maintenance dose: 100 unit/kg/mL solution infused at 1 mL/hour delivers 100 unit/kg/hour</li> </ul>							
<b>High risk medication</b>	<ul style="list-style-type: none"> <li>• Errors may result in serious patient harm</li> <li>• Check strength of product carefully as multiple concentrations exist. Incorrect product selection can result in overdose and fatal haemorrhage</li> <li>• Prescribe in unit/kg/hour (with mL/hour in brackets)<sup>2</sup></li> <li>• Dedicated line required as frequent dose adjustment needed for optimal response<sup>2</sup></li> <li>• Consult with haematologist for all dosage commencement, titration and monitoring</li> </ul>							
<b>Special considerations</b>	<ul style="list-style-type: none"> <li>• Cautions <ul style="list-style-type: none"> <li>○ If renal impairment, dose adjustment may be required<sup>4</sup></li> <li>○ Avoid IM injections and arterial stabs due to risk of haematoma formation<sup>5</sup> (if clinically necessary, apply adequate pressure post procedure)</li> <li>○ Individual patient characteristics, (e.g. bleeding risk), may require variation to monograph recommendations<sup>2</sup></li> <li>○ Check position of UVC prior to using for heparin therapy infusion (at SMO discretion)</li> </ul> </li> <li>• For patency of peripheral and umbilical arterial lines: suggested concentration 1 unit/mL</li> </ul>							
<b>Monitoring</b>	<ul style="list-style-type: none"> <li>• Prior to commencement of infusion<sup>2</sup> <ul style="list-style-type: none"> <li>○ Baseline weight, FBC, ELFT, coagulation profile, APTT, PT, fibrinogen</li> <li>○ Consider head ultrasound to exclude pre-existing intracranial bleeding (may influence choice of agent, dose and frequency of monitoring or be a contraindication)</li> </ul> </li> <li>• During infusion <ul style="list-style-type: none"> <li>○ Infusion site</li> <li>○ Signs of bleeding (e.g. invasive device sites/wounds)</li> <li>○ Vital signs (e.g. for tachycardia, hypotension, reduced capillary refill, altered alertness)</li> <li>○ Platelet count every 2–3 days<sup>6</sup> and continue post treatment if reduced</li> </ul> </li> </ul>							
<b>Compatibility</b>	<ul style="list-style-type: none"> <li>• Fluids <ul style="list-style-type: none"> <li>○ 0.9% sodium chloride<sup>3</sup>, 5% glucose<sup>3</sup></li> </ul> </li> <li>• Drugs <ul style="list-style-type: none"> <li>○ Dedicated IV line required—high risk medication<sup>2</sup></li> </ul> </li> </ul>							
<b>Incompatibility</b>	<ul style="list-style-type: none"> <li>• Dedicated IV line required—high risk medication<sup>2</sup></li> </ul>							
<b>Interactions</b>	<ul style="list-style-type: none"> <li>• Do not use concurrently with other anticoagulants as may increase risk of bleeding</li> </ul>							



<b>Stability</b>	<ul style="list-style-type: none"> <li>• Ampoule <ul style="list-style-type: none"> <li>○ Store below 25 °C<sup>7</sup></li> </ul> </li> <li>• Infusion <ul style="list-style-type: none"> <li>○ Stable for 24 hours at room temperature below 25 °C</li> <li>○ Change infusion every 24 hours<sup>2</sup></li> </ul> </li> </ul>
<b>Side effects</b>	<ul style="list-style-type: none"> <li>• Blood pathology: heparin induced thrombocytopenia (HIT)<sup>4,5</sup> (extremely uncommon) <ul style="list-style-type: none"> <li>○ If platelets decrease after 5–14 days of treatment<sup>2</sup>, consider haematologist consult</li> </ul> </li> <li>• Blood pathology: heparin resistance<sup>5</sup> <ul style="list-style-type: none"> <li>○ Demonstrated by a failure to reach therapeutic anticoagulation (using APTT or anti-Xa monitoring) despite escalating heparin doses</li> <li>○ Anti-thrombin III deficiency<sup>5</sup> is a common cause; if suspected consult haematologist</li> </ul> </li> <li>• Circulatory: bleeding<sup>4</sup> <ul style="list-style-type: none"> <li>○ If bleeding occurs, cease heparin infusion and consult haematologist urgently</li> <li>○ If reversal of heparin is advised, administer protamine sulphate (antidote)</li> </ul> </li> <li>• Skeletal: osteoporosis rare and associated with long term use<sup>8</sup></li> </ul>
<b>Actions</b>	<ul style="list-style-type: none"> <li>• Also known as unfractionated heparin (UFH)<sup>3</sup></li> <li>• Member of the glycosaminoglycan family<sup>5</sup></li> <li>• Prepared from porcine mucosa<sup>5</sup></li> <li>• Inactivates thrombin (factor IIa) and factor Xa by binding to antithrombin III <ul style="list-style-type: none"> <li>○ Low levels of antithrombin III in preterm neonates accounts for dose variations between neonates and older infants<sup>9</sup></li> </ul> </li> <li>• Clearance is greater in neonates compared to children and adults<sup>9,10</sup> (half-life 1–3 hours)</li> </ul>
<b>Antidote</b>	<ul style="list-style-type: none"> <li>• Protamine sulfate for rapid or immediate reversal. Seek haematologist advice<sup>11</sup></li> </ul>
<b>Abbreviations</b>	<p>*Current gestational age is the same as post menstrual age (PMA)  APTT: activated partial thromboplastin time, ELFT: electrolyte and liver function test, FBC: full blood count, HIT: heparin induced thrombocytopenia, IM: intramuscular injection, IV: intravenous, PAL: peripheral arterial line, PT: prothrombin time, SMO: most senior medical officer, UAC: umbilical arterial catheter, UFH: unfractionated heparin, UVC: umbilical venous catheter</p>
<b>Keywords</b>	Heparin, thrombosis, thrombus, UFH, unfractionated heparin, anticoagulant, anticoagulation, anti-Xa,

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**Therapeutic monitoring<sup>8</sup>**

Therapeutic monitoring			
<b>General principles</b>	<ul style="list-style-type: none"> <li>• If the anti-Xa does not reach target range within 24 hours seek haematologist advice<sup>2</sup></li> <li>• Initial anti-Xa level               <ul style="list-style-type: none"> <li>○ If loading dose: 4 hours post initiation<sup>2</sup></li> <li>○ If NO loading dose: 6 hours post initiation<sup>2,6</sup></li> </ul> </li> <li>• Repeat anti-Xa level               <ul style="list-style-type: none"> <li>○ 4–6 hours after any dose adjustment<sup>2</sup></li> <li>○ Daily until discontinuation of heparin therapy<sup>2</sup></li> </ul> </li> <li>• Fill coagulation tubes exactly to the specified mark to avoid erroneous results<sup>2</sup></li> <li>• Specify on pathology request that patient on heparin infusion</li> </ul>		
Anti Xa level (unit/mL)	Action required	Rate change (unit/kg/hr)	Repeat Anti Xa test
<b>Less than 0.1</b>	Increase infusion rate *Consider bolus dose	Increase by 4 unit/kg/hour	4 to 6 hours
<b>0.1–0.29</b>	Increase infusion rate	Increase by 2 unit/kg/hour	4 to 6 hours
<b>0.3–0.7</b>	<b>Target range—continue current rate</b>		<b>Daily (every 24 hours)</b>
<b>0.71–1</b>	Reduce infusion rate	Decrease by 2 unit/kg/hour	4 to 6 hours
<b>1.01–1.2</b>	Pause infusion for 30 minutes then restart at reduced rate	Decrease by 4 unit/kg/hour	4 to 6 hours
<b>1.21–2</b>	Pause infusion for 60 minutes then restart at reduced rate	Decrease by 6 unit/kg/hour	4 to 6 hours
<b>More than 2</b>	<ul style="list-style-type: none"> <li>• Stop infusion</li> <li>• Recheck syringe dilution</li> <li>• Exclude contamination</li> <li>• Repeat level with a sample taken from a non-heparinised line or peripheral site</li> <li>• Discuss urgently with QCH haematology</li> <li>• Do not restart infusion until anti-Xa less than 1 unit/mL</li> <li>• When anti-Xa less than 1 unit/mL, restart infusion at reduced rate (decrease by 6 unit/kg/hr)</li> </ul>		
*A bolus dose of 50 unit/kg (max 5,000 unit) may be considered by haematologist			

**EXAMPLE Calculations**

<b>Loading dose (100 unit/kg) for 3.5 kg baby</b>	<b>Worked example</b>
<b>Step 1. Calculate dose required for weight</b> $\text{dose (unit)} \times \text{baby weight (kg)} = \text{dose required (unit)}$	$100 \text{ (unit)} \times 3.5 \text{ (kg)} = 350 \text{ unit}$
<b>Step 2. Prepare 100 unit/kg/mL concentration solution</b> $\frac{5000 \text{ (unit)} \times \text{baby weight (kg)}}{50 \text{ mL}} = \text{unit in 1 mL}$	$\frac{5000 \text{ unit} \times 3.5 \text{ (kg)}}{50 \text{ mL}} = 350 \text{ unit/mL}$
<b>Step 3. Calculate loading dose volume</b> $\frac{\text{dose required (unit)}}{\text{solution strength (unit/mL)}} = \text{dose volume (mL)}$	$\frac{350 \text{ unit}}{350 \text{ unit/mL}} = 1 \text{ mL}$
<b>Maintenance dose (28 unit/kg/hour) for 3.5 kg baby</b>	<b>Worked example</b>
<b>Step 1. Prepare 100 unit/kg/mL concentration solution</b> $\frac{5000 \text{ (unit)} \times \text{baby weight (kg)}}{50 \text{ mL}} = \text{unit in 1 mL}$	$\frac{5000 \text{ unit} \times 3.5 \text{ (kg)}}{50 \text{ mL}} = 350 \text{ unit/mL}$
<b>Step 2. Calculate rate of maintenance infusion</b> $\frac{\text{required rate (unit/kg/hour)}}{\text{solution concentration (unit/kg/mL)}} = \text{mL/hour}$	$\frac{28 \text{ unit/kg/hour}}{100 \text{ unit/kg/mL}} = 0.28 \text{ mL/hour}$

## References

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## Document history

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