DRUG GUIDELINE

HEPARIN

SCOPE (Area): FOR USE IN: All acute wards
EXCLUSIONS: Paediatrics (seek Paediatrician advice)
SCOPE (Staff): Medical, Nursing and Pharmacy

Note: Heparin is also known as heparin sodium and unfractionated heparin.

BRAND NAMES
Heparin Sodium Injection (Hospira).
Heparin Sodium Injection (Pfizer).
Heparin pre-mixed bags (Baxter).

PHARMACOLOGY AND PHARMACOKINETICS
Unfractionated heparin (UFH) is a mixture of sulfated glycosaminoglycans, some of which possess anticoagulant properties. It is rapidly removed from the body with a half-life of 30 to 60 minutes, which increases significantly with increasing dosage. Due to this short half-life it must be given by continuous intravenous infusion with monitoring of APTT and appropriate dosage adjustments for conditions requiring full anticoagulation. Its short half-life and ability to be monitored and adjusted gives it an advantage over low molecular weight heparin (LMWH) in particular patients.

INDICATIONS
- For conditions for which full anticoagulation is required and the ability to rapidly reverse, withdraw or closely monitor the anticoagulation is desirable (via intravenous infusion).
  - Conditions include (but are not limited to) deep vein thrombosis, pulmonary embolus, mechanical heart valves (whilst waiting for long term anticoagulation to become therapeutic), acute coronary syndromes etc.
  - Patients for which rapid withdrawal, reversal or close monitoring may be useful include (but are not limited to) the morbidly obese, those with severe renal impairment, or those in whom bleeding is more likely but anticoagulation must be maintained (e.g. perioperatively).
- For the prevention of venous thromboembolism (via subcutaneous injection).
- For maintaining patency of perm catheters in haemodialysis patients (see CPG0065).
- For anticoagulation of extracorporeal circuits during dialysis treatment (ICU and Dialysis only – not covered in this guideline).

CONTRAINDICATIONS
This list is not exhaustive. Some patients may still require anticoagulation even with some of the conditions below. The risks and benefits of therapy must always be weighed up.
- History of Heparin-induced thrombocytopenia (HIT) - consult with Intensive Care or Haematology – may require alternative anticoagulant.
- Severe thrombocytopenia (platelets <50 x 10^9/L).
- Active bleeding or disease states with an increased risk of bleeding.
- History of haemorrhagic stroke.
- Recent large thromboembolic stroke.
- Severe hepatic disease or impairment (with elevated INR).
- Subacute or acute bacterial endocarditis.

PRECAUTIONS
- Thrombocytopenia – use with care (see ‘Heparin-induced thrombocytopenia’ below).
- Severe uncontrolled hypertension (BP>200/120) – use with great care.
- Intrathecal or epidural analgesia or anaesthesia, or lumbar puncture – seek specialist advice, at risk of epidural haematoma which can cause paralysis.

PREGNANCY AND BREASTFEEDING
Unfractionated heparin is considered safe to use during pregnancy and breastfeeding. However, the use of anticoagulants and thrombolytic agents during pregnancy may be associated with an increased risk of placental haemorrhage and subsequent pre-term birth or fetal loss. Prolonged use or high doses of heparin has been associated with maternal osteopenia. Consult with a haematologist for further advice regarding use during pregnancy.

Seek specialist advice before prescribing, information may update regularly.

DRUG INTERACTIONS
- Administration with other drugs that affect the clotting process may increase the risk of bleeding (Note: combined use with anti-platelets and ‘crossover’ with warfarin is, however, often indicated). See below for LMWH.
- Heparin can cause hyperkalemia, combination with other drugs that increase potassium can increase this risk, monitor potassium levels.

DOSAGE AND ADMINISTRATION

<table>
<thead>
<tr>
<th>Important Safety Information regarding Heparin</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Heparin is a high risk medication. Intravenous infusion must only be administered from premixed bags</td>
</tr>
<tr>
<td>- Heparin 25,000 unit in 5 mL ampoules will ONLY be kept on imprest in dialysis and theatre. The ampoules must be kept in a clearly labelled container and separated from similar looking ampoules, including other strengths of heparin. Concentrated ampoules will NOT be supplied to other areas of the hospital. Theatre can only store Heparin 25,000 unit in 5 ml ampoules in the “cell saver kit”.</td>
</tr>
<tr>
<td>- Intravenous infusion should only be prescribed on the Heparin Intravenous Infusion Chart (MR/700.3). The “how to” guide for medical and nursing staff is available on the second page</td>
</tr>
<tr>
<td>- Unsafe abbreviations must be avoided- always prescribe in full as “units”</td>
</tr>
<tr>
<td>- Intravenous administration of Heparin requires an Independent Double Check. See CPP 0287 Medication Administration</td>
</tr>
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</table>
Before commencing treatment:
- Check INR, APTT, full blood count, liver function tests.
  - Seek specialist advice (ICU/Haematology) if thrombocytopenia or impaired coagulation or impaired liver function present.
- Check for contraindications.
  - Ask the patient SPECIFICALLY whether they have had an adverse reaction to Heparins, including Heparin-induced thrombocytopenia, and check available records for such reactions. Record answers on the Heparin Intravenous Infusion Chart (MR/700.3) – if Yes to HIT provide detailed information in the medical record and seek Specialist advice.
- Confirm that LMWHs have not been administered in the previous 12 hours - if so, seek senior medical advice.

For PROPHYLAXIS of venous thromboembolism (see Thromboprophylaxis CPG0022):

Heparin 5,000 units in 0.2 mL subcut, two to three times a day.

For conditions requiring FULL ANTICOAGULATION administer via continuous intravenous infusion – see next page.

Administration of heparin via intravenous infusion:

1. Weigh patient and record on ‘Heparin Intravenous Infusion Chart’ (MR/700.3). For obese patients actual body weight should be used to calculate loading and initial rate.

2. Does the patient require a loading dose?
   - Loading doses enable more rapid achievement of therapeutic anticoagulation but may be omitted in stroke patients, patients ceasing warfarin therapy and post-operative patients.

3. Calculate loading dose (if required) and initial rate of infusion according to the following tables:

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<tr>
<th>Weight (kg)</th>
<th>DVT, PE, other serious thrombotic conditions</th>
<th>In place of warfarin maintenance, acute coronary syndromes</th>
<th>STEMI treated with tenecteplase*</th>
<th>PE post alteplase</th>
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<tr>
<td>40-50</td>
<td>3,500 units</td>
<td>2,500 units</td>
<td>Less than 67 kg 4,000 units</td>
<td>No bolus</td>
</tr>
<tr>
<td>51-60</td>
<td>4,500 units</td>
<td>3,500 units</td>
<td></td>
<td></td>
</tr>
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<td></td>
</tr>
<tr>
<td>71-80</td>
<td>6,000 units</td>
<td>4,500 units</td>
<td></td>
<td></td>
</tr>
<tr>
<td>81-90</td>
<td>7,000 units</td>
<td>5,000 units</td>
<td>67 kg or greater 5,000 units</td>
<td></td>
</tr>
<tr>
<td>&gt;90</td>
<td>7,500 units</td>
<td>5,000 units</td>
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* Heparin dosing varies with other thrombolytics

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**INITIAL RATE OF INFUSION**

Use heparin 25,000 units in 250 mL pre-mixed bag (100 units/mL)

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<th>STEMI treated with tenecteplase*</th>
<th>PE post alteplase</th>
</tr>
</thead>
<tbody>
<tr>
<td>40-50kg</td>
<td>800 units/hour</td>
<td>550 units/hour</td>
<td>5.5 mL/hour</td>
<td>Less than 67 kg</td>
</tr>
<tr>
<td>51-60kg</td>
<td>1,000 units/hour</td>
<td>650 units/hour</td>
<td>6.5 mL/hour</td>
<td>800 units/hour (8 mL/hr)</td>
</tr>
<tr>
<td>61-70kg</td>
<td>1,200 units/hour</td>
<td>800 units/hour</td>
<td>8 mL/hour</td>
<td>1,000 units/hour (10 mL/hr)</td>
</tr>
<tr>
<td>71-80kg</td>
<td>1,350 units/hour</td>
<td>900 units/hour</td>
<td>9 mL/hour</td>
<td>67 kg or greater</td>
</tr>
<tr>
<td>81-90kg</td>
<td>1,550 units/hour</td>
<td>1,000 units/hour</td>
<td>10 mL/hour</td>
<td></td>
</tr>
<tr>
<td>&gt;90kg</td>
<td>1,700 units/hour</td>
<td>1,000 units/hour</td>
<td>10 mL/hour</td>
<td></td>
</tr>
</tbody>
</table>

*Heparin dosing varies with other thrombolitics

3. Prescribe loading dose (if required) and initial infusion rate on ‘Heparin Intravenous Infusion Chart’ (MR/700.3).
   - Be sure to write ‘units’ in full.
   - Record the indication for anticoagulation and target APTT (60 to 80 seconds for most indications) in the relevant section at the top of the chart.
   - Record the baseline APTT and baseline platelet count in the section marked ‘Heparin monitoring’.
   - Record when the next APTT is due (6 hours from infusion commencement) in the ‘Heparin monitoring’ section. Ensure the person responsible for sampling blood for the next APTT is aware of the infusion and monitoring requirements.
   - Ensure APTT orders are marked ‘Urgent – on Heparin’.

4. After each APTT measurement:
   - Medical staff must order the necessary boluses, pauses to infusion and/or adjustments to rate (according to the table below) in the ‘Heparin monitoring’ and ‘Heparin ordering’ sections of the Heparin Intravenous Infusion Chart (MR/700.3).
   - Medical staff must immediately inform nursing staff of the outcome (e.g. increase or decrease rate, no change etc).
   - Medical staff must record the time of next APTT according to the table below, in the ‘Heparin monitoring’ section. Inform the person responsible for taking and interpreting the measurement that this is to occur.
NOMOGRAM FOR HEPARIN INFUSION DOSE ADJUSTMENT

<table>
<thead>
<tr>
<th>APTT (seconds)</th>
<th>Bolus (units)</th>
<th>Pause infusion</th>
<th>Dose change Units/ hour</th>
<th>Dose change (mL/hr of 25,000 units/250mL)</th>
<th>Recheck APTT</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 50</td>
<td>5,000 units*</td>
<td>0</td>
<td>↑ 150 units/hour</td>
<td>↑ 1.5 mL/hour</td>
<td>6 hours</td>
</tr>
<tr>
<td>50-59</td>
<td>0</td>
<td>0</td>
<td>↑ 100 units/hour</td>
<td>↑ 1 mL/hour</td>
<td>6 hours</td>
</tr>
<tr>
<td>60-80*</td>
<td>0</td>
<td>0</td>
<td>0 (Target)</td>
<td>0 (Target)</td>
<td>Next morning</td>
</tr>
<tr>
<td>81-89</td>
<td>0</td>
<td>0</td>
<td>↓ 50 units/hour</td>
<td>↓ 0.5 mL/hour</td>
<td>Next morning</td>
</tr>
<tr>
<td>90-109</td>
<td>0</td>
<td>30 minutes</td>
<td>↓ 100 units/hour</td>
<td>↓ 1 mL/hour</td>
<td>6 hours</td>
</tr>
<tr>
<td>110-130</td>
<td>0</td>
<td>30 minutes</td>
<td>↓ 150 units/hour</td>
<td>↓ 1.5 mL/hour</td>
<td>6 hours</td>
</tr>
<tr>
<td>&gt;130 (Order repeat urgent APTT)</td>
<td>0</td>
<td>120 minutes or until APTT &lt;120</td>
<td>↓ 200 units/hour</td>
<td>↓ 2 mL/hour</td>
<td>Immediately, then in 6 hours</td>
</tr>
</tbody>
</table>

*Consider omitting in stroke patients, patients ceasing warfarin therapy and post-operative patients.

# In myocardial infarction patients who have undergone thrombolysis a lower target range of 50-70 is appropriate. Seek specialist advice.

Heparin reversal
The anticoagulant effects of heparin can be reversed for patients with, or at risk of severe haemorrhage with the administration of protamine. For minor bleeding withdrawal of heparin is usually sufficient. See the Protamine Guideline (DRG0030) for further information.

Switching from LMWH to heparin and vice versa

<table>
<thead>
<tr>
<th>Changing from</th>
<th>Changing to</th>
<th>Treatment</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heparin IV</td>
<td>Dalteparin or enoxaparin subcutaneous</td>
<td>Heparin IV</td>
<td>Dalteparin or enoxaparin subcutaneous</td>
</tr>
<tr>
<td>Dalteparin or enoxaparin subcutaneous</td>
<td>Start when heparin infusion is ceased¹</td>
<td>Start when next dose is due (minimum 10 hours) without bolus</td>
<td></td>
</tr>
<tr>
<td>Heparin Subcutaneous</td>
<td>As soon as diagnosis made</td>
<td>As soon as diagnosis is made</td>
<td></td>
</tr>
<tr>
<td>Dalteparin or enoxaparin subcutaneous</td>
<td>As soon as diagnosis is made</td>
<td>Seek Consultant advice²</td>
<td></td>
</tr>
</tbody>
</table>

¹ Dose adjustment may be needed if APTT is above therapeutic range. Seek consultant advice

Heparin Infusion Cessation
When a heparin infusion in ceased this must be verbally handed over to nursing staff, and where possible documented in the progress notes. On MR/700.3 Heparin Intravenous Infusion the remaining lines should be crossed out and endorsed “ceased” with the doctor’s signature, time and date.

General Administration Information
- Infusion preparation:
  Pre-mixed bag of heparin 25,000 units in 250mL sodium chloride 0.9%. No other drugs are to be added to this bag.
Infusion stable for 24 hours once infusion commenced – change IV bag at 24 hour mark if bag is not finished.

- **Infusion pump:** Alaris PC with LVP and Guardrails
- **Routes of administration:**
  - IV injection: Yes, via Alaris PC with LVP and Guardrails (loading dose)
  - IV intermittent infusion: No
  - IV continuous infusion: Yes
  - IM injection: No
  - Subcut injection: Yes (for prophylaxis of venous thromboembolism)
- **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)
For ALL patients:
- Baseline INR, APTT, full blood count, liver function tests.
- Platelets should be monitored every two or three days between days 4 and 14 of therapy (sooner if the patient has been recently exposed to heparins), and weekly thereafter or until heparin is ceased to monitor for Heparin-induced thrombocytopenia (see below).
- Electrolytes, urea and creatinine should be monitored routinely.

For patients receiving an intravenous infusion:
- APTT requires regular monitoring to enable appropriate adjustment of dose. Specimens sent to the laboratory must be marked ‘URGENT – ON HEPARIN’.
- Heparin requirements may be large in the acute stage of a large thromboembolus. These requirements may change suddenly during treatment.

NURSING PRACTICE POINTS
- The initial heparin infusion is to commence immediately after the loading dose is given. If other bolus doses are required due to a low APTT, they are to be given at the same time the infusion rate is adjusted.
- Use the heparin 5,000 units in 5mL ampoule for the IV loading bolus dose and the 25,000 units in 250mL pre-mixed bag for the maintenance IV infusion. Heparin 5000 units in 0.2mL is for subcut administration.
- To bolus during a continuous heparin infusion press “Channel Select” on the LVP. Press the “BOLUS” button on the Alaris PC. A default dose of 5000 units (the standard and maximum dose) will appear. On the rare occasion a lesser dose is ordered, change the dose by pushing the dose button and typing in the dose. Press “Rapid Bolus” and the pump will automatically select 999ml/hr (time of 1-3 minutes depending on the dose). Press the start button and the pump will deliver the bolus over the selected time and then immediately revert back to the continuous infusion rate that was running previously.
- An unexpectedly high APTT may be due to blood being drawn from the limb into which the heparin infusion is running. Always draw blood from another limb.
- When ordering APTT tests for a patient on a heparin ensure the form is marked ‘URGENT – ON HEPARIN’.
- The heparin infusion line should be clearly labeled. Care should be taken not to confuse other lines when disconnecting and reconnecting a patient.
- Heparin has a very short half life. Interruptions to therapy must be avoided to prevent a loss of anticoagulant effect.
The initial bolus and rate of infusion and any subsequent changes must be recorded and double signed in the ‘Heparin administration’ section of the Heparin Intravenous Infusion Chart (MR/700.3).

ADVERSE EFFECTS
Bleeding, bruising, hyperkalaemia, thrombocytopenia (transient or severe HIT – see below), transient elevation of liver aminotransferases, skin necrosis (usually at injection site), osteoporosis and alopecia with long-term use, allergic reactions including urticaria and anaphylaxis.

Heparin-induced thrombocytopenia (HIT)
Heparin-induced thrombocytopenia is a rare complication of heparin therapy (including LMWH). It is an immune-mediated process and can be pro-thrombotic and life-threatening. Regular monitoring of the platelet count is mandatory during treatment with heparins or LMWH.

It usually occurs between four and 14 days following the commencement of heparin or LMWH therapy. It may occur later in some patients, or sooner in those with exposure to heparins in the previous three months, even in low doses. Delayed onset HIT has also occurred several weeks after stopping heparin.

A minor transient decrease in the platelet count is not uncommon soon after commencing heparins. Provided the platelet count does not decrease to less than half the baseline level OR below 100 x10^9/L heparin therapy can be continued with regular monitoring.

Should the platelet count decrease to either less than half the baseline level OR to below 100x10^9/L a diagnosis of Heparin-induced thrombocytopenia MUST be considered. Any indication of thrombosis in a patient on heparin must also raise the suspicion of HIT. In either of these situations immediately;
- cease heparin, and
- obtain specialist advice from a haematologist or ICU consultant.

Further testing and an alternative anticoagulant are likely to be required. For alternative treatment options please consult a haematologist or refer to the Therapeutic Guidelines: http://online.tg.org.au/ip/desktop/index.htm

If HIT is known or suspected the patient’s case should be reported to the Therapeutic Goods Administration (TGA) via https://www.tga.gov.au/reporting-problems-0#medicine

DRUG PRESENTATIONS, LOCATION AND STORAGE
Heparin sodium 25,000 units in 250 mL IV bags: 3S, 4N, 4S, ED, ICU, CVS, Radiology, Theatre
Heparin sodium 5,000 units in 5 mL: 3N, 3S, 4N, 4S, ED, ICU, Radiology, Theatre
Heparin sodium 5,000 units in 0.2 mL; various
Heparin sodium 1,000 units in 1 mL; various
Heparin sodium 5,000 units in 1 mL; various
Heparin sodium 25,000 units in 5 mL vials (for haemodialysis only – see CPG0065 and cell saver kit in theatre)
Imprest locations: pharmacy and various ward areas
Store below 25°C.
RELATED DOCUMENTS
DRG0030  Protamine
CPG0022 Thromboprophylaxis
CPG0065 Haemodialysis Perm Catheter Procedures
MR/700.3 Heparin Intravenous Infusion Chart
CPP0549 High Risk Medications
CPP0287 Medication Administration

REFERENCES
- The Northern Hospital Drug and Therapeutics Committee (rev 2009) *Heparin Pharmacy Drug Protocol*, The Northern Hospital, via personal communication.
- Dorevitch Pathology – personal communication