INTRAVENOUS UNFRACTIONATED HEPARIN RECOMMENDED STANDARD

FOR INCORPORATION INTO LOCAL GUIDELINES/PROTOCOLS

Introduction

This standard applies to inpatients aged over 16 years treated with intravenous unfractionated heparin. Do not use this standard for the management of intravenous unfractionated heparin in specific medical interventions, for example, renal replacement therapy, thermodilution catheter management (for example, Swan Ganz catheter) or Extracorporeal Membrane Oxygenation (ECMO).

This standard includes guidance on:

- unfractionated heparin indications, doses and contraindications
- monitoring requirements
- heparin products
- heparin reversal
- perioperative management and other considerations.

An example of an intravenous unfractionated heparin infusion nomogram is included. A **local nomogram** must be developed according to the local laboratory reference range.

Indications for intravenous unfractionated heparin

Treatment with an intravenous unfractionated heparin infusion is reserved for patients where treatment with low molecular weight heparin is contraindicated, for example, in severe renal impairment or when rapid offset of anticoagulant effect is required[1] for example, surgery.

Contraindications to heparin therapy include:

- Known hypersensitivity to heparin or pork products.
- History of heparin induced thrombocytopenia (HIT) (consult with haematology specialist).
- Patients with severe thrombocytopenia (consult with haematology specialist).

Commencing treatment

The following baseline laboratory tests should be performed prior to commencing treatment. The patient should be further investigated if results are abnormal:

- full blood count (FBC)
- prothrombin time (PT)
- activated partial thromboplastin time (aPTT)*
- urea, electrolytes and creatinine.

*Intravenous unfractionated heparin therapy may not be suitable if the baseline aPTT is prolonged.

Measure actual body weight.

Consider stopping antiplatelet agents due to increased risk of bleeding, if clinically appropriate.

Check if any other anticoagulants are prescribed and cease if appropriate.

Monitoring for Heparin Induced Thrombocytopenia (HIT)

Check the platelet count on commencement and then every three days while on intravenous unfractionated heparin therapy. Seek specialist haematology advice if thrombocytopenia develops or the platelet count falls more than 30 to 50 per cent below baseline [1].

Intravenous Unfractionated Heparin protocols

This standard includes two protocols (see page 2):

- A Standard Risk Protocol for use in atrial fibrillation, venous and arterial thromboembolic disease, prosthetic heart valves.
- A Higher-Bleeding Risk Protocol for circumstances where the risk of bleeding needs to be minimised, for example acute coronary syndrome.

Recommended heparin products[2]

For the intravenous bolus dose use:

- heparin sodium 5,000 units in 5 mL concentration ampoules

For the infusion use:

- commercially prepared pre-mix infusion bag of heparin 25,000 units in 250 mL normal saline (100 units per mL).

Use either the:

- Intravenous unfractionated heparin Standard Risk Protocol, *or*
- Intravenous unfractionated heparin Higher-Bleeding Risk Protocol

Intravenous unfractionated heparin Standard Risk Protocol

This protocol is for use in conditions where intravenous unfractionated heparin therapy is indicated such as atrial fibrillation, venous and arterial thromboembolic disease, and prosthetic heart valves.

Intravenous bolus dose (prior to commencing infusion)

- Administer a bolus of heparin sodium 80 units/kg[1] (maximum dose 5,000 units).

For acute thrombosis a higher weight based bolus may be required.

Seek specialist haematology advice for high body weight patients with extensive deep vein thrombosis or pulmonary emboli.

There may be circumstances where the bolus dose is omitted, for example if the patient is transitioning from another anticoagulant agent; or a delayed onset of anticoagulant effect is required.

Intravenous unfractionated heparin infusion Starting rate

- Calculate the initial infusion dose (rate) as 18 units/kg/hour[2]. Round the dose to the nearest 1 mL/hour.

Rate adjustment

- Adjust the infusion dose (rate) according to the aPTT[1] (see page 3 - Measuring the aPTT). Round the dose to the nearest 1 mL/hour.

Intravenous unfractionated heparin Higher-Bleeding Risk Protocol

This protocol is for use in conditions where intravenous unfractionated heparin therapy is indicated and the risk of bleeding needs to be minimised, for example acute coronary syndrome.

Intravenous bolus dose (prior to commencing infusion)

For patients weighing **60 kg and over**:

- Administer a bolus dose of heparin sodium 4,000 units[1].

For patients weighing **less than 60 kg:**

- Administer a bolus dose of heparin sodium 60 units/kg[1].

There may be circumstances where the bolus dose is omitted, for example if the patient is receiving another anticoagulant agent and a delayed onset of anticoagulant effect is required.

Intravenous unfractionated heparin infusion Starting rate

- Calculate the initial infusion dose (rate) as 12 units/kg/hour[1, 2]. Round the dose to the nearest 1 mL per hour.
- The *initial* hourly dose should not exceed 1,000 units/hour [i.e. 10 mL per hour (using premix infusion bag of heparin 25,000 units in 250 mL normal saline)].

Rate adjustment

- Adjust the infusion dose (rate) according to the aPTT[1] (see page 3 - Measuring the aPTT). Round the dose to the nearest 1 mL per hour.

Commercially prepared pre-mixed heparin solutions must be used wherever possible [NSW High-Risk Medicines Management Policy (PD2015-029)]. This Recommended Standard is based on pre-mix infusion bag of heparin 25,000 units in 250 mL normal saline (100 units per mL). The CEC recommends use of pre-mix infusion bags for heparin infusions. Please refer to the Frequently Asked Questions.

Measuring the aPTT

The aPTT should be repeated 4 to 6 hours after infusion commencement, and following a rate change. The medical officer should be informed if the aPTT does not reach therapeutic range within 24 hours. Following two consecutive aPTT levels in the therapeutic range, the aPTT can be checked daily.

The aPTT sample should not be collected from the same limb as the intravenous access point for the unfractionated heparin infusion.

Intravenous unfractionated heparin infusion nomogram

A local nomogram must be developed according to the local laboratory aPTT reference range. The therapeutic range is calculated as 1.5 – 2.5 times the aPTT reference range[1].

Express doses in local nomograms in units and mL/hour.

The following table is provided as an **example** of an intravenous unfractionated heparin nomogram (using pre-mix infusion bag of heparin 25,000 units in 250 mL normal saline).

Consistent with the above example, local nomograms should include:

- ongoing aPTT monitoring requirements for results outside the therapeutic range
- instructions for two levels of intravenous dose (rate) changes for aPTT results below the therapeutic range
- instructions for three levels of intravenous dose (rate) changes for aPTT results above the therapeutic range.

This **example** nomogram is for use with the Standard Bleeding Risk Protocol and the Higher-Bleeding Risk Protocol.

A local nomogram must be developed according to the local laboratory aPTT reference range.

EXAMPLE of an intravenous unfractionated heparin infusion nomogram

(using pre-mix infusion bag of heparin 25,000 units in 250 mL normal saline)

aPTT (seconds)	Intravenous dose (rate) change*	Repeat aPTT
37 - 45	INCREASE rate by 200 units (2 mL/hour) from current rate	4-6 hours
46 – 54	INCREASE rate by 100 units (1 mL/hour) from current rate	4-6 hours
55 – 90	Therapeutic range Continue current rate	4-6 hours or Daily**
91 - 105	• DECREASE rate by 200 units (2 mL/hour) from current rate	4-6 hours
106-120	• STOP infusion for 60 minutes, *then* • DECREASE rate by 200 units (2 mL/hour) from current rate	4-6 hours
Greater than 120	1. STOP infusion for 2 hours • Check patient for bleeding • Check infusion rate calculations and pump settings • Contact medical officer immediately. 2. REPEAT aPTT (after the 2 hours) If the REPEAT aPTT is LESS than 120 seconds and there is no evidence of bleeding, DECREASE rate by 300 units (3 mL/hour) less than previous rate. If the REPEAT aPTT is GREATER than 120 seconds, continue to WITHHOLD the infusion, contact the medical officer. Urgent haematology specialist advice should be sought.	4 hours

*Inform medical officer if therapeutic range is not reached within 24 hours
**Once two consecutive aPTT results in the therapeutic range

Reversal of intravenous unfractionated heparin

Specialist haematology advice should be sought if a patient requires reversal of unfractionated heparin. For potentially life threatening bleeding, administration of intravenous protamine may be appropriate. Protamine is cleared from the circulation with a half-life of about seven minutes. Because the half-life of intravenous unfractionated heparin is 60 to 90 minutes, only therapy given during the preceding several hours needs to be considered when calculating the dose of protamine that needs to be administered[3,4].

Perioperative management and other considerations[5,6]

Ceasing prior to procedure or surgery

In accordance with the surgeon or anaesthetists preference, cease the intravenous unfractionated heparin infusion 6 hours prior to surgery (if the aPTT is within the therapeutic range). If the aPTT is above the therapeutic range, a longer delay may be required before the procedure. Check that the aPTT is within the normal range.

Recommencing following surgery

The surgeon should advise when the intravenous unfractionated heparin infusion can be recommenced postoperatively. General guidance is:

Patients with a very high risk of thromboembolism (i.e. patients with a prosthetic heart valve):

- recommence the intravenous unfractionated heparin infusion (without bolus) 6 to 8 hours postoperatively.

For patients with a high bleeding risk:

- recommence the intravenous unfractionated heparin infusion 24 to 48 hours postoperatively (depending on surgical assessment).

Epidural

Specialist anaesthetic advice should be sought for patients receiving intravenous unfractionated heparin who require epidural or spinal anaesthesia. General guidance is to cease the intravenous unfractionated heparin infusion 6 hours prior to the procedure (assuming the aPTT is within the therapeutic range). Repeat aPTT immediately prior to the procedure to ensure that the aPTT is within the normal range before proceeding to surgery. If the aPTT is above the therapeutic range, a longer delay may be required before the procedure.

Lumbar puncture

Specialist haematology advice should be sought for patients receiving intravenous unfractionated heparin therapy requiring therapeutic or diagnostic lumbar puncture.

General guidance is to cease the intravenous unfractionated heparin infusion 6 hours prior to the procedure (assuming the aPTT is within the therapeutic range).

If the aPTT is above the therapeutic range, a longer delay may be required.

Recommence intravenous unfractionated heparin infusion (without bolus) after two hours (minimum) if no evidence of bleeding or a bloody tap.

References:

1. Australian Medicines Handbook Pty Ltd. *Australian Medicines Handbook*. July 2018; Available from: https://amhonline.amh.net.au.acs.hcn.com.au/.
2. NSW Health. High-Risk Medicines Management Policy Directive (PD2015_029) 2015.
3. Garcia, D.A., et al., *Parenteral Anticoagulants Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines.* Chest 2012. **141** (2 Supplement): p. e24S-43S.
4. Sanofi-Aventis, *Product information. Protamine sulfate injection B.P.*, 2017.
5. Australian and New Zealand College of Anaesthetists and Faculty of Pain Medicine. Acute pain management scientific evidence. 2015 (4th Edition)
6. Horlocker TT, Vandermeuelen E, Kopp SL, Gogarten W, Leffert LR, Benzon HT. Regional Anesthesia in the Patient Receiving Antithrombotic or Thrombolytic Therapy American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (Fourth Edition). Regional Anesthesia & Pain Medicine. 2018; 43: 263 – 309.

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Intravenous unfractionated heparin recommended standard
For incorporation into local guidelines/protocols.
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