**ANTICOAGULATION**

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- Low dose (unfractionated) heparin infusion
- Therapeutic (unfractionated) heparin infusion
- Low molecular weight heparin (LMWH)
- Warfarin
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- Adverse Events
- Forms
  - ADHB Heparin Chart (CR5620)
  - ADHB Paediatric Oral Anticoagulation Chart (CR8849)
- References

### Introduction

- These guidelines apply to infants and children in Starship Children’s Hospital.
- Refer to ADHB Newborn Services Guideline ([NW Newborn Drug Protocol - Heparin Pharmacology](#)) for infants within the newborn service.
- The following are guidelines only and may need to be adapted in individual circumstances. If you are in any doubt about a child’s anticoagulation management ask a senior medical doctor or paediatric haematologist.
- All anticoagulation needs to be prescribed. Heparin infusions must be prescribed on the ADHB Heparin chart (CR5620) and cross referenced on the medication record. Warfarin must be prescribed on the Paediatric Oral Anticoagulation chart (CR8849) and also cross referenced on the medication record.
- Prior to placement and removal of an Epidural Catheter, Heparin needs to be stopped or omitted as in the Pain Management – Epidurals & Anticoagulation – RBP

### Low dose standard/unfractionated heparin infusion (prophylaxis)

#### Indications for low dose heparin infusion

Low dose heparin infusions are used for the maintenance of central venous lines and arterial lines to prevent thrombosis.

**PICU/ PHDU/ 23B HDU**

- Cardiac children with single ventricle anatomy and central venous catheter (CVC)
- Infants < 5kg in PICU or the cardiac service with central venous catheter (CVC)
- Cardiac children with modified BT shunt, bi-directional cavopulmonary shunt and extracardiac fontan. Refer to PCCS guidelines: N:\Groups\INTRANET\Paediatric and Congenital Cardiac Service\PCCS Guidelines\Anticoagulation for Cavopulmonary aortopulmonary shunts Jan 2013 .doc)

**Post Liver Transplantation.**

- Refer to the specific Paediatric liver transplant protocol for heparin dose and monitoring: Liver Transplant Recipient Post-Op Routine Care (Paed).pdf.

**Note:** Infusion rates are not the same as the standard low dose protocol. **Do not follow the low dose heparin protocol for liver transplant patients.**
Infusion preparation for low dose heparin

Prepare the following low dose heparin solution for all of the above indications. Then refer to the appropriate management protocol.

$$\text{(500 x weight (kg)) unfractionated heparin diluted to 50mls with 5% glucose or 0.9% sodium chloride}$$

$$1\text{ml/hr} = 10 \text{ units/kg/hr}$$

Maximum 25,000 units in 50mls

Heparin infusions must be prescribed on the ADHB Heparin chart (CR5620) and cross referenced on the medication record. The only exception to this is PICU where this is charted on the 24 hour PICU flowchart.

Dose & administration of low dose heparin infusion

Obtain baseline FBC, APTT and PT prior to commencing infusion.

Recommended starting dose:

<table>
<thead>
<tr>
<th>Age</th>
<th>10 units/kg/hr</th>
<th>5 units/kg/hr</th>
<th>Do not start</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1 month</td>
<td>APTT &lt;45</td>
<td>APTT 45-55</td>
<td>APTT &gt;55</td>
</tr>
<tr>
<td>&gt; 1 month</td>
<td>APTT &lt;40</td>
<td>N/A</td>
<td>APTT &gt;40</td>
</tr>
</tbody>
</table>

Maximum dose 500 units/hour (even if patient’s weight greater than 50kg).

Administer intravenously via CVC.

Note:
- No loading dose is given
- In children who have had cardiac surgery, start infusion 4 hours after surgery if there is no significant bleeding.
- Cardiology patients weighing less than 5kg receiving aspirin should continue their low dose heparin while they have a CVC.
- Do not stop heparin infusion for sternal closure.

For further information on preparation and administration, please refer to guardrails paediatric guidelines on ADHB Reference Viewer.
Monitoring and adjusting infusion of low dose heparin infusion

- There is no ‘goal’ APTT for prophylactic (low dose) heparin infusions but APTT monitoring ensures that the patient is not therapeutically heparinised.

- Check APTT 4 hours after start of infusion and adjust as in the tables below

- Capillary APTT for ward patients should ideally be monitored around 8:30am, 1:30pm, 6:30pm or midnight.

- Patients may need more frequent APTT monitoring if they are at increased risk of bleeding, check with consultant and/or cardiac surgeon.

- Twice weekly FBC must be obtained to monitor for heparin induced thrombocytopenia.

### PICU/ PHDU

Patients less than 1 month of age

<table>
<thead>
<tr>
<th>APTT (Sec)</th>
<th>Heparin Infusion (rate)</th>
<th>Repeat APTT</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 45</td>
<td>10 unit/kg/hr</td>
<td>12 hours</td>
</tr>
<tr>
<td>45-55</td>
<td>5 units/kg/hr</td>
<td>4 hours</td>
</tr>
<tr>
<td>&gt;55</td>
<td>Stop infusion</td>
<td>4 hours</td>
</tr>
</tbody>
</table>

Patients greater than 1 month of age

<table>
<thead>
<tr>
<th>APTT (Sec)</th>
<th>Heparin Infusion (rate)</th>
<th>Repeat APTT</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 40</td>
<td>10 unit/kg/hr</td>
<td>12 hours</td>
</tr>
<tr>
<td>40-50</td>
<td>5 units/kg/hr</td>
<td>4 hours</td>
</tr>
<tr>
<td>&gt;50</td>
<td>Stop infusion</td>
<td>4 hours</td>
</tr>
</tbody>
</table>

### 23B HDU

<table>
<thead>
<tr>
<th>APTT (Sec)</th>
<th>Heparin Infusion (rate)</th>
<th>Repeat APTT</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 80</td>
<td>10 unit/kg/hr</td>
<td>Daily for 2 days then every 2 to 3 days</td>
</tr>
</tbody>
</table>
| >80 or bleeding| Stop infusion and restart: | -In children less than 1 month old if APTT < 55
|               |                         | -In children greater than 1 month old if APTT < 40  |
|               |                         | 4 hours                                       |
Therapeutic standard/unfractionated heparin infusion (Treatment)

Indications for therapeutic heparin infusion

- Treatment of venous thromboembolism such as deep vein thrombosis, pulmonary embolism and sinus venous thromboses.
- Post operative management of mechanical heart valves or Fontan surgery
- Treatment of ischaemic stroke.

Note:
If a cardiac patient is less than 21 days post-op please check with the cardiac surgeon before fully heparinising (consider ECHO if concerns of a pericardial effusion).

Infusion preparation for therapeutic heparin

For children less than 30kg

\[
(500 \times \text{weight (kg)}) \text{ in units unfractionated heparin diluted to 50mls with 5\% glucose or 0.9\% sodium chloride} \\
1\text{ml/hr} = 10 \text{ units/kg/hr}
\]

For children more than 30kg

\[
(200 \times \text{weight (kg)}) \text{ in units heparin, diluted to 50mls with 5\% glucose or 0.9\% sodium chloride} \\
1\text{ml/hr} = 4 \text{ units/kg/hr}
\]

- Heparin infusions must be prescribed on the ADHB Heparin chart (CR5620) and cross referenced on the medication record. The only exception to this is PICU where this is charted on the 24 hour PICU flowchart.
- Therapeutic heparin infusion prescriptions should include both units/kg/hr as well as the corresponding ml/hr rate.
Dose & administration of therapeutic heparin infusion

Obtain baseline FBC, APTT PT and renal function prior to commencing infusion.

### Recommended loading dose and initial maintenance dose

<table>
<thead>
<tr>
<th>Age</th>
<th>Loading dose</th>
<th>Dosing</th>
<th>Initial maintenance dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 year</td>
<td>75units/kg (maximum 7200units) over 10 minutes*</td>
<td>28 units/kg/hr</td>
<td></td>
</tr>
<tr>
<td>&gt;1 year &lt;30kg</td>
<td>20 units/kg/hr</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;30kg</td>
<td>18 units/kg/hr</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Give IV bolus 75 units/kg (max 7200units) over 10 minutes except:
- In the presence of a pre-existing coagulopathy-please discuss with senior medical doctor.
- If patient is already anticoagulated and /or converting from warfarin.
- If patient has had recent surgery - please discuss with surgeon.

If more rapid heparinisation is required then 100-200 units/kg may be given after discussion with senior medical doctor.

**Further guidance**
- Administer intravenously via dedicated peripheral or central line.
- The infusion must not be stopped or interrupted for other medication as heparin has a short half life.
- The duration of heparin therapy is dependent upon the primary problem, discuss with senior medical doctor or paediatric haematologist.
- **Usual maximum dose is 2100units/hr. In patients at increased risk of bleeding maximum dose is 1000units/hr.** Please discuss with senior medical doctor or paediatric haematologist.

For further information on preparation and administration, please refer to guardrails paediatric guidelines on ADHB Reference Viewer.

### Monitoring and adjusting therapeutic infusions of heparin

- Goal APTT is usually 60 -80 for infants less than 1 month and 50-80 for children.
- APTT is checked 4 - 6 hours after infusion has been started and adjusted as follows:

<table>
<thead>
<tr>
<th>APTT (sec)</th>
<th>Bolus (u/kg)</th>
<th>Stop Infusion (min)</th>
<th>% Rate Change</th>
<th>Repeat APTT</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 40</td>
<td>50</td>
<td>No</td>
<td>Increase by 10%</td>
<td>4 – 6 hours</td>
</tr>
<tr>
<td>40 – 49</td>
<td>No</td>
<td>No</td>
<td>Increase by 10%</td>
<td>4 – 6 hours</td>
</tr>
<tr>
<td>50 – 80</td>
<td>No</td>
<td>No</td>
<td>No change</td>
<td>Once/twice daily</td>
</tr>
<tr>
<td>81 – 90</td>
<td>No</td>
<td>No</td>
<td>Decrease by 10%</td>
<td>4 – 6 hours</td>
</tr>
<tr>
<td>91 – 115</td>
<td>No</td>
<td>30</td>
<td>Decrease by 10%</td>
<td>4 – 6 hours</td>
</tr>
<tr>
<td>&gt; 115</td>
<td>No</td>
<td>60</td>
<td>Decrease by 15%</td>
<td>4 – 6 hours</td>
</tr>
</tbody>
</table>
ENHANCEMENT

• Ensure the heparin infusion is adjusted as soon as possible after the APTT result is available and the next APTT is done 4 - 6 hours following the infusion adjustment. Nursing staff should contact relevant medical staff as soon as APTT result is available for review to ensure prompt dose changes are made as appropriate.
• Once stable the APTT must be checked twice daily for PICU/PHDU patients and daily for ward based patients.
• Capillary APTT for ward patients should ideally be monitored around 8:30am, 1:30pm, 6:30pm and midnight.
• Samples must not be taken from the same line as the heparin infusion or from veins proximal to infusion.
• Twice weekly FBC (including platelet count) are required. If there is an abrupt decrease in platelet count (approximately 50%) consider heparin induced thrombocytopenia (HIT) and discuss with paediatric haematologist.

Note:
• Avoid IM injections and arterial puncture during anticoagulant therapy. When such procedures are clinically necessary, ensure adequate external pressure is applied post-procedure.
• Avoid aspirin and anti-platelet medications during heparin therapy unless directed otherwise.

Low molecular weight heparin (LMWH)

In infants and children, the LMWH of choice at Starship is Enoxaparin (Clexane®).

Indications for LMWH

• Treatment and prophylaxis of venous thromboembolism such as deep vein thrombosis, pulmonary embolism and sinus venous thromboses.

The decision to use LMWHs instead of standard/unfractionated heparin or warfarin depends on the clinical scenario and individual patient factors such as bleeding risk or ease of venous access.

Dose & administration of LMWH

Obtain baseline FBC, APTT, PT and renal function prior to commencing.

<table>
<thead>
<tr>
<th>Age</th>
<th>Treatment dose</th>
<th>Prophylactic dose *</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 year ★</td>
<td>1.5 mg/kg/dose twice a day</td>
<td>0.75 mg/kg/dose twice a day</td>
</tr>
<tr>
<td>1 year-18 years</td>
<td>1 mg/kg/dose twice a day</td>
<td>0.5 mg/kg/dose twice a day</td>
</tr>
</tbody>
</table>

Note:
★ Require 50% larger doses possibly due to larger volume of distribution and/or reduced antithrombin levels.

# Prophylactic LMWH: Further studies are required to define the highest risk groups in paediatrics and the potential benefits of prophylaxis but in the absence of such data prophylaxis should be considered on an individual basis, particularly in older children with multiple recognised risk factors.
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Timing of commencement, and duration of therapy, should be individualised and discussed with a paediatric haematologist.

Dose is administered via subcutaneous (SC) route either via an insuflon catheter or by rotating sites of SC injections.

Round dose to the nearest syringe size where appropriate (20mg, 40mg, 60mg, 80mg, 100mg, 120mg, 150mg available).

**For doses less than 20mg:**
1. Draw 1.8 mL of 0.9% sodium chloride into a 2 mL syringe.
2. Inject enoxaparin 20 mg /0.2 mL directly into 0.9% sodium chloride syringe, making a total volume of 2 mL.
3. This equals a concentration of 10 mg/mL.
4. From the 2 mL syringe withdraw dose required with a 1 mL syringe.

Prior to any surgery, spinal or epidural procedure, two doses of LMWH should be omitted before the procedure. In patients with renal impairment it may be advisable to check the anti-Xa levels prior to surgery. Discuss with a senior medical doctor.

Prior to placement and removal of an epidural catheter LMWH needs to be stopped as in the Pain Management – Epidurals and Anticoagulation RBP

**Monitoring and adjusting LMWH (Treatment)**

- Ensure the sample is not taken from a heparin contaminated line.
- Obtain anti-Xa assay 3.5- 4 hours post morning dose and adjust as follows:

<table>
<thead>
<tr>
<th>Anti-Xa level (units/ml)</th>
<th>Hold Next Dose</th>
<th>Dose Change</th>
<th>Repeat anti-Xa level</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 0.35</td>
<td>No</td>
<td>Increase by 25%</td>
<td>4 hrs post next morning dose</td>
</tr>
<tr>
<td>0.35-0.49</td>
<td>No</td>
<td>Increase by 10%</td>
<td>4 hrs post next morning dose</td>
</tr>
<tr>
<td>0.5-1</td>
<td>No</td>
<td>No change</td>
<td>Once a week 4 hrs post a morning dose</td>
</tr>
<tr>
<td>1.1-1.5</td>
<td>No</td>
<td>Decrease by 20%</td>
<td>4 hrs post next morning dose</td>
</tr>
<tr>
<td>1.6-1.9</td>
<td>3 hrs</td>
<td>Decrease by 30%</td>
<td>Trough level pre- next dose, then 4 hrs post next morning dose</td>
</tr>
<tr>
<td>&gt;2</td>
<td>Until anti-Xa level &lt;0.5</td>
<td>Decrease by 40%</td>
<td>Trough level pre-next dose and if not &lt;0.5 repeat twice a day</td>
</tr>
</tbody>
</table>

- The APTT does not give any indication about degree of anticoagulation with LMWH.
- A platelet count should be obtained weekly for the first month. If there is an abrupt decrease in platelet count (approximately 50%) consider heparin induced thrombocytopenia (HIT) and discuss with paediatric haematologist.

**Note:**
- Avoid IM injections and arterial puncture during anticoagulant therapy. When such procedures are clinically necessary, ensure adequate external pressure is applied post-procedure.
- Avoid aspirin and other anti-platelet medications unless directed otherwise as this can potentiate the anticoagulant effect of LMWH.
- **For prophylactic LMWH monitoring please discuss with paediatric haematologist.**

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**Editor:** Dr Raewyn Gavin
**Service:** Pharmacy, Paediatric haematology
**Date Reviewed:** August 2012
Anticoagulation

**Warfarin**

Warfarin is the generic name for the most commonly used oral anticoagulant and can be used for short or long term anticoagulation. It inhibits the synthesis of vitamin K dependent coagulation factors. Maintaining stable INRs in infants less than 1 year of age can be difficult therefore low molecular weight heparin may be preferable depending on the indication.

**Indications for Warfarin**
- Treatment and prophylaxis of venous thromboembolism such as deep vein thrombosis, pulmonary embolism and sinus venous thromboses.
- Cardiac
  - Mechanical valves: aortic and mitral.
  - Post-fontan surgery.
  - Cardiomyopathy.
- Ischaemic stroke.

**Contraindications**
- Warfarin is contraindicated in pregnancy in the first and third trimester. Females of child-bearing age who are taking warfarin tablets should use effective contraception during treatment.

**Dose and Administration of Warfarin**

Obtain baseline FBC, INR, liver function tests and renal function tests prior to starting therapy.

- Warfarin for in-patient use is prescribed on the Starship warfarin chart (CR8849) and also cross referenced on the medication record.

**Loading Dose - Day 1**
- 0.2 mg/kg (maximum 5mg) at 1800 hrs.
- For cardiac patients, patients with liver dysfunction or severe renal impairment start at 0.1mg/kg (maximum 5mg) at 1800 hrs.

**Loading Dose - Day 2-4**
- Subsequent loading doses are based on individual International Normalised Ratio (INR) result. The following dose reductions are critical to avoid "over-shooting" the target range.
- If the INR is not greater than 1.5 on Day 4, the patient should be reassessed and the loading dose per kg increased based on the individual clinical need.

<table>
<thead>
<tr>
<th>INR</th>
<th>Warfarin Adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1.3</td>
<td>Repeat initial loading dose</td>
</tr>
<tr>
<td>1.4 - 3.0</td>
<td>50% of initial loading dose</td>
</tr>
<tr>
<td>3.1-3.5</td>
<td>25% of initial loading dose</td>
</tr>
<tr>
<td>3.5-4.9</td>
<td>Hold until INR &lt;3.5, then restart at 50% less than previous dose</td>
</tr>
<tr>
<td>&gt;5</td>
<td>Discuss with paediatric haematologist</td>
</tr>
</tbody>
</table>

**Note:**

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Editor: Dr Raewyn Gavin  
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- There are two brands of warfarin; Marevan® and Coumadin®. Marevan® is used at ADHB, unless patients are from French Polynesia (Tahiti) where only the Coumadin® brand is available. Marevan® and Coumadin® are not interchangeable.
- Both brands colour-code their tablets as follows:

<table>
<thead>
<tr>
<th></th>
<th>1mg</th>
<th>2mg</th>
<th>3mg</th>
<th>5mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marevan®</td>
<td>brown</td>
<td>n/a</td>
<td>blue</td>
<td>Pink</td>
</tr>
<tr>
<td>Coumadin®</td>
<td>light tan</td>
<td>lavender</td>
<td>n/a</td>
<td>Green</td>
</tr>
</tbody>
</table>

- Active warfarin is NOT evenly distributed within each tablet. Doses should be given in whole tablet sizes. Some patients will require alternate day doses or dose reduction e.g. alternating 3 mg and 4 mg daily, instead of 3.5 mg daily.
- Warfarin should be given at the same day each day usually 6pm.

Monitoring and adjusting warfarin

- INR is taken the morning after the dose.
- Most patients require 3-5 days of warfarin before achieving a stable maintenance phase.
- In the setting of acute thrombosis it is recommended that the first 7 days of warfarin therapy is covered with heparin (either unfractionated or low molecular weight heparin).
- The goal of therapy is to keep INR in range so as to minimise risk of bleeding or thrombosis.

<table>
<thead>
<tr>
<th>Indication</th>
<th>Target INR Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deep vein thrombosis/ PE</td>
<td>2-3</td>
</tr>
<tr>
<td>Mechanical valves</td>
<td></td>
</tr>
<tr>
<td>▪ Aortic</td>
<td>2-3</td>
</tr>
<tr>
<td>▪ Mitral</td>
<td>2.5-3.5</td>
</tr>
<tr>
<td>Post-Fontan surgery</td>
<td>2-3</td>
</tr>
<tr>
<td>CVL clot prophylaxis</td>
<td>1.2-2</td>
</tr>
<tr>
<td>Cardiomyopathy</td>
<td>2-3</td>
</tr>
<tr>
<td>Ischaemic stroke</td>
<td>1.5-2.5</td>
</tr>
</tbody>
</table>

Note:
- Before altering a patient's warfarin dose ensure compliance.
- Other medications may interact with warfarin necessitating a dose adjustment.
- Exclusively breastfed babies may require supplementing feeds with one formula feed a day to provide a constant intake of Vitamin K.
- Anticoagulation during the early-post-operative period (<21 days) may vary with each patient and individual surgical practice, please confirm target INR with consulting cardiac surgeon.
Discharging patients on Warfarin

1. **All patients** discharged on warfarin must be referred to an appropriate practitioner for continued INR monitoring and dosing.

   **Paediatric cardiology service (PCCS)**
   - **Auckland patients:**
     - Organise who will check the INR (parents or Community nurses).
     - Patient to be entered on the PCCS Warfarin database, and dose adjustment is via the PCCS service.
   - **Patients outside of Auckland:**
     - Organise who will check the INR (parents or Community nurses).
     - Organise who will manage dose adjustment i.e. General Practitioner, Paediatrician at base hospital, Anticoagulation Clinic (Wellington area).

   **All other patients on Warfarin**
   - Discuss with paediatric haematologist regarding target INR and duration of therapy.
   - Organise who will check the INR (Community nurses, community lab or parents if able to source a Coagucheck machine).
   - Organise who will manage dose adjustment i.e. General Practitioner, Paediatrician, Anticoagulation Clinic (Wellington area).

2. **All patients** will need to be counselled before discharge. Ensure that the patient at least understands the following:
   - That warfarin comes in 3 different colours/strengths.
   - What dose to take (in number of tablets and colours if necessary) and that the dose will be written in their red warfarin record book.
   - The date of their next INR test.
   - Procedure for their next INR test e.g. time and place of test. Also what to bring with them e.g.red warfarin record book.

   **NB:** A red warfarin record book must be given to patient prior to discharge – this is an important record of treatment and has further important patient information.
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All patients should have a Warfarin discharge checklist completed prior to discharge.

- Target INR and duration of therapy set
- Warfarin monitoring arranged (including contact re actual discharge date)
- Self INR testing arranged if applicable (including purchase of machine and education)
- Patient/caregiver has red warfarin record book
- Patient details and INR target completed in discharge summary
- Discharge prescription written
- Patient and parent/caregiver given warfarin education
- Ensure the parent/caregiver knows when an INR test is required, how to get this done and who to call with the results.

Name: ______________________________________ Designation: _______________
(print please)
Signed: ______________________________________ Date: _____________________

Adverse events

The major adverse event related to anticoagulation is bleeding. If a patient on heparin, LMWH or warfarin develops bleeding, cease therapy and seek urgent medical review and discuss with a paediatric haematologist.

Patients should also be monitored for Heparin induced Thrombocytopenia (HIT), hyperkalaemia and hypersensitivity/anaphylactoid reactions as these are possible adverse effects of heparins.

Heparin and LMWH heparin

The antidote for standard/unfractionated heparin and low molecular weight heparin is protamine sulphate. Administration of protamine sulphate should always be discussed with a paediatric haematologist.

Warfarin

The effects of warfarin are reversed by vitamin K (Phytomenadione). Other strategies that can be used include fresh frozen plasma (FFP) or prothrombin concentrate. The strategy used is dependant on the INR and the patients’ clinical status. Please discuss with senior medical staff or paediatric haematologist who will advise appropriately.
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Clinical Forms

ADHB Heparin Chart (CR5620)
ADHB Paediatric Oral Anticoagulation Chart (CR8849) L/Groups/Everyone/Starship/Nursing/PDF clinical forms/oral anticoag…

References


