SYDNEY SOUTH WEST AREA HEALTH SERVICE

Governing Body & Management

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Guidelines- Anticoagulation: Heparin & Warfarin

Table of Contents

Intravenous Standard Heparin Protocols (100 units/ml infusion)

Note: The following protocols are for infusional devices using 25,000 units of sodium heparin in 250 ml normal saline (0.9% sodium chloride) and are not suitable for infusional devices using higher concentrations. Therapy is usually initiated with a bolus intravenous dose of heparin calculated by body weight, and then a heparin infusion commenced at the rate indicated below. The initial bolus dose is usually omitted following cardiothoracic surgery. It will often be appropriate to omit the bolus dose in the early postoperative period where there is a high risk of bleeding. If in doubt, discuss this with the surgeon responsible for the patient.

A. Heparin protocol for Acute Coronary Syndrome (STEMI, non-STEMI and Unstable Angina):

DOSAGE:	**Concentration = 25,000 units heparin sodium in 250ml normal saline (0.9% sodium chloride). (100 units per ml).** **Based on 12 units/kg/hr MAX:1000units/hr**

WEIGHT (kg)	*BOLUS (units)*	*UNITS PER HOUR*	*Starting rate mL per hour**
50	3000	600	6
55	3300	660	7
60	3600	720	7
65	3900	780	8
70	4000	840	8
75	4000	900	9
80	4000	960	10
>80	4000	1000	10

- Note: millilitres per hour have been rounded to the nearest whole number.

The first APTT is taken six hours after commencing the infusion and the rate adjusted as below.

UNFRACTIONATED HEPARIN DOSAGE ADJUSTMENT PROTOCOL FOR CORONARY SYNDROME (STEMI AND NON STEMI)

Based on aPTT Normal Range of 25-35 Seconds & Infusion of 25,000units in 250mL (100 units/ml)

aPTT (seconds)	Bolus Dose IV	Stop Infusion	IV Rate Change (mL/hr)	Repeat aPTT
<35	2,000 units		increase 2 mL/hr from current rate	6 hours
35-54	Nil	NO	increase 1mL/hr from current rate	6 hours
55-75	**Therapeutic Range - No Change from current rate**			**Daily**
76-90	Nil	NO	Reduce 1mL/hr from current rate	6 hours
91-105	Nil	NO	Reduce 2mL/hr from current rate	6 hours
> 105	Nil	60 mins	Restart at 2mL/h less than previous rate	6 hrs

B. HEPARIN PROTOCOL FOR ATRIAL FIBRILLATION, VENOUS AND ARTERIAL THROMBOEMBOLIC DISEASE, PROSTHETIC HEART VALVES

DOSAGE: Concentration = 25,000 units heparin sodium in 250 normal saline (0.9% sodium chloride). (100 units per ml) Based on 18 units/kg/hour.

WEIGHT	*BOLUS*	*UNITS PER HOUR*	*Starting rate mL per hour**
50	3500	900	9
55	3500	990	10
60	5000	1080	11
65	5000	1170	12
70	5000	1260	13
75	5000	1350	13
80	5000	1440	14
85	5000	1530	15
90	5000	1620	16
95	7500	1710	17
100	7500	1800	18
110	7500	1980	20
>120	7500	2100	21

*Note: Millilitres per hour has been rounded to the nearest whole number

The first APTT is taken six hours after commencing the infusion and the rate adjusted as below.

IV UNFRACTIONATED HEPARIN DOSAGE ADJUSTMENT PROTOCOL FOR AF/VTED (TABLE 2)

Based on aPTT Normal Range of 25-35 Seconds & Infusion of 25,000units in 250mL

aPTT (seconds)	Bolus Dose IV	Stop Infusion	IV Rate Change (mL/hr)	Repeat aPTT
< 35	5,000 units	NO	increase 2mL/hr from current rate	6 hours
35-45	Nil	NO	increase 2mL/hr from current rate	6 hours
46-54	Nil	NO	increase 1mL/hr from current rate	6 hours
55-90	**Therapeutic Range - No Change from current rate**			**Daily**
91-95	Nil	NO	decrease 1mL/hr from current rate	6 hours
96-105	Nil	NO	decrease 2mL/hr from current rate	6 hours
> 105	Nil	60 mins	Restart at 2mL/h less than previous rate	6 hrs

Notes on intravenous heparin:

1) A baseline full blood count, PT and APTT should be performed prior to heparin therapy. A Haematologist should be consulted if there are significant baseline abnormalities.
2) Full blood count should be performed at least three times per week, to exclude heparin induced thrombocytopenia and a fall in haemoglobin to suggest bleeding.
3) The possibility of a retroperitoneal bleed should be considered in the absence of another identified cause of pain in the back, leg, or abdomen. A full blood count should be performed and reviewed as soon as possible, as well as urgent medical assessment and imaging of the abdomen.
4) Where the therapeutic intention is anticoagulation for venous thrombo-embolism, non-steroidal anti-inflammatory drugs (NSAIDs) should be ceased to reduce the risk of bleeding.
5) In patients who have just had cardiac or great vessel surgery, consideration should be given to omitting the bolus dose of heparin. This should be discussed with the Cardiothoracic Surgeon.
6) If the patient has had a recent surgical procedure, anticoagulation should be discussed with the Surgeon prior to initiation, where possible.

Safety Issues with infusion pumps:
Care needs to be taken that pumps are operated according to hospital protocols and the manufacturer's instructions. To reduce the risk of accidental infusion of a large volume of heparin solutions:

1. Turn off the flow occlusion device on the infusion BEFORE removing the set from the pump.
2. Set the volume to be delivered to 50 ml, to reduce the risk of accidental infusion of larger volumes.

Changing Between Intravenous Heparin and Clexane

Where a decision is made to change the patient from intravenous heparin to Clexane, the calculated dose of Clexane (see low molecular weight heparin protocol) should usually be administered as soon as the intravenous heparin is ceased, assuming the patient was not over-anticoagulated on heparin at the time.

If the patient were changed from subcutaneous Clexane to intravenous heparin, intravenous heparin would normally be commenced when the next dose of Clexane is due, assuming the patient was not over-anticoagulated at the time.

Low Molecular Weight Heparin
(Thrombo-embolism and Unstable Coronary Artery Syndromes)

Enoxaparin (Clexane) is the preferred low molecular weight heparin (LMWH) in these guidelines. Dalteparin (Fragmin) may be alternatively used where it is the preferred choice of the Attending Medical Officer. Fragmin is discussed for prophylaxis only.

AVAILABILITY:

Clexane 20mg, 40mg, 60mg, 80mg, 100mg, 120 mg, 150 mg syringes
Fragmin 2,500 units, 5,000 units

BEFORE STARTING TREATMENT:

- Baseline full blood count, PT, APTT, electrolytes, urea and creatinine. A Haematologist should be consulted if there are significant baseline abnormalities of full blood count, PT and/or APTT.
- Estimate the calculated creatinine clearance (CCR, see attached table). The eGFR is automatically calculated by many Pathology Laboratories (see http://www.kidney.org.au & Med J Aust 2005; 183:138-141) but may not be accurate at extremes of body weight, children, or with acute changes in kidney function. If in doubt CCR should be calculated.
- For patients with venous thrombo-embolism, cease antiplatelet agents unless it is specifically intended to continue these, and the benefit outweighs the risk.

DOSE:

Prophylaxis:

Clexane 20 mg daily SCI (low risk prophylaxis or body weight <50 kg) and 40 mg daily SCI (high risk prophylaxis). Care in patients of lower body weight (<50 kg) and impaired renal function (see below)
OR
Fragmin 2,500 units daily SCI (low risk prophylaxis or body weight <50 kg) and 5,000 units daily SCI (high risk prophylaxis)

Therapeutic dosing (twice daily):

Normal or near normal renal function (CCR >60 ml/min) Clexane 1 mg/kg Q12H SCI (no cap based on weight but check peak anti-Xa levels if body weight >100 kg)

Moderate renal impairment (CCR= 30-60 ml/min)

Clexane 1 mg/kg Q12H SCI (maximum 100 mg initial dose), with daily or second daily monitoring of anti-Xa levels (see below) until a stable level is achieved, with less frequent monitoring in situations where long term therapy is employed.

Severe renal impairment (CCR<30 ml/min) Avoid in most circumstances, unless in close consultation with a Renal Physician and/or Haematologist. If used, Clexane 1 mg/kg/day with daily or second daily monitoring of anti-Xa levels (see below) until a stable level is achieved.

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Therapeutic dosing (once daily – not suitable for coronary artery syndromes):

Normal renal function (CCR > 60 ml/min) Clexane 1.5 mg/kg daily (maximum 150 mg dose). If the patient's weight is >100 kg, twice daily 1 mg/kg is recommended, as above.

ADMINISTRATION:

- Clean skin with an alcohol swab.
- Inject whole length of needle vertically into a skin fold (usually the lower abdomen), holding skin fold throughout injection.
- The very small air bubble commonly found in the syringe does not need to be expelled.
- Depress plunger to recommended dose.
- Exert pressure with a swab for 1-2 minutes to reduce bruising (do not rub).

PRECAUTIONS:

- Clexane is renally excreted and accumulates in renal failure. Care is required particularly in the elderly, patients on antiplatelet drugs, and in the presence of impaired renal function.
- Calculated creatinine clearance rate (CCR) may overestimate renal function in very obese or oedematous patients. Formal assessment of renal function is recommended in these patients.
- APTT is insensitive to Clexane and cannot be used for monitoring – anti-Xa levels are required (see below).
- If the patient has had a recent surgical procedure, the Surgeon involved should be consulted before the commencement of therapeutic dose LMWH.
- Ideally enoxaparin at therapeutic dose should not be given $\leq$24 hours prior to invasive procedures.
- Vascular access sheaths should remain in situ for 6-8 hours after the administration of Clexane and doses withheld for 6-8 hours after removal.
- Extreme care in the use of Clexane in patients receiving neuroaxial anaesthesia because of the risk of bleeding (consult with an Anaesthetist).
- Heparin related thrombocytopenia and thrombosis is an uncommon but potentially serious complication of heparin therapy, requiring urgent review of anticoagulation therapy and consultation with Senior

Medical Staff (see below).

MONITORING:

- Blood should be taken 4 hours (3-5 hours) after a dose of Clexane for anti-Xa levels.
- For twice daily dosing, the therapeutic range is 0.6-1.0 IU/ml.
- For once daily dosing, the peak anti-Xa level should be 1-2 IU/ml (there is less literature on once daily dosing compared to twice daily dosing).
- A full blood count should be checked second daily on inpatients on LMWH therapy, to exclude heparin thrombocytopenia and a fall in haemoglobin to suggest bleeding. In patients receiving extended LMHW heparin therapy as an outpatient (e.g. anticoagulation during pregnancy), it is reasonable to check a full blood count weekly for three weeks and then monthly.
- The possibility of a retroperitoneal bleed should be considered in the absence of another identified cause of pain in the back, leg, or abdomen. A full blood count should be performed and reviewed as soon as possible, as well as urgent medical assessment and imaging of the abdomen.
- Where the therapeutic intention is anticoagulation for venous thrombo-embolism, non-steroidal anti-inflammatory drugs (NSAIDs) should be ceased to reduce the risk of bleeding.

Reference:

Hirsh J & Raschke R. The Seventh ACCP Conference on antithrombotic and thrombolytic therapy. Chest. 2004;126:188S-203S

The Australasian Creatinine Consensus Working Group. Chronic kidney disease and automatic reporting of estimated glomerular filtration rate: a position statement. Med J Aust 2005; 183: 138-141.

Charts for estimating GFR:

Normal Renal Function (Calculated Creatinine Clearance (CCR)>60 ml/minute

1mg/kg *twice* daily

Moderate Renal Impairment: CCR 30-60mL/min

1mg/kg twice daily. Check peak (4 hours after a dose) anti-Xa level day 2 & day 3 of therapy, and every second day after that until stable.

Severe Renal Impairment CCR < 30mL/min

1mg/kg daily. Check peak (4 hours after a dose) anti-Xa level day 2 & day 3 of therapy, and every second day after that until stable.

SERUM CREATININE <100 micromol/L and CCR

Age	Sex	Weight						
		40kg	50kg	60kg	70kg	80kg	90kg	100kg
50yrs	M							
	F							
60yrs	M							
	F							
70yrs	M							
	F	<30 ml/min		30- 50 ml/min				
80yrs	M							
	F							
90yrs	M							
	F							

SERUM CREATININE 101-150 micromol/L and CCR

Age	Sex	Weight						
		40kg	50kg	60kg	70kg	80kg	90kg	100kg
50yrs	M							
	F							
60yrs	M							
	F							
70yrs	M		<30 ml/min			30-50 ml/min		
	F							
80yrs	M							
	F							
90yrs	M							
	F							

SERUM CREATININE 151-200 micromol/L and CCR

Age	Sex	Weight						
		40kg	50kg	60kg	70kg	80kg	90kg	100kg
50yrs	M							
	F							
60yrs	M							
	F						30- 50 mL/min	
70yrs	M	<30 mL/min						
	F							
80yrs	M							
	F							
90yrs	M							
	F							

Notes:
Based on creatinine clearance calculated using the COCKCROFT–GAULT EQUATION

- Estimate calculated creatinine clearance rate (CCR) =

$$\frac{(140\text{-age}) \times \text{weight in kg}}{0.814 \times \text{creatinine in umol/l}}$$

Multiply the result by 0.85 for females.

These estimates of Glomerular Filtration Rate (GFR) are unreliable in very obese or oedematous patients. Formal assessment of renal function is recommended in these patients.

Management of Bleeding on Intravenous Standard and Low Molecular Weight Heparin

Intravenous Unfractionated Heparin

- For bleeding which is non-life threatening, heparin can be ceased. Given the short half-life of 60 minutes, there will be rapid normalisation of the APTT within 2-3 hours.
- For potentially life threatening bleeding, administration of protamine may be appropriate. 50 mg protamine will neutralise 5,000 units of heparin, and would be the appropriate dose if the patient has received a bolus in the last hour. For infusions of heparin, give 30 mg protamine for a typical infusion rate of 1250 units/hour (30,000 units per 24 hours), with proportionately more or less for the actual infusion rate.

Low Molecular Weight (LMW) Heparin

- Neutralisation of LMW heparins is incomplete with protamine, with neutralisation of only ~ 60% of the anti-Xa activity occurring.
- The suggested dosage of protamine is 1 mg protamine for each 100 anti-Xa units of LMW heparin (1 mg Clexane = 100 anti-Xa units) given in the previous 8 hours. A second dose of 0.5 mg protamine per 100 units of LMW heparin can be considered if severe bleeding continues.
- If the last dose of LMW heparin was >8 hours, a smaller dose should be given (e.g. 0.5 mg protamine per mg of Clexane).
- Protamine may not be beneficial if the last dose of LMW heparin was >12 hours ago and renal function is normal.

Precautions with protamine:

- Excess protamine may have an anticoagulant effect and should be avoided.
- Adverse reactions may occur including anaphylaxis, hypotension, dyspnoea and bradycardia. Fatal reactions have been reported. Protamine should be administered slowly over 10 minutes. Adverse reactions are said to be more common in insulin dependent diabetics, patients who have had previous vasectomy, and those with fish allergies. These patients should be pre-medicated with Phenergan 12.5 mg IVI and hydrocortisone 100 mg IVI.

Reference:

Hirsh J & Raschke R. The Seventh ACCP Conference on antithrombotic and thombolytic therapy. Chest 2004; 126: 188S-203S

Clexane prescribing information (Aventis Pharma Ltd) via MIMS Online, July 2006

INITIATION OF WARFARIN THERAPY

PRE-TREATMENT:

Check baseline INR, PT, APTT, FBC and LFTs.
A pregnancy test is recommended in women of childbearing age.

COMMENCEMENT OF THERAPY

Assess that the benefit outweighs the risk. Risk factors for bleeding include:

- Age over 65 years (especially the frail).
- Recent surgery and antibiotic therapy.
- Weight less then 50 kg.
- Concomitant drugs inhibiting warfarin metabolism (see below).
- Poor diet.
- Any other bleeding risks.
- Patients with abnormal liver function tests.
-

Guidance should be sought from **Senior Medical Staff** if there is any uncertainty or if there are multiple risk factors for prescribing anticoagulant medication.

If no risk factors exist and the patients does not have a previous known stable dose: Commence therapy at 5 mg daily with daily INR monitoring. This will attain INR of approximately 2.0 in 4-5 days.

If no risk factors exist and the patient has a previous known stable dose of Warfarin: Recommence on the same dose that the patient previously had a stable therapeutic INR, assuming that no new risk factors exist. No “loading” dose is required in this situation.

If risk factors exist (see above): A reduction of the commencement dose to 3mg daily should be considered, if the patient has never taken Warfarin, and reduction from the previous known stable dose by 1-2 mg, if the patient has previously taken Warfarin.

Warfarin dose should usually be charted at 4 PM for inpatients (morning INR ~ 16 hours after a dose), depending on the timetable of the individual ward. For outpatients the timing of Warfarin dosing may be left to patient and physician preference.

- Warfarin may be commenced on day 1 or 2 of heparin therapy.
- **Overlap warfarin with heparin** (LMWH or UFH): The consensus guidelines suggest a minimum 5 days of heparin therapy, with four days of overlapped heparin plus Warfarin.
- Heparin should usually be overlapped with Warfarin for 2 days with the INR is in the therapeutic range, before heparin is ceased. In situations judged appropriate by the managing AMO (low risk of thromboembolism and/or high risk of bleeding), it may be reasonable to cease heparin on the first day the INR is >2.
- **Document in the notes the indication and target INR as well as the planned duration of Warfarin therapy.**

In some situations, initial overlapping Warfarin/heparin therapy may not be required e.g. commencement of Warfarin following prosthetic heart valve insertion or low risk patients with atrial fibrillation commencing Warfarin electively to reduce the risk of stroke.

The Warfarin dosing algorithm below may be used to commence therapy where the target INR is 2-3, or experienced staff may initiate therapy empirically based on judgement.
If a previous stable dose for a particular patient is known, then it is preferable to start therapy at that same dose.

Initiation of Warfarin Algorithm

The algorithm below is intended for a target range of 2-3. Day 1 is the first day of Warfarin therapy. The INR will usually be checked daily on inpatients. In outpatients second daily checks of the INR may be reasonable, depending on the rate of rise of the INR.

Day	INR	Dose
1	0-1.3	5mg (*Consider reduction to 3mg if risk factors exist – see above)*
2	<1.5	5mg
	1.5-1.9	2.5mg
	2.0-2.5	1-2.5 mg
	>2.5	0
3	<1.5	5 mg
	1.5-1.9	2.5-5mg
	2.0-3.0	0-2.5mg
	>3.0	0
4	<1.5	10mg
	1.5-1.9	5-7.5 mg
	2.0-3.0	0-5 mg
	>3.0	0
5	<1.5	10 mg
	1.5-1.9	7.5-10 mg
	2.0-3.0	0-5 mg
	>3.0	0
6	<1.5	7.5-12.5 mg
	1.5-1.9	5-10 mg
	2.0-3.0	0-7.5 mg
	>3.0	0

Haematology consultation is recommended if by day 7 an adequate INR is not achieved.

References:

1. Harrison, L; Johnston, M; Massicotte, M; Crowther, M; Moffat, K; Hirsh, J. Comparison of 5-mg and 10-mg Loading Doses in Initiation of Warfarin Therapy. Ann Intern Med 1997; 126(2):133-136.
2. Crowther, M; Harrison, L; Hirsh, J . Warfarin: Less May Be Better [Letter]. Ann Intern Med 1997; 127 (4) :333
3. Harper P, Monahan K, Baker B. Warfarin induction at 5 mg daily is safe with a low risk of anticoagulant overdose: results of an audit of patients with deep vein thrombosis commencing warfarin. Intern Med J 2005; 35: 717–720.

Range of International Normalised Ratio (INR) recommended for specific applications for Warfarin Therapy *

Condition	INR Range
Preventing DVT (High risk patients eg post hip replacement)	2.0 - 3.0
Therapy after DVT or Pulmonary Embolism	2.0 - 3.0
Preventing Systemic Embolism	
Atrial Fibrillation	2.0 - 3.0
Valvular Heart Disease	2.0 - 3.0
After Myocardial Infarction	2.0 - 3.0
Tissue Heart Valves (first 3 months)	2.0 - 3.0
Mechanical Heart Valve (normal risk)	2.5 - 3.5
Mechanical Heart Valve (high risk)	3.0 - 4.5

DVT = Deep Vein Thrombosis

*Based on the 7th American College of Chest Physicians Consensus Conference (Chest 2004; 126: 401S-428S)
Reference: Gallus A et al. Med J Aust 2000; 172:600-605

Duration of Anticoagulation:

This is controversial and the Attending Medical Officer or Haematologist should make this decision. The intended duration of Warfarin therapy should be clearly documented and communicated to the patient at the time of discharge from hospital, and reviewed prior to cessation.

Risk Factor	Duration of Anticoagulation
Reversible e.g. immobilisation, postoperative state	3 months (assuming resolution of risk factor)
Idiopathic venous thrombo-embolism (VTE):	
First episode	6-12 months
Recurrent VTE	Long term
Thrombophilia & first episode of VTE:	
Factor V Leiden, prothrombin gene mutation, protein C and S deficiency & first episode VTE	6-12 months for precipitated DVT. Consider long term for unprecipitated, major thromboembolism
ATIII deficiency, antiphospholipid antibodies at moderate or high titre or combined defects, presence of a lupus inhibitor	Consider long term

PATIENT INFORMATION ON WARFARIN

Your doctor has given you Warfarin, an anticoagulant tablet to slow the clotting of your blood. There are two brands of Warfarin i.e. Coumadin and Marevan. It is important that you take the same brand at all times. The Warfarin tablet should be taken once at the same time each day (usually at night).

Important points for patients on Warfarin:

1. Have regular blood tests for INR (the INR is a blood test to measure how quickly the blood clots)
    i. It is important to have regular INR blood tests to check you are taking the right dosage.
    ii. Too many tablets may cause bleeding; too few tablets may allow blood clots to form.

2) Wear medical alert bracelet or carry medical alert card, stating you are on Warfarin.

3) Watch for signs of bleeding (eg. bruising, nose and gum bleeds, rectal bleeding and dark urine and black stool). Sudden severe headache may indicate bleeding, and you should seek immediate medical attention.

4) Eat a well balanced diet.

5) Always contact the doctor managing your Warfarin before any medical procedure (eg. any operation or any dental work or a visit to the Podiatrist). The person performing the procedure eg doctor, dentist, podiatrist etc also needs to know you are taking Warfarin.

6) Never take aspirin or medications containing aspirin unless directed by a doctor. For minor aches and pains, you may take 1-2 tablets of paracetamol up to a maximum of 8 tablets per day. If you require more see your doctor.

7) If you see a different doctor it is important they know you are taking Warfarin. Many medications can affect Warfarin. Do not change medications, take any herbal tablets or any 'over the counter' medications without discussing with your doctor.

8) Missed dose – a dose can be taken within 2 hours of your normal dosage time. If more than 2 hours, skip that day's dose until the next dose is due. DO NOT DOUBLE THE DOSE. (Record in your booklet).
9) Drink alcohol in moderation (limit to 2 standard drinks / day).

10) At the time of commencing Warfarin, clarify with your doctors the intended duration of therapy, since this is an important issue for other doctors who may look after you in the future.

11) After every blood test for INR you must ring the doctor looking after your coagulation i.e. either your GP or the hospital clinic so they can tell you if you need to change your dose.

MANAGING HIGH INR AND BLEEDING DURING WARFARIN THERAPY

Clinical Setting	Action
INR < 5 but higher than the target therapeutic range (no bleeding)	Lower the dose or omit the next dose of Warfarin. Resume therapy at a lower dose when the INR approaches the therapeutic range.
INR 5-9 (no bleeding)	• If the patient is not bleeding and is not at high risk of bleeding, the next 1-2 doses of Warfarin can be omitted and Warfarin restarted at a lower dose when the INR falls into the therapeutic range. •Alternatively if the patient is at increased risk of bleeding, omit one dose of Warfarin, give 1-2.5 mg Vitamin K orally* or 0.5-1.0 mg IV[1]. Measure INR the following day anticipating that the INR will be in the therapeutic range of 2.0-3.0 within 24 hours. Recommence Warfarin the next day at a reduced dose**.
INR >9 (no bleeding)	Stop Warfarin, give 1 mg IV Vitamin K[1] or 2.5-5 mg oral vitamin K*. Repeat the INR after 6 hours to ensure INR<9. Recommence Warfarin at reduced dose once INR is in the therapeutic range. Consider blood products, as below, if there is a high risk of bleeding.
If the patient is bleeding (any level of INR)	Stop Warfarin and give IV Vitamin K[1] (see below) and clotting factor replacement (either FFP alone/or in cases of volume overload with Prothrombinex in consultation with Haematologist), measure INR as required. Assess need to restart Warfarin. Consult senior staff as to the appropriate dose of vitamin K. A vitamin K dose in the range of 1-10 mg IVI will be appropriate.

INR = international normalized ratio.
*(use ivi formulation mixed in water, juice – see below)
** If INR <2.0 and the thrombotic risk is high, give S/C Clexane 1.5mg/kg/day or 1 mg/kg Q12H SCI until INR is >2.0, (check GFR is normal –see LMW heparin protocol).
[1]Avoid high doses of vitamin K, where the patient will require ongoing Warfarin therapy and there is a high risk of thrombo-embolism e.g. mechanical heart valve.

Blood products:

• Fresh frozen plasma (FFP) 10-15 ml/kg
OR
• Prothrombinex-HT 25-50 IU/kg plus fresh frozen plasma (FFP) 150-300 ml (this combination is particularly suitable for patients who are unlikely to cope with a large fluid volume).
OR
• If FFP is not available: Prothrombinex-HT 25-50 IU/kg (usual vial size is 500 IU of factors II, IX, X).

Vitamin K:

To provide oral doses ≤ 2 mg, use the vitamin K taken from paediatric ampoules (2 mg/0.2 ml).
When intravenous vitamin K is used, because of the small risk of anaphylactic reactions, the patient should be observed for 30 minutes after administration. If the decision has been made to cease Warfarin permanently, then 10 mg IVI or orally can be given in place of the smaller doses above.

References:

Baker R et al. Warfarin reversal: consensus guidelines, on behalf of the Australasian Society of Thrombosis and Haemostasis. Med J Aust 2004; 181: 492-497
Hirsh J et al. American Heart Association/American College of Cardiology Foundation Guide to Warfarin Therapy. Circulation. 2003;107:1692

Perioperative Management of Anticoagulant Therapy in Patients on Warfarin

Each patient requires individual assessment, with the competing risks of thrombosis and haemorrhage. Management must be discussed with the Physician managing anticoagulation to define **the thrombotic risk**, the Surgeon or the Proceduralist to define **the bleeding risk**, as well as the patient. The bleeding and thrombotic risk should be documented. It should be noted that many simple procedures, with low bleeding risk can be performed with the patient remaining on Warfarin. Uncomplicated dental work can usually be performed with a therapeutic INR. **Bridging therapy** with heparin (see below) should be offered to patients who are judged to have a high risk of thrombosis while off Warfarin. ***Because of the high thrombotic risk associated with prosthetic valves, in all cases anticoagulation should be discussed with and determined by the Cardiologist managing the patient.*** The equivalence of low molecular weight heparin therapy to Warfarin and unfractionated heparin therapy has not been established in patients with mechanical heart valves.

~Day -7

Check baseline INR, FBC, LFTs and creatinine to establish the appropriate perioperative management. Tests should be performed within 10 days in patients with stable anticoagulation of the day of surgery. Day 0 is arbitrarily defined as the day of surgery. Define the **bleeding risk** of the procedure with the operator and determine when Warfarin can be recommenced postoperatively. Define **the thrombotic risk** off Warfarin (see below). Determine whether bridging therapy with Clexane or intravenous heparin is required.

Day -5 or day -4

No Warfarin is taken from day -5 or day -4 (i.e. miss day -5 or day -4 through to day 0 inclusive). The decision as to whether to stop Warfarin from day -4 or day -5 depends on the perceived risk of thrombosis, the procedure and the baseline INR. Cessation from day -5 may be appropriate if the INR is high (>3), there is a low thrombotic risk and/or the surgery has a high bleeding risk. Cessation from day -4 may be appropriate if the INR is lower <3, there is a high thrombotic risk, and the surgery has a lower bleeding risk.

Day -3 or day -2 (only if bridging therapy is planned)

Check the INR two days after ceasing INR and commence Clexane or heparin if the INR is $\leq$2.

If the INR has not fallen sufficiently, check the INR daily, and commence bridging therapy as below when the INR has fallen to $\leq$2.

Avoid Clexane bridging therapy in patients with impaired renal function (see LMH heparin protocol).

When the INR is $\leq$2 commence either:

1) Clexane 1 mg/kg Q12H SCI (see LMW heparin protocol)
   OR
2) Therapeutic intravenous unfractionated heparin (UH) as an inpatient (see unfractionated heparin protocol).

Day -1 (all patients) Check to ensure INR < 1.8. If ≥ 1.8, 1-2 mg IV Vitamin K should be considered.
If the patient is receiving BD Clexane, the evening dose is usually omitted. If there is a high risk of thrombosis or the surgery will occur in the afternoon of the next day, then then the evening dose may be given. In most situations a gap of at least 18 hours should be allowed for twice daily Clexane dosing, with an additional six hours if neuroaxial anaesthesia is contemplated.
If the INR is < 1.5, surgery can usually proceed without rechecking the INR on the day of surgery.

Day 0 (morning of surgery)
If the patient was receiving BD Clexane, omit the morning dose (≥18 hours between surgery and last dose, and ≥ 24 hours if neuroaxial anaesthesia is being used).
If the patient is on therapeutic dose UH, stop six hours prior to the surgery.
If the INR was >1.5 on day -1, repeat the INR on the morning of surgery.
If INR > 1.5 defer surgery or if surgery is urgent, give PROTHROMBINEX-HT (25-50 IU/kg) plus FFP 150-300 ml OR FFP 10-15 ml/kg if PROTHROMBINEX-HT is not used

Day 0 (evening of procedure)
-***The bleeding risk is low*** (e.g. dental work): recommence UH (no initial bolus dose) or Clexane at the dose used pre-operatively plus the patient's usual maintenance dose of Warfarin.
-***The bleeding risk is high (e.g. following many forms of surgery):*** The surgeon must be consulted as to the appropriate timing and dose of heparin. If possible, commence UH or Clexane at prophylactic doses (e.g. Clexane 40 mg daily SCI or UH 5,000 units BD SCI). In the high thrombotic risk group, increase to therapeutic dosing UH (no initial bolus dose) or Clexane as soon as safe from a bleeding point of view (usually possible within 48 hours). Following cardiac bypass surgery, heparin is not used routinely when restarting Warfarin because of the high risk of bleeding (check with the Cardiothoracic Surgeon).
Recommence Warfarin when considered safe. Recommence at the usual maintenance dose for the patient or at reduced dose if the patient is on antibiotics or other agents when may potentiate Warfarin.
Prophylactic UH or Clexane may be used postoperatively in the low thrombotic risk group, where preoperative bridging therapy had not been used, until the INR is >2, if it is appropriate for the type of surgery (e.g. hip surgery).

Day 1+
Measure the INR daily. Cease UH or Clexane when the INR is ≥2.

THROMBOTIC RISK

The following is intended as a guide only:

High Thrombotic Risk (bridging therapy would usually be offered):

- Mechanical heart valves.
- Venous thromboembolism < 3 months since a thrombotic event (if possible delay surgical procedures to > 3 months).
- Previous arterial thrombo-embolism.
- Previous venous thromboses with high risk features (e.g. cerebral venous sinus thrombosis, mesenteric vein thrombosis, malignancy, immobility, previous thromboembolism with identified congenital or acquired thrombophilic factor, recurrent thromboembolism).
- Individual cases where the consultant managing the patient considers the thrombotic risk high.
- Atrial fibrillation with risk factors (valvular heart disease, impaired cardiac function, previous stroke, other thrombotic risk factors).

Dental Procedures:
For patients undergoing dental procedures, tranexamic acid mouthwashes can be used, usually without interrupting Warfarin therapy.

References

Kearon C, Hirsh J. Management of anticoagulation before and after elective surgery. N Engl J Med. 1997;336:1506-1511.
Kearon C. Management of anticoagulation before and after elective surgery. American Society of Hematology Education Booklet 2003 p 528-534
Baker R et al. Warfarin reversal: consensus guidelines, on behalf of the Australian Society of Thrombosis and Haemostasis. Med J Aust 2004; 181:492-497.

PERIOPERATIVE MANAGEMENT OF ANTICOAGULANT THERAPY (see guideline)

Patient name …….. MRN ……..

Planned procedure …… Date …….

Hospital for procedure …….. Usual dose of warfarin ……..mg

Reason for warfarin use……

Calculated CCR or eGFR (see LMH heparin protocol): ……

Discussed with AMO/Specialist managing anticoagulation: ☐

Notes:

THROMBOTIC RISK: ☐ Low ☐ Moderate ☐ High

Discussed with AMO/Specialist performing procedure: ☐

Notes:

BLEEDING RISK: ☐ Low ☐ Moderate ☐ High

PRE-OPERATIVE: **Last Warfarin to be taken:**

	Date	Day	WARFARIN	CLEXANE DOSE & FREQUENCY
-5			OPTIONAL (see protocol)	
-4			NO	
-3			NO	
-2			NO	
-1			NO	Omit evening dose of Clexane in most cases

Signature: …… Position:…… Date: ……

THE DAY OF SURGERY:

Last Clexane to be taken 18-24 hrs pre-operatively for therapeutic dose and >12 hours for a prophylactic dose with normal renal function.

INR on day of surgery should be ≤ 1.5 or ≤ 1.2 in high bleeding risk surgery

	Date	Day	**WARFARIN	**CLEXANE ≥ 6-12 hrs post-op
0				

**** The risk of bleeding in the immediate post-op outweighs the risk of thrombosis. Do not restart anticoagulation (unless extremely high risk of thrombosis) until instruction from the surgeon.

It is the responsibility of the surgical team to reassess the bleeding risk post surgery and to seek further consultant advice in the event of a change in the clinical circumstances.

Warfarin dose is the patient's regular dose. No loading.

POST-OPERATIVE:

	Date	Day	WARFARIN	CLEXANE DOSE & FREQUENCY
+1				
+2				
+3				
+4				
+5				

Check the following every 24-48 hours as indicated

- INR
- FBC
- anti-Xa in patients on Clexane who have significant renal impairment (GFR < 60 ml/min)
- LFTs, Albumin and Creatinine (twice weekly as indicated)

See intravenous heparin protocol for patients on standard heparin.

Signature: …… Position:…… Date: ……..

Laboratory results:

DATE	DAY	INR	Anti Xa	Notes

Intravenous Standard Heparin Protocols (300 units/ml Infusion)

Note: ***The following protocols are for infusional devices using 15,000 units of sodium heparin in 50 ml of normal saline (0.9% sodium chloride) and are not suitable for infusion pumps using lower concentrations***. Therapy is usually initiated with a bolus intravenous dose of heparin calculated by body weight, and then a heparin infusion commenced at the rate indicated below. The initial bolus dose is usually omitted following cardiothoracic surgery. It will often be appropriate to omit the bolus dose in the early postoperative period where there is a high risk of bleeding. If in doubt, discuss this with the surgeon responsible for the patient.

A. Heparin protocol for Acute Coronary Syndrome (STEMI and non-STEMI):

DOSAGE: Concentration = 15,000 units heparin sodium in 50ml normal saline. (300 units per ml)
Based on 12 units/kg/hr MAX:1000units/hr

WEIGHT (kg)	*BOLUS (units)*	*UNITS PER HOUR*	*Starting rate mL per hour**
50	3000	600	2
55	3300	660	2.2
60	3600	720	2.4
65	3900	780	2.6
70	4000	840	2.8
75	4000	900	3
80	4000	960	3.2
>80	4000	1000	3.3

The first APTT is taken six hours after commencing the infusion and the rate adjusted as below.

UNFRACTIONATED HEPARIN DOSAGE ADJUSTMENT PROTOCOL FOR CORONARY SYNDROME (STEMI AND NON STEMI)

Based on aPTT Normal Range of 25-35 Seconds & Infusion of 15,000units in 50mL 300 units/ml)

aPTT (seconds)	Bolus Dose IV	Stop Infusion	IV Rate Change (mL/hr)	Repeat aPTT
<35	2,000 units		increase 0.7 mL/hr from current rate	6 hours
<55	Nil	NO	increase 0.3 mL/hr from current rate	6 hours
55-75	**Therapeutic Range - No Change from current rate**			**Daily**
75-90	Nil	NO	reduce 0.3 mL/hr from current rate	6 hours
90-105	Nil	NO	reduce 0.7 mL/hr from current rate	6 hours
> 105	Nil	60 mins	Restart at 0.7mL/h less than previous rate	6 hrs

B. HEPARIN PROTOCOL FOR ATRIAL FIBRILLATION, VENOUS AND ARTERIAL THROMBOEMBOLIC DISEASE, PROSTHETIC HEART VALVES

DOSAGE: Concentration = 15,000 units heparin sodium in 50 normal saline (0.9% sodium chloride). (300 units per ml) Based on 18 units/kg/hour.

WEIGHT	*BOLUS*	*UNITS PER HOUR*	*Starting rate mL per hour**
50	3500	900	3
55	3500	990	3.3
60	5000	1080	3.6
65	5000	1170	3.9
70	5000	1260	4.2
75	5000	1350	4.5
80	5000	1440	4.8
85	5000	1530	5.1
90	5000	1620	5.4
95	7500	1710	5.7
100	7500	1800	6
110	7500	1980	6.6
>120	7500	2100	7

The first APTT is taken six hours after commencing the infusion and the rate adjusted as below.

IV UNFRACTIONATED HEPARIN DOSAGE ADJUSTMENT PROTOCOL FOR AF/VTED (TABLE 2)

Based on aPTT Normal Range of 25-35 Seconds & Infusion of 15,000units in 50mL

aPTT (seconds)	Bolus Dose IV	Stop Infusion	IV Rate Change (mL/hr)	Repeat aPTT
< 35	5,000 units	NO	increase 0.7 mL/hr from current rate	6 hours
35-45	Nil	NO	increase 0.7 mL/hr from current rate	6 hours
46-54	Nil	NO	increase 0.3 mL/hr from current rate	6 hours
55-90	**Therapeutic Range - No Change from current rate**			**Daily**
91-95	Nil	NO	decrease 0.3 mL/hr from current rate	6 hours
96-105	Nil	NO	decrease 0.7mL/hr from current rate	6 hours
> 105	Nil	60 mins	Restart at 0.7 mL/h less than previous rate	6 hrs

Notes on intravenous heparin:

1) A baseline full blood count, PT and APTT should be performed prior to heparin therapy. A Haematologist should be consulted if there are significant baseline abnormalities.
2) Full blood count should be performed at least three times per week, to exclude heparin induced thrombocytopenia and a fall in haemoglobin to suggest bleeding.
3) The possibility of a retroperitoneal bleed should be considered in the absence of another identified cause of pain in the back, leg, or abdomen. A full blood count should be performed and reviewed as soon as possible, as well as urgent medical assessment and imaging of the abdomen.
4) Where the therapeutic intention is anticoagulation for venous thrombo-embolism, non-steroidal anti-inflammatory drugs (NSAIDs) should be ceased to reduce the risk of bleeding.
5) In patients who have just had cardiac or great vessel surgery, consideration should be given to omitting the bolus dose of heparin. This should be discussed with the Cardiothoracic Surgeon.
6) If the patient has had a recent surgical procedure, anticoagulation should be discussed with the Surgeon prior to initiation, where possible.

Changing Between Intravenous Heparin and Clexane

Where a decision is made to change the patient from intravenous heparin to Clexane, the calculated dose of Clexane (see low molecular weight heparin protocol) should usually be administered as soon as the intravenous heparin is ceased, assuming the patient was not over-anticoagulated on heparin at the time.

If the patient were changed from subcutaneous Clexane to intravenous heparin, intravenous heparin would normally be commenced when the next dose of Clexane is due, assuming the patient was not over-anticoagulated at the time.