Peri-operative oral anticoagulant bridging

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Key Amendment

Date	Amendment	Approved by
21st January 2019	Inclusion of advice for edoxaban. Additional information for the management of medicines for diabetes	Medicines Safety Committee
25th June 2020	Document extended for 6 months during COVID-19 period.	QGC
4th January 2021	Pre-operative assessment Key Documents approved for 3 years	Pre-op Directorate Governance Meeting
27th December 2023	Extended document for 6 months whilst under review. Updated owner details.	Dr Harsha Mistry
12th November 2024	Document extended for 12 months whilst awaiting National Guidelines to inform if changes are required	Dr Harsha Mistry
6th May 2026	Document extended for 6 months to allow time for new owner Rachael Dolan to review and update	SCSD Governance

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Appendix

1. Introduction

When patients on anticoagulation require an invasive procedure the risks and benefits of stopping or continuing anticoagulation must be considered. This guideline is to be used in conjunction with the Trust Key document: *Warfarin and Other Oral Anticoagulants Guidelines and Procedures WAHT-HAE KD 017.*

This guideline gives specific advice on how to identify patients who require pre-operative anticoagulation bridging and on how to deliver that bridging. Each case should however be considered individually and haematology or cardiology should be consulted for any complex cases or in cases where there is uncertainty.

When considering bridging a patient peri-operatively it is important to consider:

1. The bleeding risk of surgery and of bridging
2. The thrombotic risk

The bridging therapy recommended for a patient is a balance of the bleeding and thrombotic risks.

The first part of the guideline gives advice on identifying bleeding and thrombotic risk. The second part of the guideline gives advice on how to bridge. This guideline recommends bridging using Low Molecular Weight Heparin, which currently is enoxaparin within Worcestershire Acute Hospitals NHS Trust.

2. Assessing Bleeding Risk

Cessation of anticoagulation and bridging therapy is usually offered to those patients whose surgery carries a risk of problematic bleeding while on anticoagulation. Some procedures may be performed on patients without interrupting their anti-coagulation. These include:

- Minor dental procedures including extractions and root canal work
- Pacemaker insertion
- Cataract surgery (unless specified by eye unit)
- Joint injections
- Soft tissue injections
- Skin biopsy on areas where pressure can be directly applied

Bridging does carry a risk of peri-procedural bleeding. A group of patients need to be carefully considered regarding whether the risks of bridging would outweigh the benefits. As per the 2017 American College of Cardiology guideline on bridging for AF these patients include[8]:

- Patients who have had a major bleed, including intra-cranial haemorrhage within 3 months
- Patients with quantitative or qualitative platelet abnormality (including aspirin use)
- Patients with labile INR which is above the therapeutic range (i.e. over 3 for most cases)
- Patients who have had a previous bleed during peri-procedural bridging therapy

3. Assessing Thrombotic Risk

The below table can be used to identify the thrombotic risk.

Table 2. Risk factors indicating Thrombotic Risk

Thrombosis Risk	Indication for Warfarin Therapy		
	Atrial Fibrillation	Thrombo-embolism	Mechanical Heart Valve
Low	- Non-valvular AF - INR target is 2-3	- Single previous VTE more than 12 months ago	
Medium	•AF associated with TIA / CVA more than 12 weeks ago •AF associated with active cancer	- Previous VTE (i.e. DVT or PE) within 12 weeks to 12 months - VTE associated with active cancer - Multiple VTE previously (i.e. 2 or more)	Bi-leaflet mechanical aortic valve with no other risk factors for stroke (i.e. no AF, / heart failure / hypertension/ diabetes / previous CVA or TIA, age under 75)
High	•Rheumatic valvular heart disease with AF - Recent ischaemic TIA/CVA within 12 weeks (discuss with haematology, ideally defer surgery, if possible) - Cardioversion or ablation for atrial fibrillation within the last month	- VTE (i.e. DVT or PE) within 12 weeks (discuss with haematology, ideally defer surgery if possible) - TIA/CVA within 12 weeks (discuss with haematology, ideally defer surgery if possible) - INR target of 3-4 - Severe thrombophilia (i.e. antithrombin deficiency or antiphospholipid antibodies) - Recurrent VTE *on* anticoagulation	- Bi-leaflet aortic valve with one or more risk factor for stroke (i.e. AF, heart failure, age >75, hypertension, diabetes, previous TIA/CVA) - Aortic caged ball/tilting disc heart valves - Mechanical mitral valve - INR target 3-4

1. **Table 3. Pre-operative Bridging Protocol according to thrombotic risk for patients taking warfarin**

Thrombus risk	Day -6	Day-5	Day-4	Day -3	Day-2	Day-1	Day 0 (day of Surgery)
Low Risk	Take last dose of normal Warfarin					**Measure INR and consider oral Vitamin K (1mg) if INR is above 1.5**	
Medium Risk	Take last dose of normal Warfarin			**Take prophylactic LMWH as per weight and renal function*** **Take at 8AM**	**Take prophylactic LMWH as per weight and renal function*** **Take at 8AM**	**Take prophylactic LMWH as per weight and renal function*** **Take at 8AM** **Measure INR – if above 1.5 please discuss with haematology consultant. Surgery may need to be deferred if safe to do so.**	**No LMWH given in the AM**
High Risk **Target INR 2-3**	Take last dose of normal Warfarin			***Commence therapeutic dose LMWH****	***continue therapeutic dose LMWH****	***Continue therapeutic dose LMWH**** **If on twice daily LMWH regime then no LMWH should be given after 8AM (i.e. omit evening dose)** **Measure INR – if above 1.5 please discuss with haematology consultant. Surgery may need to be deferred if safe to do so.**	**No LMWH given in the AM** **If IV Heparin given stop 6 hours before surgery.**
High Risk **Requires heparin infusion**	Take last dose of normal Warfarin			**Check INR:** **If INR below 2 start bridging** *Take therapeutic dose LMWH** **OR** **If INR over 2 recheck INR on day -2**	**If bridging has been started on day -3:** *continue bridging with therapeutic dose LMWH** **OR** **If INR rechecked and found to be below 2:** *start bridging with therapeutic dose LMWH**	**If bridging has been commenced:** *continue bridging with therapeutic dose LMWH** **If on twice daily LMWH regime then no LMWH should be given**	**No LMWH given in the AM** **If IV Heparin given stop 6 hrs pre op.**

				IF IV Heparin has been recommended by *cardiology consultant* then admit to ward for INR check and commence heparin as per Trust protocol	**If IV Heparin has been commenced then continue as per Trust protocol** **If INR is still above 2 then recheck on day -1**	**after 8AM (i.e. omit evening dose)** **If IV Heparin has been commenced then continue as per Trust protocol** **If INR is above 1.5 then discuss with haematology**	**Check clotting after 4-5 hrs. if bleeding risk high/neuraxial anaesthetic**

***For details of dose adjustment in renal failure or extremes of weight please see below**

2. Table. 4 Post-operative Bridging Protocol according to thrombotic risk for patients taking Warfarin

Thrombus risk	Day of Surgery	Post operatively
Low Thrombotic Risk	- Consider prophylactic LMWH if indicated for VTE prevention to be given at least 6-8 hours after wound closure - Restart Warfarin 12-24 hours after surgery at the usual maintenance dose providing haemostasis secure AND no epidural in place AND no plans to return to theatre	- Arrange for INR check after 3 days on warfarin - Patients discharge arrangements should not be affected by use of pre-operative warfarin - If a course of LMWH is indicated for postoperative VTE prevention then this should be given as usual. However once INR is therapeutic (i.e. over 2) patient should be told not to take LMWH to avoid concomitant anticoagulation
Medium Thrombotic Risk	- Commence prophylactic LMWH to be given at least 6-8 hours after wound closure when haemostasis secure - If bleeding risk is high, or haemostasis not secure, delay the first dose of enoxaparin for 24 hours and reassess bleeding risk before commencing - Restart Warfarin 12-24 hours after surgery providing haemostasis secure AND no epidural in place AND no plans to return to theatre. It is reasonable for 1st dose of postop warfarin to be double the usual dose (reduces time to therapeutic INR). - If epidural in place continue prophylactic LMWH until epidural removed (must be removed 12 hours after a prophylactic LMWH dose and 6 hours before next LMWH dose) then restart Warfarin once epidural removed as above.	- Patients discharge arrangements should not be affected by use of pre-operative warfarin - If in-patient following surgery, perform daily INR checks - If discharged (i.e. day case) arrange for INR check after 3 days on warfarin - Continue prophylactic LMWH until INR is therapeutic (i.e. over 2) - Stop prophylactic LMWH when INR is therapeutic (i.e. over 2)
High Thrombotic Risk	- Commence prophylactic LMWH to be given at least 6-8 hours after wound closure when haemostasis secure. If bleeding risk is high consider starting prophylactic LMWH 24 hours after wound closure. - If post operative bleeding risk is low: consider up-titrating LMWH to therapeutic dose on postoperative day 1 (provided haemostasis secure) - If post operative bleeding risk is high (i.e. radical prostatectomy): consider up titrating LMWH to therapeutic dose 48 hours following surgery (providing haemostatis secure). - Restart Warfarin 12-24 hours after surgery at usual maintenance dose providing haemostasis secure AND no epidural in place AND no plans to return to theatre. It is reasonable for 1st dose of postop warfarin to be double the usual dose (reduces time to therapeutic INR). - If epidural in place do not start warfarin and continue LMWH until epidural removed (must be removed 24hrs after a dose and 6 hours before next dose). These cases should be discussed with haematology.	- Check INR daily - Continue therapeutic dose LMWH until INR is therapeutic (i.e. over 2) - Ensure patient has appointment for INR follow up within 3-5 days of discharge or sooner if INR subtherapeutic - Stop treatment dose LMWH when INR therapeutic - If IV heparin infusion has been started stop when INR therapeutic

	- On specialist advice (i.e. haematology/cardiology), IV heparin infusion may be required postoperatively instead of LMWH. Follow prescribing and monitoring guidance on the dedicated prescription chart. Usually a loading dose will be needed.	

4. Dosing of Low Molecular Weight Heparin

Enoxaparin is the LMWH used within Worcestershire Acute Hospitals NHS Trust.

The standard prophylactic dose is 40mg once a day. Adjustments are required for weight and renal function - these are detailed below.

The therapeutic dose of enoxaparin recommended is 1mg/kg given every 12 hours. This has the advantage of steadier pharmacokinetics and more efficient anticoagulation than a once daily regime. Therefore this regime is particularly advantageous in patients with mechanical heart valves, recurrent thromboembolism on anticoagulation and severe thrombophillia. Dose adjustments for renal function and weight are given below. Where the 1mg/kg BD dosing regime is used it is important that the last dose is given 24 hours prior to surgery (i.e. the last dose could be given at 8AM on the day before surgery).

A once a day regime for therapeutic enoxaparin could be acceptable in some cases, for example when the patient has a strong preference for once daily injections. The recommended dose is 1.5mg/kg given every 24 hours. Dose adjustments for renal function and weight are given below. If this dosing regime is used it is important that the last dose is given 24 hours prior to surgery (i.e. the last dose could be given at 8AM on the day before surgery).

5. Enoxaparin dose adjustment in renal failure

Patients who are being considered for LMWH bridging should have a U and E checked and Creatinine Clearance calculated within 3 months of their operation date.

The Creatinine Clearance should be calculated, particularly at the extremes of weight or borderline renal function. The Cockroft Gault equation may be used:

$$\frac{(140 - \text{age}) \times \text{weight (kg)} \times 1.04 \text{ (female) or } 1.23 \text{ (male)}}{\text{serum creatinine (micromol/l)}}$$

Alternatively the patients Cr Clearance, as given by the CKD-EPI equation, can be used (provided automatically by ICE).

Table 5. Enoxaparin dose adjustments in renal impairment

eGFR – EPI formula	Enoxaparin: Treatment Dose Reduction	Enoxaparin: Prophylactic dose reduction	Anti Factor X Monitoring
< 15mls/min (and not dialysed)	D/W Haematology – unfractionated heparin will be required rather than Enoxaparin	D/W Haematology. Unfractionated heparin may be required rather than enoxaparin i.e. heparin calcium 5000units BD	Not routinely required*
20-30mls/min	1mg / KG given once a day at 8AM	Give 20mg SC given once a day	Not routinely required*
> 30mls/min	No dose reduction required	No dose reduction required	Not routinely required*

6. Enoxaparin dose adjustment according to weight

Table 6. Enoxaparin dose adjustments in extremes of weight

Weight	**Enoxaparin: therapeutic dose adjustment**	**Enoxaparin: prophylactic dose adjustment**	**Anti Factor X Monitoring**
30-50kgs	D/W Haematology	Give 20mg SC once a day	Not routinely required*
50-100kgs	Use therapeutic dose as detailed above if renal function normal	Give 40mg SC once a day	Not routinely required*
100-150 kgs	Use therapeutic dose as detailed above if renal function normal	Give 40mg SC twice a day Last dose to be given **no later than 12 hours** before surgery (i.e no later than 8 pm on day before surgery)	Consider for treatment doses in morbidly obese patients
Over 150 kgs	Use therapeutic dose as detailed above if renal function normal	Give 60mg SC twice a day Last dose to be given **no later than 12 hours** before surgery (i.e no later than 8 pm on day before surgery)	Consider for treatment doses in morbidly obese patients

*Anti Factor Xa monitoring is not routinely required as it takes many days to accumulate and is not usually required for patients who have only 3 days of pre-operative Enoxaparin

Enoxaparin comes as Clexane in 20,40,60,80 and 100 mg preparations. It is also available as 120mg/0.8ml and 150mg/ml preparations (Clexane Forte). Clexane Forte 150mg/ml has 3mg graduations on the syringe which makes it easier to titrate: a certain amount of drug can be wasted prior to administration.

The exact dose can be difficult to titrate due to availability of pre-filled syringes, therefore the following tables detail how to prescribe enoxaparin assuming the use of Clexane Forte 150mg/ml which has 3mg graduations. Guidance on 1mg/kg BD and 1.5mg/kg OD is given.

Table 7. Dose banding for Enoxaparin 1mg/kg BD Regime with Cr Clearance >30mls/minute

Patient Weight (kgs)	Recommended formulation	Syringe label	Dose	Injection Volume (ml)
40	100mg / ml Solution for Injection CLEXANE syringes	40mg / 0.4ml	40mg BD	0.4
45		60mg / 0.6ml	45mg BD	0.45
50		60mg / 0.6ml	50mg BD	0.5
55		60mg / 0.6ml	55mg BD	0.55
60		60mg / 0.6ml	60mg BD	0.6
65		80mg / 0.8ml	65mg BD	0.65
70		80mg / 0.8ml	70mg BD	0.7
75		80mg / 0.8ml	75mg BD	0.75
80		80mg / 0.8ml	80mg BD	0.8
85		100mg / 1ml	85mg BD	0.85
90		100mg / 1ml	90mg BD	0.9
95		100mg / 1ml	95mg BD	0.95
100		100mg / 1ml	100mg BD	1
105	150mg / ml Solution for Injection CLEXANE FORTE syringes	120mg / 0.8ml	105mg BD	0.7
110		120mg / 0.8ml	110mg BD	0.74
115		120mg / 0.8ml	115mg BD	0.78
120		120mg / 0.8ml	120mg BD	0.80
125		150mg / 1 ml	125mg BD	0.84
130		150mg / 1 ml	130mg BD	0.88
135		150mg / 1 ml	135mg BD	0.90
140		150mg / 1 ml	140mg BD	0.94
145		150mg / 1 ml	145mg BD	0.98
150		150mg / 1 ml	150mg BD	1

Table 8. Dose banding for Enoxaparin 1.5 mg/kg OD Regime with Cr Cl >30mls/minute

Patient Weight (kgs)	Recommended formulation	Syringe label which can be used	Ideal Dose to be prescribed	Injection Vol (ml) which must be given
40	100mg / ml Solution for Injection CLEXANE syringes	60mg / 0.6ml	60mg OD	0.6
45		80mg / 0.8ml	68mg OD	0.7
50		80mg / 0.8ml	75mg OD	0.75
55		100mg / 1ml	83mg OD	0.85
60		100mg / 1ml	90mg OD	0.9
65		100mg / 1ml	98mg OD	1
70	150mg / ml solution for injection CLEXANE FORTE SYRINGES	120mg / 0.8ml	105mg OD	0.7
75		120mg / 0.8ml	113mg OD	0.75
80		120mg / 0.8ml	120mg OD	0.8
85		150mg / 1ml	128mg OD	0.85
90		150mg / 1ml	135mg OD	0.9
95		150mg / 1ml	143mg OD	0.95
100		150mg / 1ml	150mg OD	1
105		150mg / 1ml	158mg OD	1
110	Contents of two syringes required.	100mg/1ml plus 80mg/0.8ml	165mg OD	1ml *(100mg/ml)* + 0.65ml (*80mg/0.8ml)*

115		100mg/1ml plus 80mg/0.8ml	173mg OD	1ml *(100mg/ml)*+ 0.75ml *(80mg/0.8ml)*
120		100mg/1ml plus 80mg/0.8ml	180mg OD	1ml *(100mg/ml)* + 0.8ml *(80mg/0.8ml)*
125		100mg/1ml plus 100mg/1ml	188mg OD	1ml *(100mg/ml)* + 0.9ml *(100mg/ml)*
130		100mg/1ml plus 100mg/1ml	195 OD	1ml *(100mg/ml)* + 0.95ml *(100mg/ml)*
135		120mg/0.8ml plus 100mg/ml	202mg OD	0.8ml *(120mg/0.8ml)* + 0.82ml (*100mg/ml)*
140		120mg/0.8ml plus 100mg/ml	210mg OD	0.8ml *(120mg/0.8ml)* + 0.9ml *(100mg/ml)*
145		120mg/0.8ml plus 100mg/ml	218mg OD	0.8ml *(120mg/0.8ml)* + 0.98ml *(100mg/ml)*
150		150mg/1ml plus 80mg/0.8ml	225mg OD	1ml *(150mg/ml)* + 0.75ml *(80mg/0.8ml)*

7. The timing of commencing bridging

Generally bridging is recommended once a patients INR falls below 2.

Warfarin has a long mean half life (40 hours) meaning that its offset of action is delayed for several days after stopping. In stable patients who maintain a stable INR of between 2 to 3, the INR *should* reliably start falling after 48hours off Warfarin.

As a safety precaution however the patient should be asked to have an INR check within 72 hours of the bridging plan starting. If this INR is below 4 then it is appropriate for them to commence the bridging plan as discussed. If the INR is above 4 then please discuss this with the haematology on call SpR or consultant.

In patients who maintain an INR of between 3-4 the INR could take longer to fall to below 2. In these patients it is recommended that bridging is commenced when the INR falls below 2 to avoid concomitant use of anticoagulation.

Ideally therefore the INR should be checked on day -3 before surgery in those patients who maintain an INR of 3-4. If it is found to have fallen below 2 then bridging should be commenced. If it is above 2 then the INR should be checked the following day.

In some situations it might not be possible to check the INR (i.e. day -3 will fall on a weekend for those patients having surgery on a Tuesday or Wednesday). In this situation the patient should commence

enoxaparin anticoagulation as planned on day -3 before surgery accepting the low risk of concomitant anticoagulation prior to surgery being outweighed by the benefit of bridging.

8. Prescribing bridging anticoagulation

Whenever possible the pre-operative clinic should prescribe bridging enoxaparin. If the patient lives a long distance from the hospital and will have problems in travelling to a site to collect a prescription it may be appropriate to ask the GP to prescribe enoxaparin but detailed advice must be provided. The prescription may be on a green FP10 prescription form which will enable the patient to collect their bridging therapy from their local pharmacy. Alternatively if an FP10 prescription form is not available a standard Trust prescription can be given which will enable the patient to collect their bridging therapy from the Trust pharmacy.

Usually therapeutic dose enoxaparin is commenced when the INR falls below 2. The patient must be given this information in written format. A bridging plan should be given to the patient using the BlueSpier bridging template.

A recommended format for prescribing bridging enoxaparin is to write

Enoxaparin
Inject xx mg subcutaneously XXce a day starting on the morning of xx/xx/xx
Omit the evening dose on the day before surgery (i.e. if prescribed twice a day)

For patients who undergo preoperative assessment at Kidderminster Treatment Centre the RMO may prescribe the bridging plan, only if they are given clear written instructions on what to prescribe and when this should be commenced.

9. Cancellation of surgery for patients who are on oral anticoagulants

If surgery is cancelled the admitting surgeon is responsible for arranging instructions regarding continuation of bridging or discontinuation and conversion back to an oral anticoagulant.
Generally, if surgery is to be postponed for less than 1 week then it is reasonable to continue with bridging therapy. If surgery is to be postponed for more than 1 week then it may be more appropriate to follow post-operative anticoagulation instructions as described above (i.e. restart warfarin and continue Enoxaparin until INR therapeutic for 2 consecutive readings).

10. Direct oral anticoagulant agents (DOACS) i.e. Dabigatran, Apixaban, Rivaroxaban or Edoxaban

For full guidance on bridging for patients on DOAC therapy please see Trust guideline WAHT KD 017 Warfarin and Other Oral Anticoagulants Guidelines and Procedures. A summary is included below.

Apart from Dabigatran there is no specific reversal for these anticoagulant drugs.
Their short half-life means they should be cleared from the circulation within 24 hours of the last dose (unless there is renal dysfunction). Because of the short period of discontinuation bridging with LMWH between stopping the DOAC and surgery is rarely, if ever, needed. In some cases where there is high thrombotic risk (i.e. DVT/PE/TIA or CVA within 3 months / severe thrombophilia) it is advisable to discuss with haematology about whether bridging might be required.

Current Trust guidance recommends that for elective surgery these agents should be stopped 48 hours prior to procedure. Post-operatively they can be recommenced at least 6 hours postoperatively if haemostasis secure, no epidural in place and patient is able to take oral medications. If patient is unable

to take oral medications then enoxaparin (prophylactic dose) should be considered. If patient is NBM for over 48 hours postoperatively please discuss with haematology.

Day -3	Day -2	Day -1	Day of surgery	Post-operatively
Take DOAC dose as normal (see below if dabigatran)	Withhold DOAC (see below if dabigatran)	Withhold DOAC (see below if dabigatran)	Withhold DOAC. Restart DOAC at least 6 hours after surgery if haemostasis secure and patient tolerating oral medication. If epidural in situ withhold DOAC. Prophylactic LMWH will usually be recommended.	Continue DOAC if patient tolerating oral medications. If patient NBM consider prophylactic dose Enoxaparin. If NBM for over 48 hrs then d/w haematology. Enoxaprin sc prophylaxis in patients with an epidural, must leave 4 hours after catheter removal for next dose of LMWH.

Dabigatran:

The clearance of Dabigatran is dependent on renal function and in cases where eGFR is reduced it is necessary to stop Dabigatran for longer.

Check Renal function (CrCl in ml/min):

Estimated Glomerular Filtration Rate (ml/minute)	Cessation of Dabiagtran
≥80	Stop Dabigatran for 48 hours (2 days) prior to surgery
50-79	Stop Dabigatran for 72 hours (3 days) prior to surgery
30-49	Stop Dabigatran for 96 hours (4 days) prior to surgery

Preoperatively:

- Stop dabigatran as indicated by renal function above
- Bridging anticoagulant therapy with unfractionated heparin or low molecular weight heparin (such as enoxaparin) may be needed in very high-risk thromboembolic patients who are stopping dabigatran (for example PE/DVT or ischaemic CVA within the last 3 months) and who require longer duration of anticoagulant interruption for reasons including renal insufficiency. In such patients discussion with haematology is advised.

Postoperatively:

- Start prophylactic LMWH, if indicated, when haemostasis is secure.
- Restart dabigatran at usual dose and stop LMWH when eating and no epidural in place.
- Leave 12 hours between last dose of LMWH and first dose Dabigatran

Apixaban:

Preoperatively:

- Stop apixaban 48 hours from procedure
- Check coagulation screen (PT and APTT) prior to procedure, if abnormal discuss with Clinical Haematology

Postoperatively:

- Start prophylactic LMWH when haemostasis is secure.
- Restart apixaban at usual dose and stop LMWH when eating and if no epidural in place.
- Leave 12 hours between last dose of LMWH and first dose apixaban

Rivaroxaban

Preoperatively

- Stop rivaroxaban 48 hours from procedure
- Check coagulation screen (PT and APTT) prior to procedure, if abnormal discuss with Clinical Haematology

Postoperatively

- Start prophylactic LMWH when haemostasis is secure.
- Restart rivaroxaban at usual dose and stop LMWH when eating and if no epidural in place.
- Leave 12 hours between last dose of LMWH and first dose rivaroxaban

Appendix 1

ADULT INTRAVENOUS HEPARIN TREATMENT CHART

Worcestershire NHS
Acute Hospitals NHS Trust

ADDRESSOGRAPH

Name:.....

Hosp No:

NHS No:

D.O.B..... Male Female

ALLERGIES/ADVERSE DRUG REACTIONS

NONE KNOWN ☐ Signature:

DATE	DRUG/FOOD/OTHER	REACTION DETAILS

CONSULTANT:	WARD:		WEIGHT: .....KG

INITIAL LOADING DOSE

Heparin Sodium 5000 units to be given intravenously over 5 minutes as a stat dose

Prescribed by:		Date:	Time:
Given by:	Checked by:	Date:	Time:

CONTINUATION INFUSION

Heparin Sodium 40,000 units in 40mls to be given by intravenous infusion via a syringe pump.

Initial rate ..... ml/hr. Check APTT ratio 6 hours after commencing infusion.

Prescribed by:	Date:	Time:

SYRINGE MUST BE CHANGED EVERY 24 HOURS REGARDLESS OF DOSE

Date	APTT ratio	Time	Infusion Rate ml/hour	Rate		Syringe Preparation	
				Set by SIGN	Checked by SIGN	Prepared by SIGN	Checked by SIGN

FILE IN INPATIENT SECTION OF MEDICAL NOTES

WR1762 - Version 1 - Issued:Oct 2008

ADULT INTRAVENOUS HEPARIN TREATMENT CHART

GUIDANCE FOR USE

1. Perform a Full Blood Count and coagulation screen (refer to Pathology Handbook) and document these baseline results before prescribing heparin.

2. Heparin must also be prescribed in the Regular Drugs section of the Trust Inpatient Prescription Chart, referring to this chart for prescription specifics.

DRUG (APPROVED NAME) Heparin Infusion			08:00
DOSE See IV Heparin Treatment Chart	ROUTE	DIRECTIONS	12:00
START DATE 01/06/08	SIGNATURE A. Prescriber	BLEEP 999	18:00 22:00
PHARMACY USE			

3. All Heparin Infusions must be prepared using Heparin Sodium (unfractionated Heparin) 1000 units/ml ampoules.

4. An initial IV loading dose of 5000 units should be prescribed and given over 5 minutes (by completing the preprinted prescription overleaf).

5. The continuation infusion should also be prescribed overleaf, dose and rate determined by reference to the table below (based on 18 units/kg/hour) and the time at which the initial APTT ratio should be checked should also be defined (6 hours after starting infusion).

Weight (kg)	Initial rate (ml/hour of 1000 units/ml)
41 - 50	0.8
51 - 60	1.0
61 - 70	1.2
71 - 80	1.4
> 80	1.6

5. Prepare an IV infusion 1000 units/ml i.e. 40,000 units/40mls and commence the infusion at the prescribed rate overleaf.

6. Measure the APTT ratio 6 hours after starting the infusion as above, and then adjust the rate as per the Heparin Infusion Schedule table below, to maintain the patient APTT ratio between 1.5 and 2.5

7. Once the APTT ratio is stable, the ratio can be checked daily. If the rate (dose) is changed in any respect, the ratio must be re-checked 6 hours after any change (or sooner as indicated in the heparin infusion schedule below)

HEPARIN INFUSION SCHEDULE

APTT ratio	Infusion Rate Change
<1.2	IV bolus 5000 units and increase rate by 0.4ml/hour Repeat APTT after 4 hours
1.2 - 1.4	Increase rate by 0.2ml/hour
1.5 - 2.5	**No change**
2.6 - 3.0	Reduce rate by 0.1ml/hour
3.1 - 4.0	Reduce rate by 0.2ml/hour
4.1 - 5.0	Reduce rate by 0.3ml/hour
> 5	Stop for 1 hour and reduce rate by 0.5ml/hour. Repeat APTT after 4 hours

Appendix 2. BlueSpier patient information sheet for therapeutic dose bridging

It has been recommended that you pause your blood thinning medication called Warfarin prior to surgery.

You will be asked to come off Warfarin for 5 days prior to surgery (i.e. the last dose is given on the 6th day before surgery).

It has been recommended that you take an anti-coagulation injection while you are off warfarin. This is usually an injection called clexane (or enoxaparin).

You should be provided with information and a special bin to dispose of any sharps from the injection.

Please ensure you have your INR checked within 72 hours of starting these injections. If your INR is markedly higher than normal (i.e. over 4) please discuss with your preoperative assessment nurse or clinic.

A typical schedule for stopping your anticoagulation is as follows:

Day	**Action**
Day -6	Take your last dose of warfarin
Day -5	Do not take warfarin
Day-4	Do not take warfarin
Day -3	Start anti-coagulation injection as prescribed. This will usually be either once a day at 8AM ***OR*** twice a day at 8AM and 8PM.
Day -2	Continue anti-coagulation injection as prescribed. This will usually be either once a day at 8AM ***OR*** twice a day at 8AM and 8PM.
Day -1	Continue anti-coagulation injection as prescribed BUT DO NOT TAKE ANY ANTI-COAGULATION INJECTION AFTER 8AM.
Day of Surgery	Do not take any anticoagulation injections before surgery (you may be given one afterwards)

If you have any questions about your anticoagulation plan please contact your Pre Operative Assessment Nurse or clinic.

Appendix 3. Terminology

Prosthetic heart valve: Umbrella term used to describe either bioprosthetic or mechanical heart valves which are implanted to replace a patient's own diseased valve.

Bioprosthetic valve: sometimes also called tissue valve, biological valve or xenograft. These valves are manufactured using animal tissue and usually don't require the long term use of anti-coagulation and therefore does not require bridging.

Mechanical valve: Made using synthetic metal material. May be harder wearing than bioprosthetic heart valves. There is a tendency for thrombus to form on the valve so lifelong treatment with an oral anticoagulant (i.e. warfarin) is needed to prevent this.

Bi-leaflet valve: A type of mechanical heart valve consisting of two semicircular leaflets which are attached to the valve housing. These provide more natural blood flow than other mechanical heart valves and have the lowest thrombogenic risk of all mechanical heart valves. These may be implanted into the mitral or aortic position.

Tilting disc valve: Sometimes called a Bjork-Shiley valve, these consist of a metal ring which holds a disc which opens and closes as blood is pumped through the valve. These have a high tendency to form blood clots and may require a higher target INR.

Caged ball valve: Early type of mechanical heart valve consisting of a metal cage with a ball within. These have a high tendency to form blood clots and usually require a higher target INR. They are now discontinued but may still be seen. Sometimes called a Starr Edwards valve.

Valve repair: Mitral valve repair is performed, usually for mitral valve regurgitation. The repair may be performed with or without an annuloplasty ring. Anticoagulation is usually not required unless for other reasons i.e. presence of AF. Therefore bridging is not required.

Appendix 4. Bridging for Prosthetic heart valves

Anticoagulation for patients with prosthetic heart valves during non-cardiac surgery requires careful management based on risk assessment. It is recommended not to interrupt oral anticoagulation for most minor surgical procedures (see 'Assessing Bleeding Risk' above) or in those procedures where bleeding is easily controlled.

The 2014 AHA/ACC Guideline for the Management of Patients with Valvular Heart Disease recommends that bridging anticoagulation with either Unfractionated Heparin (UFH) or subcutaneous LMWH is used during the time interval when the INR is sub-therapeutic preoperatively in patients who are undergoing invasive or surgical procedures with a 1) mechanical AVR and any thromboembolic risk factor, 2) older-generation mechanical AVR, or 3) mechanical MVR. *(Level of Evidence: C).*

The 2017 European guideline advises that UFH remains the only approved heparin treatment in patients with mechanical prostheses and that intravenous administration should be favoured over the subcutaneous route, especially where there is high thrombotic risk. However it does acknowledge that the use of subcutaneous LMWH, although off-label, is an alternative to UFH for bridging. The advantages and disadvantages of heparin and LMWH are summarised in the table below.

Table 1. Comparison of intravenous heparin infusion and low molecular weight heparin for use in heart valves

Intravenous Heparin Infusion
Advantages • Can be monitored using APTTr • Minimises time off anticoagulation, as can be stopped 6 hours before surgery • Can be reversed in the event of haemorrhagic complication Disadvantages • Variable patient response resulting in subtherapeutic anticoagulation (in around 50% of cases according to Nottingham Audit Data) • Frequent prolonged interruptions to infusion due to hardware and IV access faults (in around 50% of cases according to one paper) • Requires inpatient stay, typically for 3 days prior to surgery and post operatively until the INR is therapeutic
Low Molecular Weight Heparin
Advantages • Can be administered in an outpatient setting • More cost-effective than heparin infusion • Reliable pharmacokinetics and may offer more predictable anticoagulation Disadvantages • Remains an 'off label' use for patients with mechanical heart valves • Cannot be reversed in the event of haemorrhagic complication • Results in longer period off anticoagulation prior to the procedure, as last dose is typically given 24 hours before planned surgery

Please discuss the bridging plan with the patients regular cardiology consultant. LMWH is preferred for most patients because of its advantages over heparin infusion. However in some instances it might be necessary to arrange preoperative IV Heparin infusion on cardiology advice. Such patients typically include:

- Patients with older style caged ball valves
- Patients with multiple prosthetic cardiac valves
- Patients high higher target INR (i.e. 3-4)
- Patients who have had previous valve thrombus
- Patients who have experienced TIA/CVA when previously bridged

When IV heparin infusion is administered it should be administered according to the Trust IV Heparin protocol (WR1762) and recorded on the dedicated IV heparin treatment chart (appendix 1).

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