

# **Bridging anticoagulation: the peri-procedural management of patients on oral anticoagulants (excluding neurosurgery)**

Reproduced and Adapted from the Sheffield Bridging Anticoagulation Guideline April 2013 (with permission from the authors Joost Van Veen and Jannat Muen, Sheffield Teaching Hospitals)

Version 2.2

Working Group:

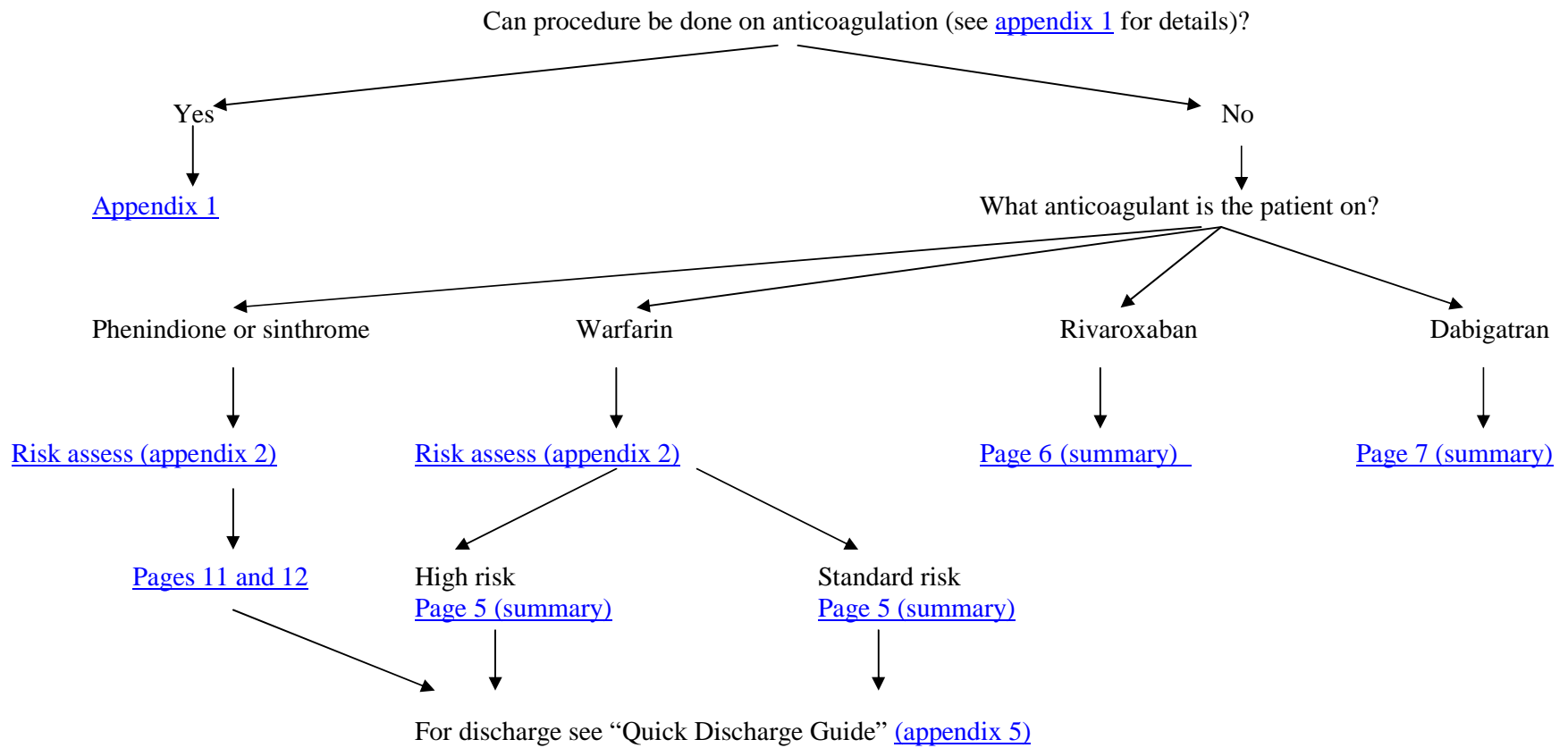
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**GPs should not be asked to prescribe or monitor bridging anticoagulation.**

Prior to the procedure, management should be by the medical/surgical team looking after the patient (maybe via pre-op assessment clinic if applicable). Following discharge from hospital, the patient should be referred to the Pre-Assessment Clinic or appropriate wards.



**SUMMARY OF BRIDGING ANTICOAGULATION FOR PATIENTS ON WARFARIN**

**Pre-operative summary for patients on warfarin**

**Standard Thrombotic Risk**

Day -5	Day -4	Day -3	Day -2	Day -1	Surgery
Last dose of warfarin	Omit warfarin	Omit warfarin	Omit warfarin	Check INR: if greater than 1.5 give 1mg oral vitamin K.  Prophylactic dalteparin at least 12 hours before surgery	Check INR if greater than 1.5 on day -1

**High Thrombotic Risk**

Day -5	Day -4 and Day-3	Day -2	Day -1	Surgery
Last dose of warfarin	Omit warfarin	Check INR:  -If greater than 2 give 1mg vit K orally and recheck day -1  - If 1.5 – 2.0 give 1mg oral vit K and recheck day -1. Start on twice daily dalteparin.  - If equal or less than 1.5 start twice daily dalteparin.	Recheck INR if greater than 1.5 on day -2 and give 1mg vit K if greater than 1.5  Last dose of therapeutic dalteparin in the morning (24 hours pre-op)	Check INR if greater than 1.5 on day -1

**Post-operative summary for patients on warfarin:**

**Standard Thrombotic Risk**

Surgery	D +1	D+2	D+3	D+4	D+5	D + 6
Prophylactic dalteparin OD 6 – 8 hrs post op	Warfarin at usual dose. Continue prophylactic dalteparin	Continue warfarin at usual doses <b>and</b> prophylactic dalteparin until INR is greater than 2.0 in patients with VTE or discharge in patients with AF.				

**High Thrombotic Risk**

Surgery	D +1	D+2	D+3	D+4	D+5	D + 6
Prophylactic dalteparin OD 6 – 8 hrs post op	Warfarin at usual dose Continue prophylactic dalteparin	Warfarin at usual dose.	Warfarin at usual dose. Increase prophylactic dalteparin as per bridging prescription chart	Warfarin at usual dose.	Warfarin at usual dose. Increase dalteparin as per bridging prescription chart. Continue until INR is greater than 2.0	

**Treatment should be reviewed daily.** Doses should only be escalated when haemostasis is secure. Pay particular attention if the patient is at high bleeding risk and seek advice if there are any concerns. If overt bleeding is present, stop anticoagulation and discuss with consultant in charge and a haematologist. After minor procedures *with* low bleeding risk, high dose LMWH and warfarin may be restarted **at earliest** 24 hours after the procedure

## SUMMARY OF BRIDGING ANTICOAGULATION FOR PATIENTS ON THERAPEUTIC RIVAROXABAN (15mg/20mg)

### Pre-operative summary for patients on rivaroxaban

#### Major Surgery or High Bleeding risk or spinal/epidural anaesthesia on 15mg OD/BD or 20mg rivaroxaban OD

<b>-3d -72hr</b> – Omit rivaroxaban if CrCl 15 – 30ml/min* – Last rivaroxaban dose if CrCl >30ml/min  * Rivaroxaban contra-Indicated if CrCl < 15ml/min	<b>-2d -48hr</b> Omit rivaroxaban	<b>-1d -24hr</b> Omit rivaroxaban	<b>Surgery</b> Omit rivaroxaban. Check PT/APTT/TT in all. (Aim normal PT) Check anti Xa if - CrCl <30ml/min and PT normal. - Co-existent coagulopathies causing PT prolongation cannot be excluded
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#### Minor procedure and Low Bleeding risk on 15mg or 20mg rivaroxaban OD

<b>-3d -72hr</b> Rivaroxaban	<b>-2d -48hr</b> Omit rivaroxaban if CrCl <30ml/min Last rivaroxaban dose if CrCl >30ml/min	<b>-1d -24hr</b> Omit rivaroxaban	<b>Surgery</b> Omit rivaroxaban. Check PT (aim normal)
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- Patients with a DVT in the previous 3 months (initial rivaroxaban dose 15 mg BD for 21 days) are at high risk of thrombosis. Consider delaying surgery for 3 months if possible. Consider IVC filter for those with a VTE in the last 4 weeks and discuss with haematology and senior anaesthetist.
- Patients on prophylactic rivaroxaban (10mg OD) should have the last dose at least 18 hours before the procedure.

### Post-operative summary for patients on rivaroxaban

#### Major or High Bleeding risk procedures.

Surgery	D +1	D+2	D+3	D+4	D+5	D + 6
<b>Prophylactic</b> dalteparin once daily starting 6 – 8 hrs post op			Stop dalteparin the day before restarting therapeutic rivaroxaban (at day 3 – 5, at earliest on day 3, depending on bleeding tendency). Check U&E/LFT. Do not restart therapeutic anticoagulation with epidural <i>in situ</i> .			

#### Minor procedures and Low Bleeding risk.

- Rivaroxaban may be restarted at earliest 24 hours after the procedure.
- If there is concern about absorption of rivaroxaban, dalteparin may be continued longer with the dose depending on the thrombotic risk group.
- Patients admitted on prophylactic doses of rivaroxaban (10 mg OD) may be re-started 6 - 8 hours post op.

**Treatment should be reviewed daily.** Doses should only be escalated when haemostasis is secure. Pay particular attention if the patient is at high bleeding risk and seek advice if there are any concerns. If overt bleeding is present, stop anticoagulation and discuss with consultant in charge and a haematologist.

## SUMMARY OF BRIDGING ANTICOAGULATION FOR PATIENTS ON DABIGATRAN (ANY DOSE)

### Pre-operative summary for patients on dabigatran

#### Major surgery or high bleeding risk or spinal/epidural anaesthesia on any dabigatran dose

<b>-4d</b> <b>-96hr</b> – Omit dabigatran if CrCl 30-50 ml/min	<b>-3d</b> <b>-72hr</b> – CrCl 30-50 ml/min: omit dabigatran – CrCl >50ml/min: last dabigatran dose in the evening	<b>-2d</b> <b>-48hr</b> Omit dabigatran	<b>-1d</b> <b>-24hr</b> Omit dabigatran	<b>Surgery (day 0)</b> Omit dabigatran. Check APTT/TT/PT in all (aim near normal TT) consider dabigatran levels if: - Normal APTT and prolonged TT
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#### Minor procedure and low bleeding risk on any dabigatran dose

<b>-4d</b> <b>-96hr</b> Dabigatran BD	<b>-3d</b> <b>-72hr</b> Dabigatran BD	<b>-2d</b> <b>-48hr</b> – CrCl 30-50ml/min omit dabigatran – CrCl >50ml/min: last dabigatran dose in the evening	<b>-1d</b> <b>-24hr</b> Omit dabigatran	<b>Surgery</b> Omit dabigatran. Check APTT (aim normal)
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Dabigatran is contraindicated at CrCl less than 30 ml/min and the half-life significantly prolonged (more than 27 hrs). Discuss with haematology.

### Post-operative summary for patients on dabigatran

#### Major or High Bleeding risk procedures

Surgery	D +1	D+2	D+3	D+4	D+5	D + 6
<b>Prophylactic</b> dalteparin 6 – 8 hrs post op			Stop dalteparin the day before restarting therapeutic dabigatran (at day 3 – 5, at earliest on day 3, depending on bleeding tendency). Check U&E/LFT. Do not restart therapeutic anticoagulation with epidural <i>in situ</i> .			

#### Minor procedures and Low Bleeding risk

- Dabigatran may be restarted at earliest 24 hours after the procedure.
- If there is concern about absorption of dabigatran, dalteparin may be continued longer at a dose depending on the thrombotic risk group.
- Patients admitted on prophylactic doses of dabigatran (150/220 mg OD) may be re-started 6 - 8 hours post op.
- Renal function *must* be checked post-operatively and dabigatran doses adjusted accordingly.

**Treatment should be reviewed daily.** Doses should only be escalated when haemostasis is secure. Pay particular attention if the patient is at high bleeding risk and seek advice if there are any concerns. If overt bleeding is present, stop anticoagulation and discuss with consultant in charge and a haematologist.

## INTRODUCTION

When patients on anticoagulation require surgery or an invasive procedure, the risks and benefits of stopping or continuing anticoagulation must be considered. In many cases it is necessary to stop the oral anticoagulant (most commonly warfarin) and replace it with low molecular weight heparin (LMWH) until after the procedure. This is known as “bridging anticoagulation”.

## SITUATIONS COVERED BY THIS GUIDELINE

**This guideline provides recommendations for the management of peri-procedural anticoagulation for patients on warfarin, rivaroxaban (Xarelto®), dabigatran (Pradaxa®), acenocoumarol (Sinthrome®) or phenindione (Dindevan®), who need interruption of anticoagulant therapy (with an INR of less than 1.5 if on warfarin) for a procedure. Additional advice may be required from a haematologist regarding acenocoumarol or phenindione.**

This guideline may also be used as guidance for the management of patients who are on long term treatment with low molecular weight heparin (LMWH).

### **This guideline does not cover the management of the following groups of patients:**

- **Patients on apixaban (Eliquis®).** Advice on the management of these patients should always be sought from a haematologist and a senior anaesthetist.
- **Pregnant patients:** advice should always be sought from a haematologist.
- **Neurosurgery:** not applicable to BHNFT
- **Pulmonary hypertension patients:** patients on the pulmonary vascular diseases unit in Sheffield are managed according to the **Sheffield pulmonary vascular disease unit bridging guideline**
- **Urology day case and outpatient procedure patients:** this group of patients should be managed according to the [Urology day case and outpatient procedure guidance on bridging anticoagulation \(Appendix 6\)](#)

This document provides guidance only. In all cases, the risks of stopping anticoagulant therapy to prevent procedure related bleeding must be balanced against the risk of a further thromboembolic event.

**If there are any uncertainties/concerns regarding these recommendations, discuss with a haematologist or/and anaesthetist**

Throughout this guideline, the terms “Standard risk” and “High risk” refer to a patient’s thrombotic risk



## PRE-OPERATIVE ASSESSMENT AND MANAGEMENT

Assessment of elective patients should be carried out at pre-operative assessment clinic. Where the procedure does not warrant a formal pre-operative assessment, the clinician ordering the procedure should ensure that the guidance is followed.

Certain procedures **may** be done whilst on therapeutic anticoagulation - see appendix 1 for further guidance.

If anticoagulation is to be interrupted, patients will need to be given clear instructions about when to take their last dose of anticoagulant:

1. **Pre-op assessment: assess whether anticoagulation needs to be interrupted for the procedure by medical staff.** Certain procedures **may** be done whilst on rivaroxaban, dabigatran and warfarin with an INR of less than 3.0 - see appendix 1 for further guidance.
2. **If anticoagulation needs to be interrupted, use the *peri-procedural bridging anticoagulation prescription chart* to determine whether a patient is in the Standard risk or High risk category** (see appendix 2 for criteria for stratification of thrombotic risk).
  - 2.1. Use the **peri-procedural bridging anticoagulation prescription** chart to prescribe the appropriate treatments.
  - 2.2. If there is any uncertainty as to which category a patient should be assigned, discuss with the cardiothoracic team (mechanical valve patients), cardiology/relevant medical team (AF and risk factors for stroke) or haematology/relevant medical team (venous thromboembolic disease patients) prior to admission. It may be appropriate to involve a senior anaesthetist at this stage.
3. **Certain patients should be discussed with senior clinicians before commencing bridging:**
  - 3.1. **Patients who are at particularly high risk of thrombosis** should be discussed with the senior clinician and anaesthetist involved; these include
    - 3.1.1. patients with a venous thrombosis in the last 3 months
    - 3.1.2. patients with recent stroke (within the previous 6 months) or any history of cardiac thromboembolism
    - 3.1.3. patients with a left-ventricular assist device
    - 3.1.4. patients within 1 month of a bare-metal stent insertion or 3 months of a drug-eluting stent insertion
  - 3.2. **Procedures which carry a very high bleeding risk:** these patients can follow the pre-operative bridging guideline but post-operative bridging may need to be individualised (e.g. spinal surgery, cardiac surgery, radical prostatectomy; **those procedures are not performed in BHNFT**).
  - 3.3. **Patients with antithrombin deficiency** should be discussed with a haematologist as treatment with antithrombin concentrates may be required.
  - 3.4. Where there is uncertainty about the management of any patient, discuss with the senior clinician and anaesthetist involved.
4. Patients without any complicating factors (e.g. renal impairment, weight greater than 150kg, etc) should follow the treatment plans as described on the **peri-procedural bridging anticoagulation prescription chart** and in appendix 7 (Standard risk) and appendix 8 (High risk).
5. Patients on therapeutic treatment with LMWH should have their dalteparin discontinued at least 24 hours prior to surgery.
6. **“High risk” patients who are expected to require epidural/spinal anaesthesia or analgesia for more than 48 hours post-operatively** should be considered for an alternative method of analgesia, as high dose dalteparin and therapeutic doses of rivaroxaban or dabigatran are incompatible with safe

removal of epidural catheters. If no other mode of anaesthesia/analgesia is suitable, the patient must be discussed with a haematologist.

## 7. Patients with renal impairment

7.1. **Standard risk patients on dalteparin should have the dose reduced if their eGFR is less than 20ml/min/1.73m<sup>2</sup>. eGFR should only be used to dose dalteparin for standard risk patients and must NOT be used to dose dalteparin for high risk patients.** Dose reductions are advised on the *peri-procedural bridging anticoagulation prescription chart*.

7.2. **High risk patients on dalteparin should have the dose reduced if their calculated creatinine clearance (CrCl) is less than 30ml/min.** These patients should be discussed with a haematologist before bridging is commenced. Renal function for high risk patients should be estimated using the following calculation:

$$\text{CrCl} = \frac{(140 - \text{age}) \times \text{weight (kg)}}{\text{Serum Creatinine (micromol/L)}} \times 1.04 \text{ (female)} = \text{_____ (mL/min)}$$
$$\text{CrCl} = \frac{(140 - \text{age}) \times \text{weight (kg)}}{\text{Serum Creatinine (micromol/L)}} \times 1.23 \text{ (male)}$$

7.3. **Patients on rivaroxaban or dabigatran with renal impairment should be managed according to the guidance given on page 6 and 7 respectively.** Renal function for all patients on rivaroxaban or dabigatran should be estimated using the above equation; eGFR should not be used to estimate renal function.

8. **Patients weighing more than 150kg should be discussed with a haematologist** as dose adjustments of dalteparin and monitoring of anti-Xa activity may be required.

9. **GPs should not be asked to prescribe or monitor bridging anticoagulation.**

9.1. Prior to the procedure, management should be by the medical/surgical team looking after the patient (may be via pre-op assessment clinic if applicable).

9.2. Following discharge from hospital, follow the guidance later in this document.

10. **If surgery is cancelled see advice in appendix 3.** It is the responsibility of the person cancelling the patient's surgery/procedure to inform the consultant responsible as patients will need advice regarding their bridging therapy.

11. **Guidance for pre-operative assessment clinics is in appendix 4**

## PRE-OPERATIVE & POST-OPERATIVE MANAGEMENT OF PATIENTS TAKING VITAMIN K ANTAGONISTS (warfarin, acenocoumarol (Sinthrome®) or phenindione (Dindevan®))

### Pre-Operative Management:

#### Pre-operative investigations

- A full blood count must be taken in the week prior to surgery (this may be performed at the same time as the pre-op INR). If the patient has acute or chronic thrombocytopenia (platelets less than  $150 \times 10^9/L$ ) then discussion with a haematologist is recommended.
- A U&E must be taken within 6 weeks prior to surgery. This should be repeated in the week prior to surgery for accurate assessment of renal function (calculated creatinine clearance).
- Obtain an accurate weight for the patient so that dosing can be carried out correctly.
- For those patients who are anticoagulated with warfarin an INR will be required on day -2 (High risk patients) and day -1 if INR was greater than 1.5 on day -2, or day -1 (Standard risk patients).

**Warfarin:** Patients should be instructed to take their last dose 5 days pre-operatively (i.e. 4 clear days before surgery) and attend for INR checks as appropriate. Patients should be advised that they may need to continue receiving injections of dalteparin after discharge from hospital until their INR is therapeutic. Patients or carers should be trained to inject dalteparin wherever possible.

**Phenindione (Dindevan®) and acenocoumarol (Sinthrome®):** These agents have shorter half-lives than warfarin, hence a shorter duration of action and more rapid onset of action. Patients should be advised to take their last dose 3 days pre-operatively (i.e. 2 clear days before surgery) and attend for INR checks as appropriate. As above these patients should be advised that they may need to continue receiving injections of dalteparin after discharge from hospital until their INR is therapeutic.

#### Pre-operative management of emergency patients taking vitamin K antagonists

For emergency procedures consider **warfarin** reversal with i.v vitamin K and/or prothrombin complex concentrate (Beriplex™) pre-operatively. Discuss warfarin reversal with a haematologist.

Post-procedure follow the guidance below

### Post-Operative Management:

1. **Follow the appropriate treatment plan according to the patient's thrombotic risk.**
  - 1.1. **Treatment should be reviewed daily.** Doses should only be escalated when haemostasis is secure. Pay particular attention if the patient is at high bleeding risk and seek advice if there are any concerns. If overt bleeding is present, stop anticoagulation and discuss with consultant in charge and a haematologist.
  - 1.2. Dalteparin doses should be adjusted according to the patient's weight and renal function – refer to specific guidance on the **peri--procedural bridging anticoagulation prescription chart**. High risk patients with renal impairment (CrCl less than 30ml/min) should be discussed with a haematologist
  - 1.3 **Patients or their carers should be trained to inject dalteparin whilst they are in hospital**
  - 1.4 Many patients are capable of self-injecting dalteparin after discharge, and failure to train them appropriately places an unnecessary burden on the community nursing service. Training should be carried out in accordance with the BBNF Self-Administration Policy.
  - 1.5. Patients with atrial fibrillation without prior stroke/TIA and patients with prosthetic bileaflet aortic valves and no other risk factors for stroke may be discharged before their INR is therapeutic if they are medically fit.

**Post-operative summary for patients on warfarin:**

**Standard Thrombotic Risk**

Surgery	D +1	D+2	D+3	D+4	D+5	D + 6
Dalteparin prophylaxis 6 – 8 hrs post op	Warfarin at usual dose. Continue dalteparin	Continue warfarin at usual doses <b>and</b> prophylactic dalteparin until INR is greater than 2.0 in patients with VTE or discharge in patients with AF.				

**High Thrombotic Risk**

Surgery	D +1	D+2	D+3	D+4	D+5	D + 6
Prophylactic dalteparin OD 6 – 8 hrs post op	Warfarin at usual dose Continue prophylactic dalteparin		Warfarin at usual dose. Increase prophylactic dalteparin as per bridging prescription chart		Warfarin at usual dose. Increase dalteparin as per bridging prescription chart. Continue until INR is greater than 2.0	

**Warfarin should be re-started at the patient’s usual dose on the first day post-procedure.** It will take up to 2 weeks for the INR to become therapeutic. Additional loading or boost doses of warfarin are not recommended. Dalteparin should be continued until the INR is greater than 2 for all patients including those with a higher INR target range. After minor procedures *with* low bleeding risk, high dose LMWH and warfarin may be restarted **at earliest** 24 hours after the procedure.

**1.6. Post-operative summary for patients on phenindione (Dindevan®) and acenocoumarol (Sinthrome®):**

**Standard Thrombotic Risk**

Surgery	D +1 to +4	D +3-5
Dalteparin prophylaxis 6 – 8 hrs post op	Continue prophylactic dalteparin	Restart phenindione/acenocoumarol at usual doses between day 3-5 (at earliest day 3) <b>and</b> continue prophylactic dalteparin until INR is greater than 2.0 in patients with VTE or discharge in patients with AF. May be restarted day +1 following <u>very minor</u> procedures (discuss with Haematologist)

**High Thrombotic Risk**

Surgery	D +1	D+2	D3+5
Prophylactic dalteparin OD 6 – 8 hrs post op	Continue prophylactic dalteparin		Increase prophylactic dalteparin as per bridging prescription chart. Continue until INR is greater than 2.0. Restart phenindione/ acenocoumarol at usual dose between day 3-5 (at earliest day 3).

## PRE-OPERATIVE & POST-OPERATIVE MANAGEMENT OF PATIENTS TAKING RIVAROXABAN (XARELTO®) & DABIGATRAN (PRADAXA®)

### Pre-Operative Management:

#### Pre-operative investigations:

- A full blood count must be taken in the week prior to surgery (this may be performed at the same time as the pre-op INR). If the patient has acute or chronic thrombocytopenia (platelets less than  $150 \times 10^9/L$ ) then discussion with a haematologist is recommended.
- A U&E must be taken within 6 weeks prior to surgery. This should be repeated in the week prior to surgery for accurate assessment of renal function (calculated creatinine clearance).
- Obtain an accurate weight for the patient so that post-operative dalteparin dosing can be carried out correctly.
- Patients on rivaroxaban and dabigatran should have the PT, APTT and thrombin time checked pre-operatively. Selected patients may need drug levels as shown below.

**Rivaroxaban (Xarelto®):** Patients should be given instructions on when to take their last dose, dependent on the type of procedure and their usual dose of rivaroxaban.

### Major surgery or High Bleeding risk or spinal/epidural anaesthesia on 15mg/20mg rivaroxaban OD

<b>-3d -72hr</b> – Omit rivaroxaban if CrCl 15 – 30ml/min* – Last rivaroxaban dose if CrCl >30ml/min  * Rivaroxaban contra-indicated if CrCl < 15ml/min	<b>-2d -48hr</b> Omit rivaroxaban	<b>-1d -24hr</b> Omit rivaroxaban	<b>Surgery</b> Omit rivaroxaban. Check PT/APTT/TT in all. (Aim normal PT) Check anti Xa if - CrCl <30ml/min and PT normal. - Co-existent coagulopathies causing PT prolongation cannot be excluded
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### Minor procedure and Low Bleeding risk on 15mg or 20mg rivaroxaban OD

<b>-3d -72hr</b> Rivaroxaban	<b>-2d -48hr</b> Omit rivaroxaban if CrCl <30ml/min Last rivaroxaban dose if CrCl >30ml/min	<b>-1d -24hr</b> Omit rivaroxaban	<b>Surgery</b> Omit rivaroxaban. Check PT (aim normal)
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- Patients with a DVT in the previous 3 months (initial rivaroxaban dose 15 mg BD for 21 days) are at high risk of thrombosis. Consider delaying surgery for 3 months if possible. Consider IVC filter for those with a VTE in the last 4 weeks and discuss with haematology and senior anaesthetist.
- Patients admitted on prophylactic rivaroxaban (10mg OD) should have the last dose at least 18 hours before the procedure

**Dabigatran (Pradaxa®):** Patients should be given instructions on when to take their last dose, dependent on the type of procedure and their usual dose of dabigatran.

**Major surgery or High Bleeding risk or spinal/epidural anaesthesia on any dabigatran dose**

-4d -96hr – Omit dabigatran if CrCl 30-50 ml/min	-3d -72hr – CrCl 30-50 ml/min: omit dabigatran – CrCl >50ml/min: last dabigatran dose in the evening	-2d -48hr Omit dabigatran	-1d -24hr Omit dabigatran	Surgery (day 0) Omit dabigatran. Check APTT/TT/PT in all (aim near normal TT) consider dabigatran levels if: - Normal APTT and prolonged TT
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**Minor procedure and Low Bleeding risk on any dabigatran dose**

-4d -96hr Dabigatran BD	-3d -72hr Dabigatran BD	-2d -48hr – CrCl 30-50ml/min omit dabigatran – CrCl >50ml/min: last dabigatran dose in the evening	-1d -24hr Omit dabigatran	Surgery Omit dabigatran. Check APTT (aim normal)
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- Dabigatran is contraindicated at CrCl less than 30 ml/min and the half-life significantly prolonged (more than 27 hrs). Discuss with haematology.

**Pre-operative management of emergency patients taking rivaroxaban or dabigatran:**

For patients on **rivaroxaban**, please refer to the “Guidelines for management of rivaroxaban-related bleeding” and discuss with haematology.

For patients on **dabigatran**, please refer to the “Guidelines for management of dabigatran-related bleeding” and discuss with haematology.

Post-procedure follow the guidance below

**Post-Operative Management:**

2. **Follow the appropriate treatment plan according to the patient’s thrombotic risk.**
  - 2.1. **Treatment should be reviewed daily.** Doses should only be escalated when haemostasis is secure. Pay particular attention if the patient is at high bleeding risk and seek advice if there are any concerns. If overt bleeding is present, stop anticoagulation and discuss with consultant in charge and a haematologist.
  - 2.2. Dalteparin doses should be adjusted according to the patient’s weight and renal function – refer to specific guidance on the peri--procedural bridging anticoagulation prescription chart. High risk patients with renal impairment (CrCl less than 30ml/min) should be discussed with a haematologist

### 2.3 Post-operative summary for patients on rivaroxaban

#### Major or High Bleeding risk procedures on therapeutic dose of rivaroxaban

Surgery	D +1	D+2	D+3	D+4	D+5	D+6
Prophylactic dalteparin once daily starting 6 – 8 hrs post op			Stop dalteparin the day before restarting therapeutic rivaroxaban (at day 3 – 5, at earliest on day 3, depending on bleeding tendency). Check U&E/LFT. Do not restart therapeutic anticoagulation with epidural <i>in situ</i> .			

- After minor procedures *with* low bleeding risk, rivaroxaban may be restarted at earliest 24 hours after the procedure.
- If there is concern about absorption of rivaroxaban, dalteparin may be continued longer with the dose depending on the thrombotic risk group.
- Patients admitted on prophylactic doses of rivaroxaban (10 mg) may be re-started 6 - 8 hours post op.

### 2.4 Post-operative summary for patients on dabigatran

#### Major or High Bleeding risk procedures on therapeutic dose of dabigatran

Surgery	D +1	D+2	D+3	D+4	D+5	D+6
Prophylactic dalteparin 6 – 8 hrs post op			Stop dalteparin the day before restarting therapeutic dabigatran (at day 3 – 5, at earliest on day 3, depending on bleeding tendency). Check U&E/LFT. Do not restart therapeutic anticoagulation with epidural <i>in situ</i> .			

- After minor procedures *with* low bleeding risk, dabigatran may be restarted at earliest 24 hours after the procedure.
- If there is concern about absorption of dabigatran, dalteparin may be continued longer with the dose depending on the thrombotic risk group.
- Patients admitted on prophylactic doses of dabigatran (150/220 mg OD) may be re-started 6 - 8 hours post op.
- Renal function *must* be checked post-operatively and dabigatran doses adjusted accordingly.

### 3.0 MONITORING FOR HEPARIN-INDUCED THROMBOCYTOPENIA (HIT)

All patients receiving dalteparin must have a full blood count performed in the week prior to starting treatment. Full blood counts must be repeated every 3 to 4 days (i.e. twice weekly) for the first two weeks of treatment with dalteparin as inpatients. Patients discharged from hospital on LMWH only require HIT monitoring if they have undergone cardiothoracic surgery or they have received unfractionated heparin (prophylactic or treatment doses) within the last 90 days. If the platelet count falls by 30-50% or to less than  $150 \times 10^9/L$ , and/or the patient develops new signs of thrombosis, suspect HIT: contact a haematologist for advice.

### MANAGEMENT OF SPINAL OR EPIDURAL ANAESTHESIA OR ANALGESIA

The risks of spinal haematoma with spinal/epidural anaesthesia are greatest at times of needle/catheter insertion and removal.

#### 1.1 Patients on low dose dalteparin (i.e. any “standard risk” patients, or “high risk” patients receiving treatment on days 0, 1 or 2 post-operatively):

1.1.1 Spinal/epidural catheters must be inserted or removed at least 12 hours after the last dose of prophylactic dalteparin

1.1.2 The next dose of dalteparin must be given at least 4 hours after inserting or removing a spinal/epidural catheter

1.1.3 If a patient is on twice daily dosing of low dose dalteparin, a dose should be delayed by 4 hours to allow removal of the spinal/epidural catheter

#### 1.2. Patients on high dose dalteparin (i.e. “high risk” patients from day 3 post-operatively)

If a “high risk” patient is expected to require spinal/epidural analgesia for more than 48 hours post-operatively then an alternative route of analgesia should be considered. High dose dalteparin is incompatible with safe removal of spinal/epidural catheters.

1.2.1 If a patient receiving high dose dalteparin still has a spinal/epidural catheter in situ, advice should be sought from a haematologist and anaesthetist regarding management of the patient.

1.2.2 Spinal/epidural catheters must be inserted or removed at least 24 hours after the last dose of high dose dalteparin.

1.2.3 High dose dalteparin must not be administered within 12 hours of insertion or removal of a spinal/epidural catheter.

#### 1.3 Patients taking rivaroxaban or dabigatran

1.3.1 For patients taking therapeutic doses of **rivaroxaban** (15 or 20mg OD or 15mg BD) and who have a creatinine clearance of greater than 30ml/min there should be an interval of at least 48 hours between the last dose of rivaroxaban and insertion of spinal/epidural catheters. For patients with a creatinine clearance of 15-30ml/min the interval should be at least 72 hours. Patients taking prophylactic rivaroxaban (10mg OD) should have an interval of at least 18 hours between the last rivaroxaban dose and insertion of spinal/epidural catheters.

1.3.2 For patients taking any dose of **dabigatran** and who have a creatinine clearance of greater than 50 ml/min there should be an interval of at least 60 hours between the last dabigatran dose and insertion of spinal/epidural catheters. For patients with a creatinine clearance of 30-50ml/min the interval should be at least 96 hours.

1.3.3 **Patients taking rivaroxaban or dabigatran should have a PT, APTT and TT checked when epidural catheters are inserted or removed.** These parameters should be in the normal range but selected patients require drug level measurement (see guidance above)

#### 1.4 Patients taking warfarin should have an INR of 1.5 or less when epidural catheters are inserted or removed.

**1.5 Be vigilant for the signs of spinal cord compression due to spinal haematoma:** backache, leg weakness, loss of perineal and leg sensation, loss of bladder control. These must be acted upon promptly with urgent referral to the on-call anaesthetist



## DISCHARGING PATIENTS

1. **Standard risk patients with a previous VTE and high risk patients should remain on dalteparin treatment until their INR is greater than 2.0, if they are taking warfarin. Standard risk patients with atrial fibrillation can stop dalteparin on discharge provided continuing thromboprophylaxis for other reasons is not indicated**

### **INR > 2.0**

If the patient's INR is greater than 2.0 at the time of discharge, patients should be referred back to their usual anticoagulation provider.

Patients are referred to the Pharmacy Anticoagulant clinic using the **BHNFT Anticoagulation Referral Form**. Patients must have an INR check within 7 days of discharge (sooner if clinically indicated).

For patients whose INR monitoring is undertaken by their general practitioners, those patients can be referred to their general practitioners using the same **BHNFT Anticoagulation Referral Form**. The Referral Form must be faxed to the appropriate GP Surgeries. It is essential that confirmation is received from the GP Surgeries that their patients will be seen within 7 days of discharge (sooner if clinically indicated) and the date and time of appointment is given to the patients on discharge.

### **INR < 2.0**

If the INR is less than 2.0, it will be the responsibility of the clinical staff of the appropriate departments to arrange for INR checks (and also other appropriate blood tests as advised, e.g HIT monitoring, UEs) and to inform the appropriate medical staff of the Specialty of the results and for advice on dosing of warfarin, until the INR is > 2.0. **If there are concerns about the anticoagulation, the middle grade staff/consultant looking after the patients must speak directly with a haematologist.**

- N.B: - Patients who are still requiring LMWH for their bridging anticoagulation must not be discharged back to their General Practitioners**
- Patients who are not medically fit or/and require frequent monitoring should remain in hospital until the INR is > 2.0**

Ensure adequate supply (10 days) of Dalteparin and warfarin are prescribed on the TTO. If further supply of Dalteparin is required, it will be the responsibility of the medical staff of the appropriate surgical/medical departments to issue the prescription.

Patients (or their carers) should be trained to administer Dalteparin wherever possible; otherwise patients will need to be referred to District Nurses (extension number 3211).

Patients with atrial fibrillation without prior stroke/TIA and patients with prosthetic bileaflet aortic valves and no other risk factors for stroke may be discharged before their INR is therapeutic if they are medically fit. The patient's warfarin should be restarted at their usual dose and they can be referred to their regular anticoagulation provider for INR monitoring. These patients do not need to be "bridged" with Dalteparin on discharge from hospital. For further guidance, see appendix 5.

## 2. **Patients taking rivaroxaban or dabigatran:**

- Patients taking prophylactic doses of rivaroxaban (10mg OD) or dabigatran (150/220mg OD) should be restarted 6-8 hours post-op and discharged once they are medically fit.
- Patients taking treatment doses of rivaroxaban (15 or 20mg OD or 15mg BD) or dabigatran (110 or 150mg BD) who have had a major or high bleeding risk procedure, should receive **only** dalteparin until at least the third day post-procedure, at which time their normal dose of rivaroxaban/dabigatran can be restarted and patients can be discharged once medically fit. Patients who have had a minor and low bleeding risk procedure may restart their rivaroxaban/dalteparin at the earliest 24 hours after the procedure.
- Dalteparin **MUST** be **discontinued** the day(24 hours) before rivaroxaban/dabigatran is restarted.
- INR monitoring is not required in patients who are taking rivaroxaban or dabigatran.

## BACKGROUND AND RATIONALE FOR RECOMMENDATIONS

### Introduction

The purpose of this document is to provide recommendations for the management of peri-procedural anticoagulation for patients on oral anticoagulant therapy who need to stop anticoagulation prior to surgery (INR of less than 1.5 prior to the procedure or interruption of dabigatran/rivaroxaban). They are part of a trust wide initiative to implement NPSA guidance for safer anticoagulation and are adapted from the guidelines by the American College of Chest Physicians (Douketis *et al*, 2012), the British Committee for Standards in Haematology (Keeling *et al*, 2011) and expert opinion (Spyropoulos 2012).

There are an estimated 500,000 patients in the UK using oral anticoagulants, the majority for atrial fibrillation (AF) and mechanical heart valves (Baglin *et al*, 2007). In the USA approximately 10% of patients on oral anticoagulants are thought to require surgery or invasive procedures annually (Douketis *et al*, 2012) making peri-operative bridging anticoagulation a common occurrence. A risk assessment by the National Patient Safety Agency demonstrated wide variation in practice of the peri-operative management of patients on oral anticoagulation both between and within hospital trusts as well as deficiencies in training of staff dealing with anticoagulation issues (National Patient Safety Agency, 2006). This can lead to potentially unnecessary admissions for pre-procedural anticoagulation, delays in discharge because of unstable anticoagulation, and unsafe anticoagulation management with potentially increased morbidity and mortality.

For patients on oral anticoagulant therapy requiring invasive procedures, the risk of a thromboembolic event in the peri-operative period when anticoagulation is interrupted must be balanced against the risk of bleeding when these are continued. If the risk of procedure-related bleeding whilst continuing oral anticoagulation is thought to be small, anticoagulation may be continued. This applies to some minor dental (Douketis *et al*, 2012; Perry *et al*, 2007), ophthalmic (Douketis *et al*, 2012) and dermatological (Douketis *et al*, 2012) procedures and should be discussed with the relevant team. Recent guidelines from the British Society of Gastroenterology suggest that diagnostic endoscopic procedures with or without biopsy, biliary or pancreatic stenting and diagnostic endoscopic ultrasound can also be performed whilst the patient is on therapeutic anticoagulation (Veitch *et al*, 2008). Similarly, patients requiring invasive cardiology procedures may be at low risk of bleeding and these procedures can be done whilst anticoagulated. These patients should be discussed with the cardiology team before anticoagulation is altered. Patients requiring diagnostic angiography also have a low risk of bleeding and procedures can generally be done on warfarin provided the INR is less than 3 and the guidance as given by vascular radiology should be followed. A list of procedures that may be undertaken whilst a patient's INR is less than 3 is given below, and in appendix 1 of this document.

If the risk of procedure-related bleeding is thought to outweigh the risk of thromboembolic events, anticoagulation should be stopped and bridging anticoagulation considered depending on the thrombotic risk. If bridging anticoagulation is instituted, this should be done in a manner whereby both the time without anticoagulation and the bleeding risk are minimised. The peri-procedural management therefore depends both on individual patient characteristics and the type of procedure done.

## Bleeding risk associated with procedures

Note that this list is not comprehensive and is intended as guidance only.

Very high risk <sup>1</sup>	High risk	Low risk <sup>2</sup>	Procedures which may be performed on warfarin <sup>3</sup>
Cardiac surgery	Major orthopaedic surgery	Minor procedures as specified by treating surgeon/physician	Diagnostic GI endoscopic procedures ± biopsy (Veitch <i>et al</i> , 2008)
Neurosurgery	Major vascular surgery		Biliary or pancreatic stenting (Veitch <i>et al</i> , 2008)
Spinal surgery	Major gynaecological and urological surgery		Diagnostic EUS (Veitch <i>et al</i> , 2008) minor dermatological surgery (Douketis <i>et al</i> , 2012)
Radical prostatectomy	Major cancer surgery		Minor dental surgery (Perry <i>et al</i> , 2007) Minor ophthalmological surgery (cataract extraction) (Douketis <i>et al</i> , 2012)
	Other major abdominal and thoracic surgery		
	Renal biopsy		

<sup>1</sup> Procedures with very high bleeding risk can follow this guideline pre-operatively. Post operative dalteparin should not be escalated before day +3 and some may need an individualised decision. Please note that these procedures are not performed in BHNFT.

<sup>2</sup> Minor procedures at low risk of bleeding but where warfarin needs to be stopped should be identified by the treating physician or surgeon. In patients with a high thrombotic risk undergoing a low risk procedure high dose dalteparin **may** be restarted **at earliest** 24 hours after the procedure. Caution may be needed with procedures that appear to have a low bleeding risk but have been associated with higher bleeding rates. These include resection of large pedunculated polyps or broad based flat (sessile) polyps requiring EMR and pacemaker or defibrillator implantation.

<sup>3</sup> Guidelines on selected procedures that may be done whilst on warfarin are available from the British Society for Gastroenterology (Veitch *et al*, 2008), ACCP (Douketis *et al*, 2012) and British Committee for Standards in Haematology (Perry *et al*, 2007) (Keeling *et al*, 2011). Other minor vascular and cardiological procedures may also be possible whilst on warfarin but should be discussed with the relevant team.

## Assessment of thrombotic risk

This guideline recommends stratification of thrombotic risk as **Standard risk** or **High risk**.

### *Mechanical heart valves*

The risk of thrombosis is highest in mechanical mitral valve prosthesis and aortic valve prosthesis using caged ball or tilting disc devices. The risk is lower in modern bileaflet aortic valves. Most studies assessing the use of low molecular weight heparin (LMWH) as bridging anticoagulation have used therapeutic dose regimens (for a review see Douketis *et al*, 2012). Two studies have used low dose LMWH (including patients with mitral valve prosthesis) but it is not clear if this is sufficient as it can be argued that higher doses of LMWH are needed for the prevention of arterial thrombosis. The latter however is also not established.

This guideline therefore classifies all patients with mechanical valve prosthesis as high risk **except** those with bileaflet aortic valves without any other risk factors for stroke.

### *Atrial Fibrillation*

Patients at highest risk for stroke are those with a previous stroke/TIA or rheumatic valvular heart disease. These patients should be bridged according to the high risk guideline. For others, the optimal bridging regimen is unclear. The BCSH guidelines (Keeling *et al*, 2011) suggest no bridging in patients without prior stroke or TIA (unless multiple risk factors present), whereas the ACCP guidelines suggest that either no bridging or bridging is acceptable in patients with a CHADS2 score up to 4 depending on the bleeding risk of the procedure (Douketis *et al*, 2012).

For patients on warfarin, this guideline recommends using prophylactic doses of LMWH whilst an inpatient in all patients with AF except those with previous stroke, TIA or rheumatic valvular heart disease. The latter should be bridged as per the high risk protocol. If there is any uncertainty as to which category a patient should be assigned, this should be discussed with the cardiology team/relevant medical team prior to admission.

#### *Previous venous thrombotic events (VTE)*

In contrast to arterial thrombotic events, there is evidence that prophylactic dose LMWH therapy decreases the post-operative thrombotic risk. Therefore there is a clear role for the use of prophylactic dose LMWH in patients with a previous VTE who are on long term anticoagulation with warfarin and have a target INR of 2 – 3.

Patients with VTE in the previous 2 – 3 months are at high risk of recurrence and any procedures (for which interruption of anticoagulation is necessary) should preferably be delayed for 2 – 3 months. If this is not possible, a temporary IVC filter should be considered after discussion with a Haematologist/Anaesthetist prior to admission.

Patients with antiphospholipid syndrome (who have had either arterial or venous thrombotic events) and those with recurrent thrombosis whilst on warfarin (who are managed with a target INR of 3.5) are at high risk of recurrence: they should be managed according to the high risk guideline. Patients with antithrombin deficiency may require peri-procedural antithrombin concentrate and should also be discussed with a Haematology Coagulation Consultant prior to admission.

#### **The use of low molecular weight heparin (LMWH) for bridging anticoagulant therapy**

LMWH given subcutaneously has a 90 – 100% bioavailability and a more predictable anticoagulant response than unfractionated heparin (UFH). It has a half life of approximately 4 hours and is given in weight adjusted doses. Dosage monitoring is generally not necessary except in patients with renal failure, at extremes of body weight, and during pregnancy. Compared to unfractionated heparin, it has a favourable benefit to risk ratio in animal models and when used to treat VTE (Hirsh *et al*, 2008). In addition LMWH can be given in the outpatient setting. Because of these advantages LMWH is recommended in preference to unfractionated heparin (UFH) for anticoagulation bridging.

Standard risk patients should receive prophylactic doses of LMWH until oral anticoagulation has become therapeutic (INR greater than 2.0). In patients taking rivaroxaban or dabigatran, the last LMWH dose should be 24 hours before restarting dabigatran or rivaroxaban.

High risk patients should receive LMWH with the dose increasing at increments post-operatively until full therapeutic doses have been achieved. LMWH should continue in patients taking warfarin until it has become therapeutic (INR greater than 2.0). In patients taking rivaroxaban or dabigatran, the last LMWH dose should be 24 hours before restarting dabigatran or rivaroxaban. Both the creatinine clearance and liver function tests should be checked before restarting rivaroxaban or dabigatran and their doses checked against these parameters.

Dose adjustments for LMWH are necessary for patients with renal impairment. Patients requiring low “**prophylactic**” doses of dalteparin should have doses reduced if their eGFR is less than 20ml/min/1.73m<sup>2</sup>, and additional monitoring of anti-Xa levels carried out. Advice should be sought from a Haematologist regarding the management of these patients.

For patients who require high dose (“**therapeutic dose**”) LMWH and who have renal impairment (creatinine clearance less than 20 ml/min), the use of unfractionated heparin infusion may be preferable. Patients requiring therapeutic doses of dalteparin and who have a CrCl between 20-29 ml/min can have reduced doses of dalteparin (discuss with a Haematologist) if additional monitoring of anti-Xa levels is readily available. Alternatively unfractionated heparin infusion should be considered.

## Timescale for peri-operative anticoagulation

### *Stopping warfarin*

Prospective cohort studies stopped warfarin 5 – 6 days prior to surgery (for a review see Douketis *et al*, 2008). One study stopping anticoagulation 5 days before surgery found that 7% of patients had an INR greater than 1.5 the day before surgery which was corrected with 1mg oral vitamin K (Kovacs *et al*, 2004). In another retrospective study including 43 patients with an INR of 1.5 – 1.9, administration of 1mg oral vitamin K resulted in INR normalization in 91% of the patients (Woods *et al*, 2007). An INR greater than 1.5 on the day of operation is more likely in patients with a higher INR target (e.g. mechanical heart valves and patients with recurrent VTE whilst on warfarin) and elderly patients. This guideline recommends taking the last dose of warfarin 5 days prior to surgery (4 clear days), checking the INR the day prior to surgery and giving 1mg oral vitamin K if INR greater than 1.5. Patients at high thrombotic risk should have their INR checked on day -2 and should be started on LMWH; their INR should be rechecked on day -1 if INR was greater than 1.5 on day -2. Advice on starting LMWH is detailed below.

Other vitamin K antagonists (i.e. phenindione and acenocoumarol) have shorter half-lives and a shorter duration of action. They should be stopped closer to the date of surgery; advice should be sought from a Haematologist about the management of patients on these anticoagulants.

### *Other oral anticoagulants (e.g. rivaroxaban, dabigatran, apixaban)*

The newer oral anticoagulants have a different mode of action to vitamin K antagonists, and require different management. They are renally excreted and therefore the timescale for stopping and re-starting peri-operatively is partly dependent on renal function.

Both rivaroxaban and dabigatran have shorter half-lives in comparison to warfarin and an onset of action within 2 hours if intestinal absorption is normal. As a result, it can be assumed that interrupting coagulation with dabigatran or rivaroxaban is sufficient to ensure haemostasis and that surgery is safe (Schulman & Crowther 2012).

This guideline recommends that for patients taking therapeutic doses of rivaroxaban (15 or 20mg OD) and who have a creatinine clearance of greater than 30 ml/min who are to undergo major surgery or procedures with high bleeding risk, the last dose should be given on day -3 (where the procedure day is day 0).

In patients with a creatinine clearance of 15 – 30 ml/min undergoing a major procedure or procedures with high bleeding risk the last rivaroxaban dose should be given on day -4.

Patients who are to undergo minor procedures with a low bleeding risk and a creatinine clearance greater than 30 ml/min whilst taking therapeutic rivaroxaban, should omit the dose on the day prior to the procedure (day -1).

Patients who are to undergo minor procedures with a low bleeding risk and a creatinine clearance of 15 – 30 ml/min should have the last dose of rivaroxaban on day -2.

Patients taking prophylactic doses of rivaroxaban (10mg OD) must have taken their last dose of rivaroxaban at least 18 hours prior to the procedure (Spyropoulos 2012).

Patients taking therapeutic doses of dabigatran who have a creatinine clearance of greater than 50 ml/min who require major surgery or a procedure with a high bleeding tendency should have their last dose on day -3 of the procedure.

Those with a creatinine clearance of 30 – 50 ml/min should have the last dose on day -5 before surgery.

Those requiring minor surgery with low bleeding risk and who have a creatinine clearance of greater than 50 ml/min should have the last dabigatran dose on day -2 before surgery and those with a creatinine clearance of 30 – 50 ml/min on day -3 of surgery (Spyropoulos 2012).

Advice should always be sought from a Haematologist and a consultant anaesthetist regarding the management of patients taking apixaban (Eliquis®).

### *Influence of rivaroxaban and dabigatran on routine coagulation testing.*

Of the routine coagulation tests (prothrombin time (PT), activated partial thromboplastin time (APTT) and thrombin time (TT)), the PT is most sensitive for rivaroxaban. A normal PT makes therapeutic anticoagulation *unlikely* (Baglin *et al*, BJ Haem 2012, doi:10.1111/bjh.12052) but does not exclude this.

**For all patients the aim is to avoid major procedures unless the PT is normalised. Additionally we recommend specific anti Xa levels for patients on therapeutic rivaroxaban requiring emergency surgery and in patients having major procedures who have a creatinine clearance of 15 – 30**

Bridging anticoagulation: the peri-procedural management of patients on oral anticoagulation (excluding neurosurgery)

ml/min even in the presence of a normal PT. Anti Xa levels should also be considered in those whom a (even marginal) prolongation of the PT may be due to other causes to exclude anticoagulation with rivaroxaban.

For dabigatran the APTT and the TT are the most sensitive tests. A normal APTT makes therapeutic anticoagulation unlikely whilst a normal TT excludes the presence of dabigatran. **The aim for patients requiring major surgery or high bleeding risk procedures is a normal TT. We suggest measurements of dabigatran levels by Hemoclot assay in patients requiring major surgery with a normal APTT but raised TT.**

#### *Restarting anticoagulation and bleeding risk*

When to restart anticoagulation after a procedure depends on the bleeding risk associated with the type of procedure and the proximity of surgery. The ultimate dose is dependent on the thrombotic risk of the patient. The risk of bleeding is highest in patients who receive therapeutic doses of anticoagulation in the immediate post-operative period. **The ACCP and BCSH guidelines suggest that therapeutic-dose LMWH should not be restarted within 24 hours of minor procedures with a low bleeding risk and not within 48 – 72 hours of surgery with a high bleeding risk.**

Very little data are available on surgery with a very high bleeding risk. There continue to be concerns about potential high bleeding rates in patients where therapeutic anticoagulation has been started post-operatively. Studies are underway randomising patients with high risk AF and mechanical heart valves to bridging with low molecular weight heparin versus no bridging [The BRIDGE study (<http://clinicaltrials.gov/ct2/show/NCT00786474>) and PERIOP-2 study (<http://clinicaltrials.gov/ct2/show/NCT00432796>)].

Provided surgical haemostasis is secure, low dose prophylactic LMWH can usually be restarted 6 – 8 hours after surgery. Patients at high risk of thrombosis should initially be started on low-dose LMWH; the dose can subsequently be escalated at 72 hours provided haemostasis is secure and full dose LMWH can be given on day 5 and continued until the INR is greater than 2.

Warfarin can be restarted at the patient's usual dose on the day after surgery (day +1) provided haemostasis is secure. Loading or boost doses of warfarin should be avoided as these increase the risk of over-anticoagulation. It will take 1 to 2 weeks for the patient's INR to become therapeutic. LMWH should be continued until the INR is greater than 2.0, irrespective of the target INR in all high risk patients with VTE. LMWH can be discontinued in standard risk patients with AF without previous stroke/TIA provided there is no indication for prolonged thromboprophylaxis

Prophylactic doses of rivaroxaban (10mg OD) and dabigatran (150/220mg OD) may be restarted 6-8 hours post-op provided haemostasis is secure. Patients who normally take therapeutic doses of rivaroxaban (15 OD or BD or 20mg OD) or dabigatran (110 or 150mg BD) should receive LMWH until at least the third to fifth day post-op, at which point their normal dose of anticoagulant can be resumed. **LMWH MUST be discontinued once rivaroxaban/dabigatran have been restarted.**

Other oral anticoagulants (i.e. phenindione, acenocoumarol and apixaban) should be re-started later after surgery due to their short half-lives and more rapid onset of action. Patients on these anticoagulants should be discussed with a Haematologist.

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## Appendix 1

### PROCEDURES WHICH MAY BE PERFORMED ON WARFARIN WITH AN INR LESS THAN 3.0

**Diagnostic angiographic procedures by vascular radiology:** guidance given in the vascular handbook should be followed, i.e.

Check INR in pre-assessment clinic

If INR less than 3.0, check the INR on the day-ward, proceed with angiography and discharge on usual dose of warfarin

If the INR is greater than 3.0 and the patient is non-urgent, adjust dose accordingly and proceed when the INR is less than 3.0

If the INR is greater than 3.0 and the patient is urgent discuss with Radiologist and a Haematologist

**Some invasive cardiology procedures may be done whilst the patient is anticoagulated on warfarin:** these patients should be discussed with the cardiology team before anticoagulation is altered.

**Minor dental, ophthalmic, (cataract surgery) and dermatological surgery:** these patients should be discussed with the relevant team before anticoagulation is altered.

**Diagnostic GI endoscopies, biliary or pancreatic stenting and diagnostic endoscopic ultrasound:** these patients should be discussed with the relevant team before anticoagulation is altered.

### PROCEDURES WHICH MAY BE PERFORMED ON RIVAROXABAN OR DABIGATRAN

Minor procedures with low bleeding risk for which clear guidelines exist to be done whilst on warfarin may also be possible to do on rivaroxaban and dabigatran. Although this is recommended internationally (Spyropoulos 2012), evidence of safety is lacking. These procedures include:

**Dental procedures** including minor oral surgery or up to 3 dental extractions, Prosthodontics, conservation, endodontics, hygiene phase therapy and orthodontics.

**Minor ophthalmic, (cataract surgery) and dermatological surgery.**

**Diagnostic GI endoscopies.**

**In patients on rivaroxaban or dabigatran, we suggest omitting the dose taken in the morning of the procedure and restarting/continuing after the procedure provided there are no concerns about bleeding.**



**Appendix 2  
ASSESSMENT OF THROMBOTIC RISK**

Reason for being on oral anticoagulants	STANDARD RISK	HIGH RISK
<input type="checkbox"/> <b>Prosthetic heart valve</b>	<ul style="list-style-type: none"> <li>● Bileaflet mechanical aortic valve and no other risk factors for stroke and more than 3 months after implantation</li> </ul>	<ul style="list-style-type: none"> <li>● Recent stroke or TIA (within 6 months) – discuss with senior clinician and anaesthetist</li> <li>● Any mechanical mitral valve</li> <li>● Caged ball or tilting disc aortic valve</li> <li>● Bileaflet mechanical aortic valve <b>and</b> one or more of the following stroke risk factors:               <ul style="list-style-type: none"> <li><input type="checkbox"/> chronic atrial fibrillation</li> <li><input type="checkbox"/> left ventricular dysfunction</li> <li><input type="checkbox"/> age over 75 years</li> <li><input type="checkbox"/> hypertension</li> <li><input type="checkbox"/> diabetes</li> <li><input type="checkbox"/> prior stroke or TIA</li> </ul> </li> <li>● Any mechanical valve within 3 months of implantation</li> </ul>
<input type="checkbox"/> <b>Chronic atrial fibrillation</b>	<ul style="list-style-type: none"> <li>● Atrial fibrillation without prior stroke/TIA or rheumatic valvular heart disease</li> </ul>	<ul style="list-style-type: none"> <li>● Atrial fibrillation with previous stroke/TIA</li> <li>● Atrial fibrillation with rheumatic valvular heart disease</li> </ul>
<input type="checkbox"/> <b>Venous thromboembolism or antiphospholipid syndrome</b>	<ul style="list-style-type: none"> <li>● Previous VTE and now on long term anticoagulant therapy (target INR 2.5) <i>(Patients with previous VTE who are no longer on oral anticoagulation should be treated according to the <b><u>BHNFT Guidelines for the Prevention of Venous Thromboembolic Disease</u></b>)</i></li> </ul>	<ul style="list-style-type: none"> <li>● Recent episode of VTE (within 3 months) – discuss with senior clinician and anaesthetist: consider postponing surgery or placing an IVC filter</li> <li>● Antiphospholipid syndrome with a history of venous or arterial thrombosis</li> <li>● Recurrence of VTE on oral anticoagulation (target INR 3.5)</li> </ul>
<input type="checkbox"/> <b>Pulmonary hypertension</b> (undergoing a procedure that is <i>not</i> for investigation or management of PH)	<ul style="list-style-type: none"> <li>● <b>PH patients with chronic thromboembolic pulmonary hypertension or IVC filter in situ:</b> discuss with PH consultants in Sheffield regarding risk stratification, then manage according to this guideline.</li> <li>● <b>Pulmonary hypertension patients with other risk factors:</b> risk stratify according to the risk factors as above</li> <li>● <b>Pulmonary hypertension patients who are on warfarin for survival benefit only:</b> anticoagulation bridging is not required.</li> </ul>	
<input type="checkbox"/> <b>Antithrombin deficiency</b>	<p><b>All patients with antithrombin deficiency should be discussed with a Haematologist before bridging is commenced, as some may require antithrombin replacement.</b></p>	

**Appendix 3**  
**CANCELLATION OF SURGERY**

*Patients on warfarin*

Cancellation of surgery will lead to an increased period of bridging (even if warfarin is restarted). There is the potential for patients to receive inadequate anticoagulation or no anticoagulation during this time. This would put them at increased risk of thromboembolic events.

- Cancellation should be avoided if at all possible.
- If cancellation is unavoidable, postpone the surgery or procedure for a **maximum** of 1 week.
- The person cancelling the surgery or procedure must inform the relevant consultant immediately.
- Teach patients or carers to inject dalteparin wherever possible.
- If surgery is to be postponed for more than 1 week, contact a Haematologist for advice: a decision on an individual basis should be made.

<b>Dalteparin dosing for HIGH RISK PATIENTS who have been cancelled and rescheduled within 1 week</b> with calculated Creatinine Clearance 30ml/min or greater					
<b>less than 46kg</b>	<b>46-65 kg</b>	<b>66-99 kg</b>	<b>100-120 kg</b>	<b>121-150 kg</b>	<b>greater than 150kg</b>
5,000 units am 2,500 units pm	5,000 units BD	7,500 units BD	10,000 units BD	12,500 units BD	Discuss with a Haematologist
The last dose should be given in the morning on the day prior to procedure/surgery					

<b>Dalteparin dosing for HIGH RISK PATIENTS who have been cancelled</b> with calculated Creatinine Clearance less than 30ml/min
Discuss with a Haematologist.

<b>Dalteparin dosing for STANDARD RISK PATIENTS with eGFR 20ml/min/1.73m<sup>2</sup> or greater who have been cancelled and rescheduled within 1 week</b>			
<b>Weight less than 45kg</b>	<b>Weight 45 – 100kg</b>	<b>Weight 101 – 150kg</b>	<b>Weight greater than 150kg</b>
Dalteparin 2,500 units <b>once daily</b> in the evening	Dalteparin 5,000 units <b>once daily</b> in the evening	Dalteparin 7,500 units <b>once daily</b> in the evening	Dalteparin 5,000 units <b>twice daily</b> in the evening
The last dose should be given in the evening on the day prior to procedure/surgery			

<b>Dalteparin dosing for STANDARD RISK PATIENTS who have been cancelled</b> with eGFR less than 20 ml/min/1.73m <sup>2</sup>
Anti-Xa monitoring may be required: discuss with a Haematologist
Dalteparin 2,500 units <b>once daily</b> in the evening
The last dose should be given in the evening on the day prior to procedure/surgery

*Patients on rivaroxaban or dabigatran*

If surgery is cancelled for patients on rivaroxaban or dabigatran and either drug has been stopped, it should be re-started as soon as possible. Dalteparin is not necessary given the short onset of action of these drugs.

## **Appendix 4**

### **NOTES FOR PRE-OPERATIVE ASSESSMENT CLINICS**

Patients on anticoagulants should be assessed by medical staff for thrombotic risk using the Peri-procedural bridging anticoagulation prescription chart. This chart should then be placed in the patient's notes with the pre-assessment prescription chart.

Pre-assessment clinic staff will ensure the last three INR results are included in the pre-operative document, along with the current dose of warfarin.

Pre-assessment clinic staff will identify which patients need to have U&E, FBC and INR checks and when.

When patients are dated for surgery the pre-assessment nurse will book patients for INR checks in either pre-assessment clinic, or the designated area at the weekends where the case notes should be available.

Arrangements **must** be made to ensure that the patient knows when to take their last dose of warfarin, rivaroxaban or dabigatran. In addition to this, patients **must** be informed on when they are to restart taking their anticoagulant.

Patients will have an appointment made on PAS to attend the pre-assessment clinic and will be entered as a ward attender when they return to the main hospital for checks.

#### ***Where INR and FBC checks will take place:***

Monday to Friday: patients to attend pre-assessment clinic

Weekends: patients to attend appropriate wards

#### ***Appointment Times:***

**Standard risk patients** will attend the day prior to surgery at 08:00 to 10:00 (to give Vitamin K the necessary time to take effect if it is necessary). Any necessary treatment will be given at this time.

**High risk patients** will attend 48 hours pre-surgery date for bloods and treatment at 08.00 as identified on the prescription chart. Pre-assessment clinic staff will make individual patient arrangements for the 2<sup>nd</sup> dose of Dalteparin at 20:00 injection. If patient or carer is administering the dalteparin they must be trained and provided with a sharps bin.

High risk patients may need to return for a further INR check on the day prior to surgery at 08.00 (depending on the previous day's INR) and again any necessary treatment will be given.

#### ***Prescriptions***

The Peri-procedural anticoagulation bridging prescription chart sets out what treatment is required. It should be used to prescribe vitamin K (if required) and dalteparin.

The BHNFT Warfarin Prescription and Monitoring Chart should be used to prescribe the patient's warfarin.

#### ***Prescriptions for Dalteparin***

All prescriptions will be completed on receipt of U&E/Cr (within last 6 weeks) and INR result.

All prescriptions will be completed by the medical staff in pre-assessment clinic. On the weekend prescriptions to be completed by medical staff in the appropriate wards.

Ward areas to keep stock of dalteparin 2,500 units and dalteparin 5,000 units and Vitamin K 1mg (phytomenadione 2mg/0.2mL).

Dalteparin for high risk patients will need to be ordered from pharmacy on an individual basis.

If there are any questions/queries when patient attends for INR check, these should be discussed by the appropriate medical staff with the anaesthetist first. If needed, advice can be sought from a Haematologist

### ***Admission Plan***

All patients can be admitted on the day of surgery, unless they have other co-morbidities that require them to be admitted earlier.

**All patients will need to have their INR checked on day of surgery and bridging therapy continued as per the treatment plan throughout admission.**

### ***Cancellations:***

**It is the responsibility of the person cancelling the patient's surgery to inform the consultant responsible as patients will need advice regarding their bridging therapy.**

**Please remember patients will have stopped their warfarin 5 days prior to their day of surgery.**

Avoid cancellation if at all possible: patients are to be given high priority by clinical staff/general managers/bed managers when considering which patients to cancel due to lack of beds. This will be managed by the individual specialities.

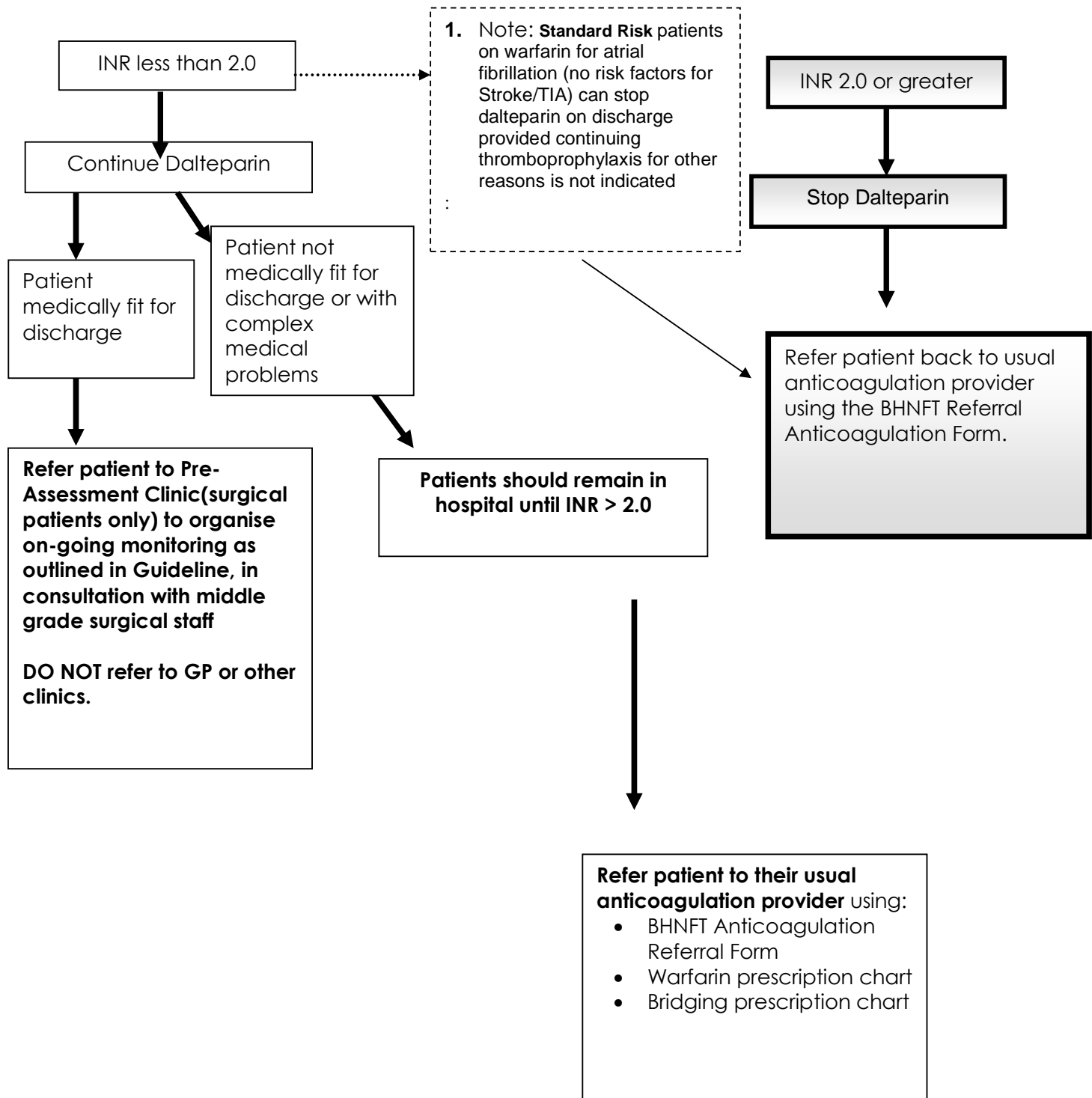
See Appendix 3 for further advice regarding cancellation.

### **Other issues**

Patients with co-morbidities and complications which are likely to affect control of INR must be managed as in-patients throughout their bridging anticoagulation

## Quick Guide to DISCHARGING ON PERI-PROCEDURAL ANTICOAGULATION BRIDGING

(Restart patient on usual dose of Warfarin: do NOT give loading or boost doses)



## Appendix 6

### **Urology Day case / Outpatient procedure guidance on bridging anticoagulation in patients treated with Warfarin.**

This guidance is reproduced and adapted from the Sheffield Teaching Hospital Guideline on bridging anticoagulation for **day case** procedures in Urology (version 3.0 November 2012), for use in BHNFT, including:

- Circumcision/ inguinoscrotal procedures
- TURBT/ bladder biopsy
- Lithotripsy
- TRUS biopsy
- Vasectomy

Three groups of patients treated with Warfarin are identified for the purposes of this document.

## 1. Standard risk patients without previous venous thrombosis

- Patients on warfarin for non-valvular atrial fibrillation (AF) without prior stroke/TIA.
- Patients on warfarin with bileaflet aortic valve replacement AVR without risk factors for stroke (AF, prior stroke/TIA, congestive cardiac failure, hypertension, diabetes, age over 75).

### Assessment

These patients are at low risk of thrombosis and the risk of bleeding when bridged postoperatively with low molecular weight heparin generally outweighs the risk of thrombosis.

### Guidance

There is no indication for bridging with low-molecular weight heparin.

Stop warfarin 4 days before procedure (i.e. last dose is taken 5 days before procedure)

Check INR on day of procedure at least 1 hour before procedure.

Give Vitamin K, 1mg orally if INR > 1.4

Restart warfarin at normal dose when no visible bleeding.

Refer to usual anticoagulation provider for follow up. Patient should stay on their usual dose of warfarin until they reach their target INR and loading or boost doses should not be used.

For lithotripsy where further treatment may be required 2 weeks later – stay off warfarin until treatment complete then recommence at usual dose.

**VTE prophylaxis in patients having day case surgery with no reduction in usual mobility is not required.**

## 2. Standard risk patients with previous venous thrombosis

Includes patients in the previous group but in addition have

- Previous DVT over 3 months ago but still on warfarin (target INR 2-3).

**(Patients with antithrombin deficiency are at high risk for thrombosis and should be discussed with haematology before any procedures).**

### Assessment

These patients are at moderate risk of thrombosis and the time spent off anti-coagulation should be limited.

### Guidance

As before, there is no indication for bridging with low-molecular weight heparin **BEFORE** the procedure.

Stop warfarin 4 days before procedure (i.e. last dose is taken 5 days before procedure)

Check INR on day of procedure at least 1 hour before procedure.

Give Vitamin K, 1mg orally if INR > 1.4

When no visible bleeding (e.g. haematuria), commence on daily prophylactic dalteparin (dose dependent on weight) as well as usual dose of warfarin.

### 3. High risk patients

- AF with previous TIA or Stroke
- Mechanical mitral valve
- Bileaflet aortic valves with risk factor for stroke
- Non bileaflet aortic valves
- DVT/PE within the last 3 months
- Rheumatic valve disease/valvular AF
- Antiphospholipid syndrome.
- Venous thrombosis on warfarin with target INR 3.5 (range 3-4)

**(Patients with antithrombin deficiency must be discussed with haematology before any procedures.)**

#### **Assessment**

These patients are NOT suitable to be managed as outpatients as their risks of bleeding and thrombosis are difficult to balance. Serious consideration should be given to whether or not the procedure is essential.

#### **Guidance**

**The case needs to be discussed at consultant level between Urology and Coagulation re: high risk bridging management prior to procedure. Admission pre- procedure for loading/ bridging is likely to be the norm.**



**Appendix 7**  
**TREATMENT GUIDELINES FOR STANDARD RISK PATIENTS**

Use eGFR to assess renal function.

Prescribe treatment on the Peri-procedural Bridging Anticoagulation Prescription Chart (available from Intranet).

<b>TREATMENT PLAN FOR STANDARD RISK PATIENTS</b> <b>with eGFR 20ml/min/1.73m<sup>2</sup> or greater</b>				
<b>Day</b>	<b>Weight less than 45kg</b>	<b>Weight 45 – 100kg</b>	<b>Weight 101 – 150kg</b>	<b>Weight greater than 150kg</b>
<b>-5</b>	Last dose of warfarin (4 clear days) (if on acenocoumarol or phenindione: see page 11)			
<b>-4</b>	No warfarin			
<b>-3</b>				
<b>-2</b>				
<b>-1</b>	<b>Check INR:</b> if greater than 1.5: give vitamin K 1mg orally stat. Re-check INR on day 0 Start dalteparin if INR is less than 2.0 (give last dose at least 12 hours before procedure)			
	Dalteparin 2,500 units OD	Dalteparin 5,000 units OD	Dalteparin 7,500 units OD	Dalteparin 5,000 units BD
<b>0</b> (day of procedure)	Dalteparin 2,500 units 6 – 8 hours post-operatively	Dalteparin 5,000 units 6 – 8 hours post-operatively	Dalteparin 7,500 units 6 – 8 hours post-operatively	Dalteparin 7,500 units 6 – 8 hours post-operatively
<b>+1 onwards</b>	Dalteparin 2,500 units <b>once daily</b>	Dalteparin 5,000 units <b>once daily</b>	Dalteparin 7,500 units <b>once daily</b>	Dalteparin 5,000 units <b>twice daily</b>
	Restart warfarin at patient's usual dose. (if on acenocoumarol or phenindione: see page 12) Continue dalteparin as per day +1 until INR is greater than 2.0			

**Dalteparin must only be started post-operatively when haemostasis is secure.**

<b>TREATMENT PLAN FOR STANDARD RISK PATIENTS</b> <b>with eGFR less than 20 ml/min/1.73m<sup>2</sup></b>	
Anti-Xa monitoring may be required: discuss with a haematologist	
<b>Day</b>	<b>Recommended treatment</b>
<b>-5</b>	Last dose of warfarin (4 clear days) (if on acenocoumarol or phenindione: see page 11).
<b>-4</b>	No warfarin
<b>-3</b>	
<b>-2</b>	
<b>-1</b>	Check INR: if greater than 1.5: give vitamin K 1mg orally stat. Re-check INR on day -1. Start dalteparin 2,500 units OD if INR is less than 2.0 (give last dose at least 12 hours before procedure)
<b>0</b> (day of procedure)	Dalteparin 2,500 units 6 – 8 hours post-operatively
<b>+1 onwards</b>	Dalteparin 2,500 units <b>once daily</b>
	Restart warfarin at patient's usual dose. (if on acenocoumarol or phenindione: see page 12). Continue dalteparin as per day +1 until INR is greater than 2.0

**Appendix 8  
TREATMENT GUIDELINES FOR HIGH RISK PATIENTS**

Use calculated Creatinine Clearance to assess renal function.

$\text{CrCl} = \frac{(140 - \text{age}) \times \text{weight (kg)}}{\text{Serum Creatinine (micromol/L)}} \times 1.04 \text{ (female)}$ $= \text{_____ (mL/min)}$
$\text{CrCl} = \frac{(140 - \text{age}) \times \text{weight (kg)}}{\text{Serum Creatinine (micromol/L)}} \times 1.23 \text{ (male)}$

Prescribe treatment on the Peri-procedural Bridging Anticoagulation Prescription Chart (available from Intranet).

<b>TREATMENT PLAN FOR HIGH RISK PATIENTS with calculated Creatinine Clearance 30ml/min or greater</b>						
<b>Day</b>	<b>less than 46kg</b>	<b>46-65 kg</b>	<b>66-99 kg</b>	<b>100-120 kg</b>	<b>121-150 kg</b>	<b>greater than 150kg</b>
<b>-5</b>	Last dose of vitamin K antagonist (4 clear days) (if on acenocoumarol or phenindione: see page 13)					
<b>-4</b>	No warfarin					
<b>-3</b>						
<b>-2</b>	Check INR: if greater than 1.5: give Phytomenadione (vitamin K) 1mg orally stat and re-check INR on day -1. Start dalteparin if INR is less than 2.0					
	5,000 units am 2,500 units pm	5,000 units BD	7,500 units BD	10,000 units BD	12,500 units BD	Discuss dosing with a haematologist
<b>-1</b>	5,000 units in the morning	5,000 units in the morning	7,500 units in the morning	10,000 units in the morning	12,500 units in the morning	
<b>0 (day of procedure)</b>	Dalteparin 2,500 units 6 – 8 hours post-op	Dalteparin 5,000 units 6 – 8 hours post-op	Dalteparin 5,000 units 6 – 8 hours post-op	Dalteparin 7,500 units 6 – 8 hours post-op	Dalteparin 7,500 units 6 – 8 hours post-op	
<b>+1</b>	Restart warfarin at patient's usual dose on day +1 (if on acenoumarol or phenindione: see page 14).					
	2,500 units once daily	5,000 units once daily	5,000 units once daily	7,500 units once daily	7,500 units once daily	Discuss dosing with a haematologist
<b>+2</b>	2,500 units twice daily	2,500 units twice daily	5,000units twice daily	7,500 units twice daily	7,500 units twice daily	
<b>+3</b>						
<b>+4</b>						
<b>+5 onwards</b>	5,000 units am 2,500 units pm	5,000 units twice daily	7,500 units twice daily	10,000 units twice daily	12,500 units twice daily	

**Dalteparin must only be started or increased post-operatively when haemostasis is secure.**

<b>Dalteparin dosing for high risk patients with calculated Creatinine Clearance 20 - 29 ml/min</b>
Discuss with a haematologist or use unfractionated heparin infusion

<b>Dalteparin dosing for high risk patients with calculated Creatinine Clearance less than 20 ml/min</b>
Use unfractionated heparin infusion