Bridging Anticoagulation: The Peri-Procedural Management of Patients on Oral Anticoagulants

Dr Stuti Kaul – Consultant Haematologist
Dr Ruth Medlock – Consultant Haematologist
Lee Wilson – Consultant Pharmacist
(With thanks to colleagues at Sheffield Teaching Hospitals NHS FT on whose guidance this guideline is heavily based)

Issued - July 2017
Review Date - July 2019
Table of contents

INTRODUCTION .................................................................................................................. 3
SITUATIONS COVERED BY THIS GUIDELINE .................................................................. 3
PRE-OPERATIVE ASSESSMENT AND MANAGEMENT & DAY SURGERY GUIDANCE ............ 4
  Pre-op assessment ............................................................................................................... 4
  Determining whether a patient is in the Standard risk or High risk category .................. 4
  Patients who are at particularly high risk of thrombosis ................................................. 4
  Procedures which carry a very high bleeding risk ......................................................... 4
  Patients with antithrombin deficiency ............................................................................. 4
  Patients with renal impairment ..................................................................................... 4
DAY SURGERY GUIDANCE .................................................................................................. 5
PRE-OPERATIVE & POST-OPERATIVE MANAGEMENT OF VITAMIN K ANTAGONISTS ......... 6
  Pre-operative investigations ............................................................................................ 6
  Pre-operative management of warfarin .......................................................................... 6
  Pre-operative management of phenindione and acenocoumarol ................................... 7
  Pre-operative management of emergency patients taking vitamin K antagonists .......... 7
  Post-operative management ......................................................................................... 7
  Post-operative summary for warfarin ............................................................................ 7
  Post-operative summary for phenindione and acenocoumarl ....................................... 8
PRE-OPERATIVE & POST-OPERATIVE MANAGEMENT OF PATIENTS TAKING DOACs ......... 9
  Pre-operative investigations ............................................................................................ 9
  Pre-operative management of apixaban, edoxaban, or rivaroxaban ............................. 9
  Pre-operative management of dabigatran ..................................................................... 9
  Pre-operative management of emergency patients taking DOACs ............................... 9
  Post-operative management ......................................................................................... 9
MONITORING FOR HEPARIN -INDUCED THROMBOCYTOPENIA (HIT) ............................... 10
MANAGEMENT OF SPINAL OR EPIDURAL ANALGESIA OR ANAESTHESIA ...................... 11
DISCHARGING PATIENTS ................................................................................................... 12
BACKGROUND AND RATIONALE FOR RECOMMENDATIONS .......................................... 13
  Introduction .................................................................................................................... 13
  Bleeding risk associated with procedures .................................................................... 14
  Assessment of thrombotic risk ..................................................................................... 14
  Low molecular weight heparin (LMWH) bridging anticoagulant therapy .................... 16
  Timescale for peri-operative anticoagulation ............................................................... 17
  Stopping warfarin .......................................................................................................... 17
  Other oral anticoagulants (e.g. apixaban, dabigatran, edoxaban and rivaroxaban) ....... 17
  Restarting anticoagulation and bleeding risk ................................................................. 18
REFERENCES ..................................................................................................................... 20
Appendix 1 - Procedures which may be performed with an INR less than 3.0 ..................... 22
Appendix 2 - Assessment of thrombotic risk ................................................................ 23
Appendix 3 - Treatment guidelines for Standard Risk patients on warfarin ..................... 24
Appendix 4 - Treatment guidelines for High Risk patients on warfarin ......................... 25
Appendix 5 - Cancellation of surgery .............................................................................. 26
Appendix 6 - Endoscopy Patients ................................................................................... 28
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, acenocoumarol (Sinthrome®), phenindione (Dindevan®), apixaban (Eliquis®) dabigatran (Pradaxa®), edoxaban (Lixiana®), or rivaroxaban (Xarelto®), who need interruption of anticoagulant therapy (with an INR of less than 1.5 if on warfarin, acenocoumarol or phenindione) for a procedure. Additional advice may be required from a haematologist regarding acenocoumarol or phenindione.

Management of peri-operative antiplatelet therapy is beyond the scope of this guidance but some pragmatic guidance can be found here.

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

- **Pregnant patients:** advice should always be sought from an Obstetrician or Haematologist
- **Endoscopy patients:** see Appendix 6
- **Bronchoscopy patients:** see link

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.**

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

**GPs should not be asked to prescribe or monitor bridging anticoagulation**
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. Certain procedures may be done whilst on rivaroxaban, dabigatran, apixaban and warfarin with an INR of less than 3.0 – see appendix 1 for further guidance.

2. If anticoagulation needs to be interrupted, determine whether a patient is in the Standard risk or High risk category (see appendix 2 for criteria for stratification of thrombotic risk).

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:
      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)
      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, radical prostatectomy).
   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 in appendix 3 (Standard risk), appendix 4 (High risk) and appendix 5 (cancellation of surgery).

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 is 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 should have doses reduced if eGFR is less than 20ml/min/1.73m².
   7.2. High risk patients should use IV unfractionated heparin if their calculated creatinine clearance is less than 30ml/min/1.73m². 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:
(140 – age__) x weight__(kg) X 1.04 (female) = _____ (mL/min)

Serum Creatinine (micromol/L) __ X 1.23 (male) = _____ (mL/min)

7.3 **Patients on apixaban, dabigatran, edoxaban or rivaroxaban with renal impairment should be managed according to the guidance below.**

8. Patients weighing more than 150kg should follow the treatment plans described in appendix 3 (Standard risk), appendix 4 (High risk) and appendix 5 (cancellation of surgery).

9. **If surgery is cancelled, see advice in appendix 5.** It is the responsibility of the person cancelling the patient to inform pre-assessment clinic staff as patients will need advice regarding their bridging therapy.
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 x10^9/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:

  - Pre-operative management for patients at **high thrombotic risk**

<table>
<thead>
<tr>
<th>Day -5</th>
<th>Day -4/-3</th>
<th>Day -2</th>
<th>Day -1</th>
<th>Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Last dose of warfarin</td>
<td>Omit warfarin until D+1</td>
<td>Check INR: If greater than 2 give phytomenadione 1mg (vitamin K) orally and recheck on day -1 If INR is between 1.5 and 2.0 (inclusive of these levels) give phytomenadione 1mg (vitamin K) and recheck on day -1. Start on twice daily dalteparin. - If less than 1.5 start twice daily dalteparin.</td>
<td>Recheck INR if greater than 1.5 on day -2 and give a second dose of phytomenadione 1mg (vitamin K) orally if greater than 1.5 Last dose of therapeutic dalteparin in the morning (24 hours pre-op)</td>
<td>Check INR if greater than 1.5 on day -1</td>
</tr>
</tbody>
</table>

  - Preoperative management for patients at **standard thrombotic risk**

<table>
<thead>
<tr>
<th>Day -5</th>
<th>Day -4</th>
<th>Day -3</th>
<th>Day -2</th>
<th>Day -1</th>
<th>Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Last dose of warfarin</td>
<td>Omit warfarin until D+1</td>
<td>Check INR: if greater than 1.5 give phytomenadione 1mg (vitamin K) orally Prophylactic dalteparin at least 12 hours before surgery</td>
<td>Check INR if greater than 1.5 on day -1</td>
<td>Check INR if greater than 1.5 on day -1</td>
<td></td>
</tr>
</tbody>
</table>

- Near patient testing is acceptable however, the patient must have a venous INR on either day -1 or -2 pre-operatively. Post operatively the patient must have venous samples undertaken whilst an inpatient but may return to near patient testing once discharged.

**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/acenocoumarol/phenindione reversal with vitamin K and/or prothrombin complex concentrate (Beriplex™) pre-operatively. Consider discussing with a haematologist.

**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 a haematologist.
   1.2. Dalteparin doses should be adjusted according to the patient’s weight and renal function.
   1.3. Patients undergoing cardiac surgery should not be given dalteparin on the day of surgery.

1.4. **Patients or their carers should be trained to inject dalteparin whilst they are in hospital.**
   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.

1.5. Patients with atrial fibrillation without prior stroke/TIA or rheumatic valvular heart disease 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.

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

Post-operative warfarin management for patients at **standard thrombotic risk**

<table>
<thead>
<tr>
<th>Surgery</th>
<th>D +1</th>
<th>D +2</th>
<th>D +3</th>
<th>D +4</th>
<th>D +5</th>
<th>D + 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dalteparin prophylaxis 6–8hrs post op</td>
<td>Warfarin at usual dose</td>
<td>Continue prophylactic dalteparin</td>
<td>Continue warfarin at usual doses and prophylactic dalteparin until INR is greater than 2.0 in patients with VTE or until discharge in patients with standard risk AF (without prior stroke/TIA or rheumatic valvular heart disease).</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Post-operative warfarin management for patients at **high thrombotic risk**

<table>
<thead>
<tr>
<th>Surgery</th>
<th>D +1</th>
<th>D +2</th>
<th>D +3</th>
<th>D +4</th>
<th>D +5</th>
<th>D + 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dalteparin prophylaxis 6–8hrs post op</td>
<td>Warfarin at usual dose</td>
<td>Continue prophylactic dalteparin</td>
<td>Warfarin at usual dose. Increase prophylactic dalteparin as per Appendix 4 (high risk)</td>
<td>Warfarin at usual dose. Increase dalteparin as per Appendix 4 (high risk)</td>
<td>Continue until INR is greater than 2.0</td>
<td></td>
</tr>
</tbody>
</table>
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 the earliest 24 hours after the procedure.

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

Post-operative phenindione/acenocoumarol management for patients at standard thrombotic risk

<table>
<thead>
<tr>
<th>Surgery Dalteparin prophylaxis 6–8hrs post op</th>
<th>D +1</th>
<th>D+2</th>
<th>D3/4/5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continue prophylactic dalteparin</td>
<td></td>
<td></td>
<td>Restart phenindione/acenocoumarol at usual doses between day 3-5 (at earliest day 3) and 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 very minor procedures (decision to be made in conjunction with the operating surgeon and haematologist)</td>
</tr>
</tbody>
</table>

Post-operative phenindione/acenocoumarol management for patients at high thrombotic risk

<table>
<thead>
<tr>
<th>Surgery Dalteparin prophylaxis 6–8hrs post op</th>
<th>D +1</th>
<th>D+2</th>
<th>D3/4/5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continue prophylactic dalteparin</td>
<td></td>
<td></td>
<td>Increase prophylactic dalteparin as per Appendix 4 (high risk) Continue until INR is greater than 2.0. Restart phenindione/acenocoumarol at usual dose between day 3-5 (at the earliest day 3)</td>
</tr>
</tbody>
</table>
PRE-OPERATIVE & POST-OPERATIVE MANAGEMENT OF PATIENTS TAKING APIXABAN (ELIQUIS®), DABIGATRAN (PRADAXA®), EDOXABAN (LIXIANA®) & RIVAROXABAN (XARELTO®)

Pre-Operative Management:

Pre-operative investigations:
1. A full blood count must be taken in the week prior to surgery. If the patient has acute or chronic thrombocytopenia (platelets less than 150 x10⁹/L) then discussion with a haematologist is recommended.
2. 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).
3. Obtain an accurate weight for the patient so that post-operative dalteparin dosing can be carried out correctly.

<table>
<thead>
<tr>
<th>Creatinine Clearance (ml/min)</th>
<th>Low bleeding risk procedure</th>
<th>High bleeding risk procedure (including spinal/epidural anaesthesia)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apixaban/Edoxaban/Rivaroxaban:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;30 ml/min</td>
<td>Omit for at least 24 hours</td>
<td>Omit for at least 48 hours</td>
</tr>
<tr>
<td>15 - 30ml/min</td>
<td>Omit for at least 48 hours</td>
<td>Omit for at least 72 hours</td>
</tr>
<tr>
<td>&lt; 15ml/min: contra-indicated</td>
<td>Discuss with Haematology</td>
<td>Discuss with Haematology</td>
</tr>
<tr>
<td>Dabigatran:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;80 ml/min</td>
<td>Omit for at least 24 hours</td>
<td>Omit for at least 48 hours</td>
</tr>
<tr>
<td>50-80 ml/min</td>
<td>Omit for at least 24-48 hours</td>
<td>Omit for at least 48-72 hours</td>
</tr>
<tr>
<td>30-50 ml/min</td>
<td>Omit for at least 48-72 hours</td>
<td>Omit for at least 96 hours</td>
</tr>
<tr>
<td>&lt; 30ml/min (contra-indicated)</td>
<td>Discuss with Haematology</td>
<td>Discuss with Haematology</td>
</tr>
</tbody>
</table>

Pre-operative management of emergency patients taking DOACs:
Refer to the “Guidelines for Management of Bleeding and Excessive Anticoagulation with Oral Anticoagulation” and discuss with haematology.

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 a haematologist.
   2.2. Dalteparin doses should be adjusted according to the patient’s weight and renal function. High risk patients with renal impairment (CrCl less than 30ml/min) should be discussed with a haematologist.

Post-operative summary for patients on DOACs for procedures with major bleeding risk

<table>
<thead>
<tr>
<th>Surgery (D 0)</th>
<th>D +1</th>
<th>D+2</th>
<th>D+3</th>
<th>D+4</th>
<th>D+5</th>
<th>D + 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dalteparin prophylaxis starting 6–8hrs post op</td>
<td>Restart DOAC at the earliest on day +3, depending on bleeding tendency. Check U&amp;E/LFT and do not restart if epidural in situ.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Post-operative management of DOACs after minor procedures and low bleeding risk:

- DOACs may be restarted at the earliest 24 hours post-procedure.
- If there is concern about absorption of DOAC, dalteparin may be continued longer at a dose depending on the thrombotic risk group. Dalteparin must still be discontinued 24 hours prior to restarting DOAC.
- Prophylactic doses of rivaroxaban (10mg OD) and dabigatran (150/220mg OD) may be restarted 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 a haematologist.

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 received unfractionated heparin (prophylactic or treatment doses) within the last 100 days. If the platelet count falls by 30-50% or to less than 150x10^9/L, and/or the patient develops new signs of thrombosis, suspect HIT, and 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 apixaban, dabigatran, edoxaban or rivaroxaban

<table>
<thead>
<tr>
<th>Creatinine Clearance (ml/min)</th>
<th>Interval between inserting or removing spinal/epidural catheter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rivaroxaban:</td>
<td></td>
</tr>
<tr>
<td>&gt;30ml/min</td>
<td>48 hours</td>
</tr>
<tr>
<td>&lt;30ml/min</td>
<td>72 hours</td>
</tr>
<tr>
<td>Apixaban:</td>
<td></td>
</tr>
<tr>
<td>&gt;30ml/min</td>
<td>48 hours</td>
</tr>
<tr>
<td>&lt;30ml/min</td>
<td>72 hours</td>
</tr>
<tr>
<td>Edoxaban:</td>
<td></td>
</tr>
<tr>
<td>&gt;30ml/min</td>
<td>48 hours</td>
</tr>
<tr>
<td>&lt;30ml/min</td>
<td>72 hours</td>
</tr>
<tr>
<td>Dabigatran:</td>
<td></td>
</tr>
<tr>
<td>&gt;80ml/min</td>
<td>48 hours</td>
</tr>
<tr>
<td>50-80ml/min</td>
<td>48-72 hours</td>
</tr>
<tr>
<td>30-50ml/min</td>
<td>96 hours</td>
</tr>
</tbody>
</table>

Patients taking a DOAC should be managed according to the DOAC bridging protocol when spinal/epidural catheters are to be removed or inserted (see table above – previous page)

1.4 Patients taking warfarin should have an INR of 1.4 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. Patients taking Warfarin:

Standard risk patients with atrial fibrillation (without prior stroke/TIA or rheumatic valvular heart disease) can stop dalteparin on discharge provided continuing thromboprophylaxis for other reasons is not indicated. All other standard risk patients should remain on dalteparin treatment until their INR is greater than 2.0 if they are taking warfarin. If INR is greater than 2 at the time of discharge, patients should be referred back to their usual anticoagulation provider. Patients must have an INR check within 7 days of discharge (sooner if clinically indicated). If INR is 2 or less, suitable discharge arrangements should be made.

- Ensure supply of dalteparin is prescribed on the TTO
- Train patient/carer to administer dalteparin wherever possible, or refer to a District Nurse
- Monitoring requirements (INR and HIT monitoring) should be considered.

Patients with atrial fibrillation without prior stroke/TIA or rheumatic valvular heart disease 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 MUST be referred to their regular anticoagulation provider for INR monitoring. These patients do not need to be “bridged” with dalteparin on discharge from hospital.

2. Patients taking DOACs (apixaban, dabigatran, edoxaban or rivaroxaban):

- Patients taking DOACs should be managed according to the peri-operative guidance within this guideline.
- Dalteparin MUST be discontinued the day before rivaroxaban, dabigatran, apixaban or edoxaban is restarted.
- INR monitoring is not required in patients who are taking rivaroxaban, dabigatran, apixaban or edoxaban and there is no referral required on discharge.
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) and the British Committee for Standards in Haematology (refer to: Peri-operative management of anticoagulation and antiplatelet therapy. Keeling, Tait, Watson, and on behalf of the British Committee of Standards for Haematology. BrJHaem 2016, Volume 175(4), p602–613).

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.

<table>
<thead>
<tr>
<th>Very high risk¹</th>
<th>High risk</th>
<th>Low risk²</th>
<th>Procedures which may be performed on warfarin ³</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac surgery</td>
<td>Major orthopaedic surgery</td>
<td>Minor procedures as specified by treating surgeon/physician</td>
<td>Diagnostic GI endoscopic procedures ± biopsy (Veitch et al, 2008)</td>
</tr>
<tr>
<td>Neurosurgery</td>
<td>Major vascular surgery</td>
<td></td>
<td>Biliary or pancreatic stenting (Veitch et al, 2008)</td>
</tr>
<tr>
<td>Spinal surgery</td>
<td>Major gynaecological and urological surgery</td>
<td></td>
<td>Diagnostic EUS (Veitch et al, 2008)</td>
</tr>
<tr>
<td>Radical prostatectomy</td>
<td>Major cancer surgery</td>
<td></td>
<td>Minor dermatological surgery (Douketis et al, 2012)</td>
</tr>
<tr>
<td></td>
<td>Other major abdominal and thoracic surgery</td>
<td></td>
<td>Minor dental surgery (Perry et al, 2007)</td>
</tr>
<tr>
<td></td>
<td>Renal biopsy</td>
<td></td>
<td>Minor ophthalmological surgery (cataract extraction) (Douketis et al, 2012)</td>
</tr>
</tbody>
</table>

¹ 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.

² 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.

³ 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. Bridging with therapeutic doses should be considered for those at highest thrombotic risk (Keeling et al, 2016):
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 in the last 3 months, patients with rheumatic valvular heart disease and patients who suffered a previous TIA/stroke over 3 months ago and who have 3 of the following risk factors:

- Congestive cardiac failure
- Hypertension (>140/90 mmHg or on medication)
- Age >75 years
- Diabetes mellitus

These patients should be bridged according to the high risk guideline (BCSH guidelines). The BRIDGE trial showed that bridging is associated with a significant risk of major bleeding whilst it does not reduce the risk of stroke in patients with a CHADS2 score of up to and including 4. There were too few patients to draw conclusions with a CHADS2 score of 5 and 6 (Douketis et al 2015).

For all other patients with AF this guideline recommends using prophylactic doses of LMWH whilst an inpatient. 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 3 months are at high risk of recurrence and any procedures (for which interruption of anticoagulation is necessary) should preferably be delayed for 3 months. If this is not possible, a temporary IVC filter should be considered following discussion with a Consultant Haematologist 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 DOACs (apixaban, dabigatran, edoxaban or rivaroxaban), the last LMWH dose should be 24 hours before restarting the DOAC.

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 DOACs (apixaban, dabigatran, edoxaban or rivaroxaban), the last LMWH dose should be 24 hours before restarting the DOAC. Both the creatinine clearance and liver function tests should be checked before restarting apixaban, dabigatran, edoxaban or rivaroxaban and the DOAC dose 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/1.73m². 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 30ml/min), the use of unfractionated heparin infusion is usually preferable.
**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 1.4 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. apixaban, dabigatran, edoxaban, and rivaroxaban):**

<table>
<thead>
<tr>
<th>Renal Function CrCl ml/min</th>
<th>Estimated half-life (hours)</th>
<th>Low bleeding risk</th>
<th>High bleeding risk</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Dabigatran</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;80</td>
<td>13</td>
<td>24 hours</td>
<td>48 hours</td>
</tr>
<tr>
<td>&gt;50 to &lt;80</td>
<td>15</td>
<td>24-48 hours</td>
<td>48-72 hours</td>
</tr>
<tr>
<td>&gt;30 to &lt;50</td>
<td>18</td>
<td>48-72 hours</td>
<td>96 hours</td>
</tr>
<tr>
<td><em>Rivaroxaban</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;30</td>
<td>9</td>
<td>24 hours</td>
<td>48 hours</td>
</tr>
<tr>
<td>&lt;30</td>
<td></td>
<td>48 hours</td>
<td>72 hours</td>
</tr>
<tr>
<td><em>Apixaban</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;30</td>
<td>8</td>
<td>24 hours</td>
<td>48 hours</td>
</tr>
<tr>
<td>&lt;30</td>
<td></td>
<td>48 hours</td>
<td>72 hours</td>
</tr>
<tr>
<td><em>Edoxaban</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;30</td>
<td>10-14</td>
<td>24 hours</td>
<td>48 hours</td>
</tr>
<tr>
<td>&lt;30</td>
<td></td>
<td>48 hours</td>
<td>72 hours</td>
</tr>
</tbody>
</table>

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.
Apixaban, dabigatran, edoxaban and rivaroxaban 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 anticoagulation with apixaban, dabigatran, edoxaban and rivaroxaban is sufficient to ensure haemostasis and that surgery is safe (Schulman & Crowther 2012).

**Apixaban, edoxaban & rivaroxaban**

This guideline recommends that for patients taking therapeutic doses of apixaban, edoxaban and rivaroxaban and who have a creatinine clearance of greater than 30 ml/min and are to undergo major surgery or procedures with high bleeding risk. Should omit these drugs for at least 48 hours.

In patients with a creatinine clearance <30ml/min undergoing a major procedure or procedures with high bleeding risk should omit these drugs for at least 72 hours.

Patients who are to undergo minor procedures with a low bleeding risk and a creatinine clearance greater than 30 ml/min whilst taking therapeutic apixaban, edoxaban, or rivaroxaban should omit these drugs for at least 24 hours.

Patients who are to undergo minor procedures with a low bleeding risk and a creatinine clearance of <30 ml/min should omit these drugs for at least 48 hours.

Patients taking prophylactic doses of rivaroxaban (10mg OD) must have taken their last dose of rivaroxaban at least 18 hours prior to the procedure (Keeling et al 2016). These drugs are contraindicated in a creatinine clearance of less than 15ml/min and these patients should be discussed with haematology.

**Dabigatran**

Patients taking therapeutic doses of dabigatran who have a creatinine clearance of greater than 80ml/min who require major surgery or a procedure with a high bleeding tendency should omit dabigatran for at least 48 hours.

Those with a creatinine clearance of 50-80ml/min should omit dabigatran for at least 48 – 72 hours and those patients with a creatinine clearance 30 – 50 ml/min should omit dabigatran for at least 96 hours.

Those requiring minor surgery with low bleeding risk and who have a creatinine clearance of greater than 80 ml/min should omit dabigatran 24 hours and those with a creatinine clearance of 50 – 80 ml/min for at least 24 – 48 hours and those with a creatinine clearance of 30 – 50 ml/min for at least 48 – 72 hours (Keeling et al 2016). Dabigatran is contra-indicated in patients with a creatinine clearance of less than 30ml/min and these patients should be discussed with Haematology.

**Influence of apixaban, dabigatran, edoxaban and rivaroxaban on routine coagulation testing**

A normal thrombin time effectively excludes the presence of dabigatran but a normal APTT and PT do not exclude significant concentrations of apixaban, rivaroxaban or edoxaban in a sample (Keeling et al 2016). Specific drug level measurements may be considered after discussion with haematology, for example, for emergency surgery when omission of the drug by the timescales in this guidance is not feasible, or acute renal failure when there is concern about drug accumulation.

**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 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. LMWH can be discontinued in standard risk patients with AF 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), dabigatran (110 or 150mg BD), apixaban (2.5 or 5mg BD) or edoxaban (30 or 60mg OD) should receive LMWH for at least 48 hours, at which point their normal dose of anticoagulant can be resumed provided there is no concern about bleeding at that point. LMWH must be discontinued 24 hours prior to restarting apixaban/dabigatran/edoxaban/rivaroxaban.
REFERENCES


Appendix 1

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

Diagnostic angiographic procedures by vascular radiology:
- 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.

Bronchoscopy patients: see link
Endoscopic procedures: see Appendix 6

PROCEDURES WHICH MAY BE PERFORMED ON APIXABAN, DABIGATRAN, EDOXABAN OR RIVAROXABAN

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, dabigatran or apixaban. 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 apixaban, dabigatran, edoxaban or rivaroxaban, 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

<table>
<thead>
<tr>
<th>Reason for being on oral anticoagulants</th>
<th>STANDARD RISK</th>
<th>HIGH RISK</th>
</tr>
</thead>
</table>
| **Prosthetic heart valve** | • Bileaflet mechanical aortic valve and no other risk factors for stroke and more than 3 months after implantation | • Any mechanical mitral valve  
• Caged ball or tilting disc aortic valve  
• Bileaflet mechanical aortic valve and one or more of the following stroke risk factors:  
  - chronic atrial fibrillation  
  - left ventricular dysfunction  
  - age over 75 years  
  - hypertension  
  - diabetes  
  - prior stroke or TIA  
• Any mechanical valve within 3 months of implantation |  
• Bioprosthetic valves with no other risk factors for stroke – anticoagulation not required. Thromboprophylaxis if indicated. |

| **Chronic atrial fibrillation** | • Atrial fibrillation without prior stroke/TIA or rheumatic valvular heart disease | • Atrial fibrillation with previous stroke/TIA within the last 3 months.  
• Atrial fibrillation with previous stroke/TIA & 3 or more of following risk factors:  
  - age >75  
  - congestive cardiac failure  
  - hypertension (>140/90mmHg or on medication)  
  - diabetes mellitus  
• Atrial fibrillation with rheumatic valvular heart disease |  |

| **Venous thromboembolism or antiphospholipid syndrome** | • Previous VTE and now on long term anticoagulant therapy (target INR 2.5) | • Recent episode of VTE (within 3 months) – discuss with senior clinician and anaesthetist: consider postponing surgery or placing an IVC filter  
• Antiphospholipid syndrome with a history of venous or arterial thrombosis  
• Recurrence of VTE on oral anticoagulation (target INR 3.5)  
• Patients with anti-thrombin deficiency should be discussed with haematology. |  |
| Pulmonary hypertension (undergoing a procedure that is not for investigation or management of PH) | PH patients with chronic thromboembolic pulmonary hypertension or IVC filter in situ: discuss with PH consultants regarding risk stratification, then manage according to this guideline.

- Pulmonary hypertension patients with other risk factors: risk stratify according to the risk factors as above
- Pulmonary hypertension patients who are on warfarin for survival benefit only: anticoagulation bridging is not required. |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Antithrombin deficiency</td>
<td>All patients with antithrombin deficiency should be discussed with a Haematologist before bridging is commenced, as some may require antithrombin replacement.</td>
</tr>
</tbody>
</table>
Appendix 3
TREATMENT GUIDELINES FOR STANDARD RISK PATIENTS

Use eGFR to assess renal function.

### TREATMENT PLAN FOR STANDARD RISK PATIENTS

**with eGFR 20ml/min/1.73m² or greater**

<table>
<thead>
<tr>
<th>Day</th>
<th>Weight less than 46kg</th>
<th>Weight 46 – 120kg</th>
<th>Weight 120 – 150kg</th>
<th>Weight greater than 150kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>-5</td>
<td>Last dose of warfarin/Vitamin K antagonist (4 clear days) – ensure patient has clear instructions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-4</td>
<td>No warfarin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| -1  | Check INR: if greater than 1.5: give phytomenadione (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) |
| 0   | Dalteparin 2,500 units **once daily** (pm)  
Dalteparin 5,000 units **once daily** (pm)  
Dalteparin 7,500 units **once daily** (pm)  
Dalteparin 5,000 units **twice daily** |
| +1 onwards | Dalteparin 2,500 units **once daily** (pm)  
Dalteparin 5,000 units **once daily** (pm)  
Dalteparin 7,500 units **once daily** (pm)  
Dalteparin 5,000 units **twice daily** |

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

### TREATMENT PLAN FOR STANDARD RISK PATIENTS

**with eGFR less than 20 ml/min/1.73m²**

<table>
<thead>
<tr>
<th>Day</th>
<th>Recommended treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>-5</td>
<td>Last dose of warfarin/Vitamin K antagonist (4 clear days)</td>
</tr>
<tr>
<td>-4</td>
<td>No warfarin</td>
</tr>
<tr>
<td>-3</td>
<td></td>
</tr>
<tr>
<td>-2</td>
<td></td>
</tr>
</tbody>
</table>
| -1  | Check INR: if greater than 1.5: give phytomenadione (vitamin K) 1mg orally stat. Re-check INR on day 0  
Start dalteparin 2,500 units **once daily** (pm) if INR is less than 2.0 (give last dose at least 12 hours before procedure) |
| 0   | Dalteparin 2,500 units 6–8 hours post-operatively |
| +1 onwards | Dalteparin 2,500 units **once daily** (pm)  
Restart warfarin at patient’s usual dose.  
Continue dalteparin as per day +1 until INR is greater than 2.0 |
### Appendix 4

**TREATMENT GUIDELINES FOR HIGH RISK PATIENTS**

**CALCULATE CREATININE CLEARANCE USING THE COCKCROFT-GAULT EQUATION OR**

[Click here to access the online CrCl calculator]

#### TREATMENT PLAN FOR HIGH RISK PATIENTS

with calculated CrCl ≥ 30 ml/min

<table>
<thead>
<tr>
<th>Day</th>
<th>less than 46kg</th>
<th>46-65 kg</th>
<th>66-99 kg</th>
<th>100-120 kg</th>
<th>121-150 kg</th>
<th>Greater than 150 kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>-5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Last dose of warfarin/ Vitamin K antagonist (4 clear days) – ensure patient has clear instructions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-2</td>
<td>Check INR: if greater than 1.5: give Phytomenadione (vitamin K) 1mg orally stat and re-check INR on day -1. Start twice daily dalteparin if INR is less than 2.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>5,000 units am 2,500 units pm</td>
<td>5,000 units twice daily</td>
<td>7,500 units twice daily</td>
<td>10,000 units twice daily</td>
<td>12,500 units twice daily</td>
<td>12,500 units twice daily</td>
</tr>
<tr>
<td>-1</td>
<td>5,000 units in the morning</td>
<td>5,000 units in the morning</td>
<td>7,500 units in the morning</td>
<td>10,000 units in the morning</td>
<td>12,500 units in the morning</td>
<td>12,500 units in the morning</td>
</tr>
<tr>
<td>0 (day of procedure)</td>
<td>Dalteparin 2,500 units 6 – 8 hours post-op</td>
<td>Dalteparin 5,000 units 6 – 8 hours post-op</td>
<td>Dalteparin 5,000 units 6 – 8 hours post-op</td>
<td>Dalteparin 7,500 units 6 – 8 hours post-op</td>
<td>Dalteparin 7,500 units 6 – 8 hours post-op</td>
<td></td>
</tr>
<tr>
<td>+1</td>
<td>Restart warfarin at patient’s usual dose on day +1. Continue dalteparin until the INR &gt; 2.0 on 2 consecutive days.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2,500 units once daily</td>
<td>5,000 units once daily</td>
<td>5,000 units once daily</td>
<td>5,000 units once daily</td>
<td>7,500 units once daily</td>
<td>7,500 units once daily</td>
</tr>
<tr>
<td>+2</td>
<td>2,500 units twice daily</td>
<td>2,500 units twice daily</td>
<td>5,000 units twice daily</td>
<td>5,000 units twice daily</td>
<td>7,500 units twice daily</td>
<td>7,500 units twice daily</td>
</tr>
<tr>
<td>+3</td>
<td>2,500 units twice daily</td>
<td>2,500 units twice daily</td>
<td>5,000 units twice daily</td>
<td>5,000 units twice daily</td>
<td>7,500 units twice daily</td>
<td>7,500 units twice daily</td>
</tr>
<tr>
<td>+4</td>
<td>5,000 units am 2,500 units pm</td>
<td>5,000 units twice daily</td>
<td>7,500 units twice daily</td>
<td>10,000 units twice daily</td>
<td>12,500 units twice daily</td>
<td>12,500 units twice daily</td>
</tr>
<tr>
<td>+5 onwards</td>
<td>5,000 units am 2,500 units pm</td>
<td>5,000 units twice daily</td>
<td>7,500 units twice daily</td>
<td>10,000 units twice daily</td>
<td>12,500 units twice daily</td>
<td>12,500 units twice daily</td>
</tr>
</tbody>
</table>
COCKCROFT-GAULT EQUATION:

\[ \text{CrCl} = \frac{((140 - \text{age in years}) \times \text{wt in kg}) \times 1.23}{\text{serum creatinine in micromol/l}} \]

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

<table>
<thead>
<tr>
<th>Dalteparin dosing for high risk patients with calculated CrCl less than 30 ml/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use unfractionated heparin infusion</td>
</tr>
</tbody>
</table>
Appendix 5
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.
- Teach patients or carers to inject dalteparin wherever possible, to avoid unnecessary community nurse workload.

| Dalteparin dosing for HIGH RISK PATIENTS & STANDARD RISK AF PATIENTS who have been cancelled and rescheduled within 1 week with calculated Creatinine Clearance 30ml/min or greater |
|---|---|---|---|---|---|
| less than 46kg | 46-65 kg | 66-99 kg | 100-120 kg | 121-150 kg | greater than 150kg |
| 5,000 units am | 5,000 units |7,500 units BD | 10,000 units BD | 12,500 units BD | Discuss with a Haematologist |
| 2,500 units pm BD | BD | BD | BD | |

The last dose should be given in the morning on the day prior to procedure/surgery

<p>| Dalteparin dosing for HIGH RISK PATIENTS &amp; STANDARD RISK AF who have been cancelled with calculated Creatinine Clearance less than 30ml/min |
|---|---|
| Discuss with a Haematologist. |</p>
<table>
<thead>
<tr>
<th>Weight less than 45kg</th>
<th>Weight 45 – 100kg</th>
<th>Weight 101 – 150kg</th>
<th>Weight greater than 150kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dalteparin 2,500 units once daily in the evening</td>
<td>Dalteparin 5,000 units once daily in the evening</td>
<td>Dalteparin 7,500 units once daily in the evening</td>
<td>Dalteparin 5,000 units twice daily in the evening</td>
</tr>
</tbody>
</table>

The last dose should be given in the evening on the day prior to procedure/surgery

<table>
<thead>
<tr>
<th>Dalteparin dosing for STANDARD RISK PATIENTS with eGFR less than 20 ml/min/1.73m²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-Xa monitoring may be required: discuss with a Haematologist</td>
</tr>
<tr>
<td>Dalteparin 2,500 units once daily in the evening</td>
</tr>
<tr>
<td>The last dose should be given in the evening on the day prior to procedure/surgery</td>
</tr>
</tbody>
</table>

Patients on a DOAC (apixaban, dabigatran, edoxaban or rivaroxaban)
If surgery is cancelled for patients on apixaban, dabigatran, edoxaban or rivaroxaban 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 6
ENDOSCOPY PATIENTS

COAGULATION PATHWAY FOR ENDOSCOPY PATIENTS

Please indicate which Pathway to follow: __________________________

Date: __________________________

Doctor’s Signature: __________________________

Dr Al-Najar, Dr A. Agrawal

June 2013

Review: June 2015

LOW RISK PROCEDURES
- Diagnostic gastroscopy +/- biopsy
- Biliary or Pancreatic stenting (confirmed diagnosis of cancer)

PATHWAY 1
- Warfarin
- Continue warfarin
- Check INR on arrival to Endoscopy
- If INR 2.5 (within therapeutic range) then biopsies can be taken

PATHWAY 2
- Nimesulide
- Dabigatran

PATHWAY 3
- Low-risk procedure and creatinine < 120
- Stop for 1 day

PATHWAY 4
- Warfarin
- Stop warfarin 5 days before endoscopy
- Restart warfarin
- Fast track APTT/PT
- Result should be normal
- Must have afternoon appointment

Please note: Patients who are on low molecular weight Heparin should have drug omitted on day of procedure.

HIGH RISK PROCEDURES
- All colonoscopy procedures
- ERCP

PATHWAY 5
- Warfarin
- Stop warfarin 5 days before endoscopy
- Non Valvular AF: ≥ 3 months after VTE

PATHWAY 6
- Warfarin
- Stop warfarin 5 days before endoscopy
- High-risk condition
-冠状动脉
- CVD
- PVD

PATHWAY 7
- Triangular Clopidogrel
- Stop warfarin 5 days before endoscopy
- High-risk condition
- Coronary artery
- Stents

PATHWAY 8
- Triangular Clopidogrel
- Stop warfarin 5 days before endoscopy
- High-risk condition
- Coronary artery
- Stents

Nursing staff: On yellow book, please state date when Warfarin stopped.

NHS Number: __________________________

District Number: __________________________

Surname: __________________________

Address: __________________________

DoB: __________________________

Review: June 2015