Perioperative management of Anticoagulant and Antiplatelet medication
GL067

Approval

<table>
<thead>
<tr>
<th>Approval Group</th>
<th>Job Title, Chair of Committee</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaesthetics Clinical Governance</td>
<td>Chair, Anaesthetics Clinical Governance</td>
<td>November 2016</td>
</tr>
</tbody>
</table>

Change History

<table>
<thead>
<tr>
<th>Version</th>
<th>Date</th>
<th>Author, job title</th>
<th>Reason</th>
</tr>
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<tbody>
<tr>
<td>7</td>
<td>Jan 2016</td>
<td>Jennie Rechner, Consultant Anaesthetist, Rebecca Sampson, Consultant Haematologist</td>
<td>Update and Review</td>
</tr>
<tr>
<td>8</td>
<td>November 2016</td>
<td>Jennie Rechner, Consultant Anaesthetist, Rebecca Sampson, Consultant Haematologist</td>
<td>Update</td>
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</table>
The following are guidelines only. If in doubt, cases should be discussed with the duty Consultant Haematologist and Cardiologist.

Anticoagulants (warfarin and direct oral anticoagulants) and antiplatelets (aspirin, clopidogrel, prasugrel, ticagrelor) affect either the coagulation cascade or platelet activity. They are not necessarily interchangeable and a patient may require both types of drug. Each patient needs to have their risk of thrombosis and risk of bleeding assessed (see table below and appendix A). A decision can then be made as to whether they will need to stop their anticoagulant/antiplatelet prior to surgery and whether they will require bridging with perioperative tinzaparin. Elective surgery should be avoided until treatment of venous thromboembolism (VTE) is complete (2-6 months) and for one month after arterial thromboembolism. An IVC filter should be considered for high thrombotic risk patients who are unable to receive bridging tinzaparin.

<table>
<thead>
<tr>
<th>High Thrombotic Risk</th>
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<tbody>
<tr>
<td>• Mechanical heart valves</td>
</tr>
<tr>
<td>In the mitral position</td>
</tr>
<tr>
<td>Any position with placement in the preceding 3 months</td>
</tr>
<tr>
<td>Older aortic valves (tilting discs, ball and cage) or bileaflet valves with AF, impaired LV, previous VTE)</td>
</tr>
<tr>
<td>Multiple valves</td>
</tr>
<tr>
<td>• Venous or arterial thromboembolism (VTE)</td>
</tr>
<tr>
<td>Within preceding 3 months</td>
</tr>
<tr>
<td>Recurrent thromboembolism (2 or more episodes)</td>
</tr>
<tr>
<td>• Known hypercoagulable state</td>
</tr>
<tr>
<td>Antiphospholipid antibody</td>
</tr>
<tr>
<td>Homozygous factor V Leiden</td>
</tr>
<tr>
<td>Protein C or S deficiency</td>
</tr>
<tr>
<td>Multiple genetic defects of above</td>
</tr>
<tr>
<td>• Acute intracardiac thrombus (within 12 weeks)</td>
</tr>
<tr>
<td>• Atrial Fibrillation with history of:</td>
</tr>
<tr>
<td>Stroke, TIA or VTE</td>
</tr>
<tr>
<td>With mechanical valve</td>
</tr>
<tr>
<td>• Active cancer</td>
</tr>
<tr>
<td>• Orthopaedic surgery leading to prolonged immobilisation</td>
</tr>
<tr>
<td>• Combination of moderate and low thrombotic risk factors</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Moderate Thrombotic Risk Group.</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Venous thromboembolism within preceding 3-6 months</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Low Thrombotic Risk Group.</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Atrial fibrillation without risk factors as defined above</td>
</tr>
<tr>
<td>• Heterozygous factor V Leiden</td>
</tr>
<tr>
<td>• Newer bileaflet aortic valves without risk factors as defined above</td>
</tr>
</tbody>
</table>
Patients on warfarin or acenocoumarol

Minor skin surgery, minor hand surgery, minor dental surgery and cataracts: INR ≤ 2.5 for hand surgery; within therapeutic range for minor skin, dental and cataract surgery.

Patients can usually continue warfarin. The INR should be checked in the preoperative assessment clinic and again on the morning of surgery. If the INR is usually more than 2.5 for hand surgery or more than 3.5 for minor skin/ dental/cataract surgery, bridging tinzaparin may be required. Minor skin surgery is confined to removal of skin lesions, minor hand surgery confined to the following under local anaesthesia (including biers block) only (primary carpal tunnel, trigger finger, Dupuytren's contracture and peripheral soft tissue lesions) and minor dental surgery (not extraction of wisdom teeth). If in doubt as to the bleeding risk of the operation please discuss with the surgeon. Patients having hand surgery under regional block need to discontinue warfarin and start bridging tinzaparin if required.

For cataract surgery the INR should be within the therapeutic range. Patients should be advised of the increased risk of haemorrhage.

All other surgery: requires an INR ≤1.5.

Please note why the patient is taking warfarin and whether they are at high, moderate or low risk of thrombosis. This determines whether they need bridging therapy (therapeutic subcutaneous tinzaparin).

Low thrombotic risk group
Omit 4 doses of warfarin; check that INR is ≤1.5 prior to surgery. Postoperatively restart warfarin as below.

Moderate thrombotic risk group
As for low thrombotic risk group unless the patient has a combinations of low and moderate risk factors; then manage as for high thrombotic risk group.

High thrombotic risk high – requires bridging tinzaparin perioperatively.

Preoperatively:
1. Omit 4 doses of warfarin and start tinzaparin 175 units/kg once per day sub. Cut. for two days prior to surgery using the pre-printed prescription label available (round up to nearest 1000units; use actual body weight; maximum dose is 25,000 units).
2. Prescribe the tinzaparin for 8am preoperatively.
3. Tinzaparin is omitted on the day of surgery.
4. Patients with an eGFR of <20ml/min need a reduced dose of tinzaparin of 100 units/kg for a maximum of 7 days.
5. Include postoperative doses in the prescription for patients having day surgery so that they can be discharged following surgery without needing to wait for further injections to be prescribed i.e. prescribe seven doses in total. Please complete the ‘Anticoagulants in ADSU’ proforma for these patients and place this in the surgical pathway.
6. All patients prescribed therapeutic tinzaparin need an ‘alert’ stickers placed on the front of the drug chart, anaesthetic chart and care pathway to alert the admitting team. The patient can be taught to self-inject at preoperative assessment clinic and there are packs available to facilitate this.

**Day of surgery:** No tinzaparin should be given on the day of surgery; there will therefore be a safe window for surgery (>20 hours).

**Postoperatively:** Restart both therapeutic tinzaparin and warfarin as soon as the risk of surgical haemorrhage is deemed to have passed, usually 12-48 hrs postoperatively. Continue the tinzaparin until the INR is > 2.0 or has reached the patient’s usual therapeutic level. If the surgery is day-case the patient will need to continue to inject tinzaparin at home until a therapeutic INR has been confirmed. The patient will usually require 3-5 doses of tinzaparin. These will have been prescribed in preoperative assessment clinic. Patients should restart their warfarin as follows:

<table>
<thead>
<tr>
<th>Normal warfarin dose</th>
<th>High thrombotic risk</th>
<th>Moderate thrombotic risk</th>
<th>Low thrombotic risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;5mg/day</td>
<td>10mg, 10mg, normal</td>
<td>10mg, 10mg, normal</td>
<td>10mg, 10mg, normal</td>
</tr>
<tr>
<td>≤5mg/day</td>
<td>5mg, 5mg, normal</td>
<td>5mg, 5mg, normal</td>
<td>Normal dose</td>
</tr>
</tbody>
</table>

The nurses on ADSU need to complete the ‘Anticoagulants in ADSU’ proforma before discharge.

**Emergency surgery in patients on warfarin:** Seek advice from the duty Consultant Haematologist. In general these patients need PCC (Prothrombin Complex Concentrates) available via Haematology Consultant on-call plus Vitamin K (prescribe as phytomenadione 5 - 10 mg by slow IV). FFP is no longer a first line treatment.

**Patients on direct oral anticoagulants (DOACs) – dabigatran (direct thrombin inhibitor) rivaroxaban, apixaban (Xa inhibitors)**

DOACs are anticoagulant drugs used in the management of thrombosis. Their perioperative management is important to avoid patient harm. The clinical consequences of a thrombotic or bleeding event must be taken into consideration. If patient has multiple risk factors for thrombosis and needs to stop the DOAC for more than 48-72 hrs the patient may require bridging tinzaparin.
There is a range of alternatives available to try to reverse DOACs depending on the DOAC. Timing is critical and must be planned and communicated carefully. Seek advice from duty Consultant Haematologist for emergency patients so that suitable reversal agents such as Idaracuzimab, beriplex and FEIBA can be discussed.

**Calculating creatinine clearance.** If the patient’s eGFR is greater than 50 there is no need to check creatinine clearance. If eGFR<50 calculate the creatinine clearance as follows.

\[
1.23 \times (140 - \text{age}) \times \text{weight} \times 0.85 \text{ if female}
\]

serum creatinine

(Age in years; weight in kg; creatinine in μ mol/l)

**Elective surgery**

Minor procedures including cataracts under local and selected hand / dental surgery under local – as warfarin; do not stop.

All other procedures – anticoagulation must be stopped. If the patient falls into a ‘high thrombotic risk’ category or has a combination of moderate and low thrombotic risk factors, bridging tinzaparin may be required as the current guidelines for cessation of the DOACS expose some patients to a prolonged period of inadequate anticoagulation. If patients are likely to receive a neuraxial block perioperatively, the anticoagulant will need to be stopped for longer. Please see separate guideline for anticoagulants and neuraxial blockade.

NB. See the individual drug Summary of Product Characteristics for detailed prescribing information. These can be found at [http://www.medicines.org.uk/emc/](http://www.medicines.org.uk/emc/)

**Dabigatran**

AF: 110-150mg bd

Since it is renally excreted, the time to stop depends on the patient’s renal function. See below for details on risk of bleeding. If eGFR<50 please calculate creatinine clearance as detailed above.

<table>
<thead>
<tr>
<th>Renal function (CrCl mL/min)</th>
<th>Last dose before surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low risk of bleeding</td>
</tr>
<tr>
<td>&gt;50</td>
<td>2 days (miss 2 doses)</td>
</tr>
<tr>
<td>30 - 50</td>
<td>3 days (miss 4 doses)</td>
</tr>
</tbody>
</table>

No dabigatran to be taken on the morning of surgery. Dabigatran must be stopped for 2-4 days depending on renal function if neuraxial blockade is likely.
Rivaroxaban

Postoperative prophylaxis: 10mg od
AF: 20mg od

<table>
<thead>
<tr>
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<th>Last dose before surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low risk of bleeding</td>
</tr>
<tr>
<td>&gt;30</td>
<td>2 days (miss 1 dose)</td>
</tr>
<tr>
<td>15-30</td>
<td>3 days (miss 2 doses)</td>
</tr>
</tbody>
</table>

No rivaroxaban to be taken on the morning of surgery. Rivaroxaban must be stopped for 24-48 hrs (depending on whether 10 or 20mg) if neuraxial blockade likely.

Apixaban

Postoperative prophylaxis: 2.5mg bd
AF: 5mg bd (>80 years with weight ≤60kg, 2.5mg bd)

<table>
<thead>
<tr>
<th>Renal function (CrCl mL/min)</th>
<th>Last dose before surgery</th>
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<tbody>
<tr>
<td></td>
<td>Low risk of bleeding</td>
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</tr>
<tr>
<td>15-30</td>
<td>3 days (miss 4 doses)</td>
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</table>

No apixaban to be taken on the morning of surgery. Apixaban must be stopped for 48 hrs (depending on renal function) if neuraxial blockade likely.
Edoxaban

<table>
<thead>
<tr>
<th>Renal function (CrCl mL/min)</th>
<th>Last dose before surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low risk of bleeding</td>
</tr>
<tr>
<td>&gt;50</td>
<td>1 day</td>
</tr>
<tr>
<td>15-50</td>
<td>2 days</td>
</tr>
</tbody>
</table>

No edoxaban to be taken on the morning of surgery. Edoxaban must be stopped for 48 hrs (depending on renal function) if neuraxial blockade likely.

Postoperative resumption of new oral anticoagulants

NB. See the individual drug Summary of Product Characteristics for detailed prescribing information. These can be found at [http://www.medicines.org.uk/emc/](http://www.medicines.org.uk/emc/)

Bridging tinzaparin should be prescribed postoperatively in the same way as for those on warfarin until the direct oral anticoagulants are restarted.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Low bleeding risk surgery</th>
<th>High bleeding risk surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dabigatran</td>
<td>Resume on day after surgery (24 h postoperative), 110-150 mg twice daily</td>
<td>Resume 2-3 days after surgery (48-72 h postoperative), 150 mg twice daily</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>Resume on day after surgery (24 h postoperative), 10-20 mg once daily</td>
<td>Resume 2-3 days after surgery (48-72 h postoperative), 20 mg once daily</td>
</tr>
<tr>
<td>Apixaban</td>
<td>Resume on day after surgery (24 h postoperative), 5 mg twice daily</td>
<td>Resume 2-3 days after surgery (48-72 h postoperative), 5 mg twice daily</td>
</tr>
</tbody>
</table>

Urgent surgery

- Stop anticoagulation
- Check FBC, U&Es, Ca, full coagulation screen including fibrinogen. Indicate timing of last dose on request card.
- Delay surgery if possible until coagulation screen normal.
- Consult Haematology if surgery immediately necessary. They may recommend Beriplex® (human prothrombin complex) or Factor VIII Bypassing agent (FEiBA)
Patients on drugs inhibiting platelet activity

Low dose aspirin should be continued peri-operatively whenever possible, in particular for high-risk patients.

Patients undergoing surgery for whom bleeding may have catastrophic consequences (e.g. closed space surgery such as spinal surgery, cervical nerve root blocks) should be discussed with the relevant specialists (surgery, anaesthesia, cardiology). The patient should be counselled concerning the risks of stopping aspirin.

Low dose aspirin may be continued for patients undergoing neuraxial blockade such as caudals.

Patients who are at high risk of event (e.g. cardiac, MI, VTE) if aspirin withheld:
≤ 6 weeks after MI, PCI, bare metal stents, CABG
≤ 6 weeks after above if complications
≤ 2 weeks after stroke
≤12 months following drug-eluting stent

Patients who are at intermediate risk of event if aspirin withheld:
≤ 6-24 weeks after MI, PCI, bare metal stents, CABG, stroke
≤ 12 months following drug eluting stents, high-risk stents, low ejection fraction, diabetes.

Patients who are at low risk of event if aspirin withheld:
≥ 6 months after MI, PCI, BMS, CABG, stroke
≥ 12 months after the above if complications

If appropriate, stop aspirin for 7 days.

**NSAIDS:** Patients undergoing spinal surgery should stop NSAIDS for 3 days.

**Dipyridamole:** Stop dipyridamole 48 hours before surgery if other antiplatelet medication is to be stopped.

**Clopidogrel, prasugrel and ticagrelor:** Patient may receive dual antiplatelet therapy for a specified period or alternatively may receive clopidogrel/ticagrelor as monotherapy if intolerant of aspirin. The former group are likely to be at high risk of thrombosis and premature discontinuation of medication may lead to significant harm. Please note indications for taking these agents:

- Acute coronary syndrome & drug-eluting stent – 12 months
- Bare metal stent – 4 weeks minimum, preferably 3 months
- Post CVA either as dual therapy or if aspirin not tolerated
- Most NSTEMIs require dual antiplatelet therapy for 1 year regardless of stenting
- Post TAVI (Trans catheter aortic valve implantation)
• Superior mesenteric artery stent – lifelong
• Alternative to aspirin as monotherapy for secondary prevention of stroke/MI

Elective surgery after acute coronary syndrome and after inserting a drug-eluting stent should be delayed for 6-12 months. Discuss premature discontinuation of antiplatelet therapy with a cardiologist prior to surgery. The risks depend not only on the time since the stent but where the stent has been placed.

Emergency surgery on patients taking antiplatelet therapy following a recent acute coronary syndrome or coronary stent implant: discuss with a cardiologist prior to surgery.

Patients having an angioplasty and stent for peripheral vascular disease can remain on dual antiplatelet therapy throughout.

Patients prescribed clopidogrel/ticagrelor as monotherapy for secondary prevention should continue perioperatively if the risk of bleeding is low. Aspirin may be a suitable alternative if there are no contraindications.

Patients undergoing surgery with a significant risk of bleeding or for whom bleeding may have catastrophic consequences (e.g. closed space surgery such as spinal surgery, cervical nerve root blocks) should be discussed with the relevant specialists (surgery, anaesthesia, cardiology). The patient should be counselled about the risks of stopping dual antiplatelet therapy.
Clopidogrel, prasugrel, if they are to be stopped, should be stopped for 7 days. Ticagrelor should be stopped for 5 days.

What is the risk of an adverse event if clopidogrel (or prasugrel/ticagrelor) is stopped perioperatively?

**HIGH RISK**
Indication: Drug eluting stent, mesenteric artery stent, recently implanted bare metal stent (<4 weeks) or recent troponin +ve ACS

- Is indication for clopidogrel temporary?
  - NO
  - YES

- Is surgery essential?
  - NO
  - YES

- Can surgery be delayed for this length of time?
  - NO
  - YES

- Consider delaying surgery until patient has finished taking clopidogrel for 1 month

**LOW RISK**
Indication: Atrial fibrillation, long term prophylaxis for stroke or myocardial infarction, primary prevention in patients intolerant of aspirin

Discuss with cardiologists and surgeons and make a combined decision
1. Relative risks of thrombosis (if clopidogrel stopped) vs bleeding (if clopidogrel continues) vs cancelling surgery
2. Benefits of central neuraxial blockade (clopidogrel needs to be stopped for 7 days) vs continuing clopidogrel

Discuss risks and benefits of treatment

**Stop clopidogrel:**
- Advise patient of increased risk of thrombosis during surgery
- Stop clopidogrel 7 days preop
- Continue aspirin through surgery if at all possible
- Restart clopidogrel as soon as possible after surgery (once epidural and high risk central venous lines removed and risk of haemorrhage minimised).

**Continue clopidogrel:**
- Advise patient of increased risk of bleeding during surgery
- Avoid central neuraxial blockade
- Consider site of central venous access (avoid subclavian route) and technique (USS guided)
- Ensure X-matched platelets are available at short notice during surgery should catastrophic haemorrhage occur.
Appendix A

Suggested risk stratification for perioperative bleeding

High (2-day risk of major bleed 2%-4%)
- Neurosurgical/urologic/head and neck/abdominal/breast cancer surgery
- Joint arthroplasty
- Spinal surgery
- Transurethral prostate resection
- Kidney biopsy
- Polypectomy, variceal treatment, biliary sphincterectomy, pneumatic dilatation
- PEG placement
- Endoscopically guided fine-needle aspiration
- Multiple tooth extractions
- Any major operation (procedure duration > 45 minutes)

Low (2-day risk of major bleed 0%-2%)
- Laparoscopic cholecystectomy
- Gastrointestinal endoscopy ± biopsy, enteroscopy, biliary/pancreatic stent without sphincterotomy, endosonography without fine-needle aspiration
- Pacemaker and cardiac defibrillator insertion and electrophysiological testing
- Simple dental extractions
- Carpal tunnel repair
- Knee arthroscopy
- Hysteroscopy
- Skin cancer excision
- Abdominal hernia repair
- Haemorrhoidal surgery
- Hydrocele repair
- Cataract and non-cataract eye surgery

This table is based on definitions derived from surgical/subspecialty societies in anticoagulant bridging or anticoagulant bridging management studies

References:
5. Horlocker T. Regional anaesthesia in the patient receiving antithrombotic and antiplatelet therapy. BJA 2011; 107: i96-i106
6. The Handbook of Peri-Operative Medicines. UK Clinical Pharmacy Association
8. Korte W et al. Peri-operative management of antiplatelet therapy in patients with coronary artery disease. Joint position paper by members of the working group on Perioperative Haemostasis of the Society on Thrombosis and Haemostasis Research (GTH), the working group on Perioperative Coagulation of the Austrian Society for Anesthesiology, Resuscitation and Intensive Care (ÖGARI) and the Working Group Thrombosis of the European Society for Cardiology (ESC)