

Quick reference guide for the administration of anticoagulants and antiplatelet medication in the perioperative period

| CATEGORY: | Clinical Guidelines |
|------------------------------|---------------------------|
| CLASSIFICATION: | Clinical |
| Controlled Document Number: | CG331 |
| Version Number: | 1 |
| Controlled Document Sponsor: | Clinical Guidelines Group |
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| Approved By: | Clinical Guidelines Group |
| On: | May 2018 |
| Review Date: | May 2021 |

Introduction

As the number of anticoagulant medications is ever increasing, the guidance pertaining to their use in the perioperative period has become increasingly complicated. This is a brief guide designed primarily for the use of the anaesthetic department. It seeks to cover the appropriate management of oral anticoagulation and antiplatelet medication throughout the perioperative period, including whom to contact for further advice and the referral process for the anticoagulation bridging clinic. It also provides a brief overview of the agreements with the surgical subspecialties regarding when to stop medication perioperatively.

Rationale

Optimum perioperative management of anticoagulants and antiplatelet medication must balance the risk of thrombosis associated with stopping the drug with the risk of bleeding associated with the procedure. Whilst each case must be evaluated on its own merits, and expert consensus sought where there is any doubt, this guideline provides some basic principles to which anaesthetists can adhere.

Anaesthetists are frequently concerned with the safety of performing central neuraxial blockade in patients who are anticoagulated. Increasingly the importance of making the correct decision regarding withholding of medication perioperatively falls under our remit and responsibilities.

This guideline does not cover patients undergoing emergency surgery: the urgent nature of the situation and the inability to instigate appropriate bridging therapy necessitate a discussion with the team who instigated the anticoagulant or antiplatelet medication and also the haematology registrar or consultant on call. It also does not cover patients being admitted to Birmingham Women's Hospital although the principles underpinning the management may be similar.

Indications for instigating anticoagulants or antiplatelet medication

Patients are started on these medications for a relatively small number of reasons:

- 1. Venous thromboembolic (VTE) treatment or prophylaxis
- 2. Atrial fibrillation
- 3. Metallic heart valve
- 4. Following stroke or transient ischaemic attack (TIA)
- 5. Post-insertion of cardiac stents
- 6. Following myocardial infarction (MI), coronary artery bypass graft (CABG) or other cardiac procedure.

Weighing up the risks

When considering the perioperative management of patients taking anticoagulants or antiplatelet medication the risk of incurring a thrombosis must be weighed up against the risk of bleeding during the procedure. In addition to surgical risk, the appropriateness of regional anaesthetic techniques should also be evaluated.

Risk of thrombosis 1,2,3,4

| Low risk | Intermediate risk |
|-------------------------------------|--|
| Six months after CABG or MI without | Six months after CABG or MI with |
| complications | complications |
| Twelve months after stroke without | Greater than one year after drug-eluting |
| complications | stent insertion |
| Primary prevention of stroke or MI | Greater than four weeks after bare metal |
| | stent insertion |
| | Diabetes mellitus |
| | Malignancy |
| | Low ejection fraction (<40%) |
| | Greater than three months following |
| | DVT/PE |

| High risk | |
|---------------------------------------|---|
| Six weeks after MI or CABG | Within one year of drug-eluting stent |
| Two weeks after stroke | insertion |
| AF with previous stroke | Within four weeks of bare metal stent |
| Thrombophilias: antiphospholipid | insertion |
| syndrome, antithrombin III deficiency | High risk stents: |
| Patients with LVAD | History of stent thrombosis |
| Non-AF source of cardiac thrombus | More than one stent |
| within the last month | Long stent |
| Mitral or aortic metallic valve | Stent placed at bifurcation |
| Carotid stenosis | Stent in left main artery or within |
| Within three months of diagnosis of | small arteries |
| DVT/PE | 31113111 3111333 |

NB: Estimated mortality following stent thrombosis is 50%.

Risk of bleeding in non-cardiac surgery based on procedure^{5,6}

| Low risk | Intermediate risk | High risk |
|----------------------------|-------------------|------------------------|
| Dental | Visceral | Spinal or neurosurgery |
| Dermatological | Cardiovascular | Posterior chamber |
| biopsies | Major orthopaedic | ophthalmic |
| Minor orthopaedic eg joint | ENT | Hip arthroplasty |
| injections and soft tissue | Urology | Transurethral |
| aspirations | | prostatectomy |
| Anterior chamber | | |
| ophthalmic | | |
| Endoscopy | | |
| | | |

Central neuraxial blockade should be considered as major bleeding risk requiring complete haemostasis⁷.

Guidance for stopping anticoagulants and antiplatelet medication preoperatively

A comprehensive account of when medications should be stopped is found here: http://uhbpolicies/assets/OralAnticoagulantAntiplateletGuideline.pdf

Further information on direct oral anticoagulant drugs (DOACs) can be found here: http://uhbpolicies/assets/DoacsInitiationMonitoring.pdf

For patients undergoing procedures at low risk of bleeding, anticoagulants and antiplatelet medication can be continued throughout the perioperative period.

Where patients are at intermediate or high risk of bleeding, consideration needs to be given as to the risk of thrombosis. Those at low risk of thrombosis are likely able to be managed by discontinuing their usual medication preoperatively and it being replaced with a low molecular weight heparin (LMWH) such as tinzaparin in the postoperative period if their VTE assessment requires it before recommencing their usual medicines.

Patients at intermediate and high risk of thrombosis in who it is felt necessary to stop anticoagulant and antiplatelet medication are those that need to be considered for perioperative bridging therapy. A referral to bridging clinic should be completed if stopping oral or parenteral anticoagulants. The process of how to achieve this is listed in Appendix 3. Therapeutic anticoagulation is not recommended within 72 hours following major surgery associated with a bleeding risk or with an epidural catheter in situ due to the risk of bleeding and epidural haematoma formation: if this is felt necessary then each case must be evaluated on its merits and discussed with the relevant specialties involved in the patient's care.

Please note in patients considered to be at very high risk of thromboembolism the Trust guidance recommends stopping clopidogrel for five days instead of the usual

seven and aspirin stopped for three days or not at all. These cases are best discussed with the relevant specialties with knowledge of the indication for commencing antiplatelet treatment and the risks of pausing it before any medication is stopped.

Regional anaesthesia

Of paramount concern to anaesthetists is the safety of performing central neuraxial blockade. As before, the risk of thrombosis and the overall appropriateness of performing a regional technique must be balanced. Where a central neuraxial blockade is to be performed, it is imperative the correct medications are stopped preoperatively and in many cases not resumed until after an epidural catheter has been removed where one has been sited. The table in appendix 1 lists the necessary time lines and when the medication can be safely reinstated postoperatively.⁷

Where it is desirable to resume therapeutic anticoagulation (therapeutic dose LMWH or unfractionated heparin (UFH)) within 72 hours following surgery then epidural analgesia is likely best avoided.

Epidural care, and pertinently their removal, is covered in the Trust guideline "Expanded Practice Protocol for the Care of a Continuous Epidural Infusion for the Management of Acute Pain".

http://uhbpolicies/assets/EppCareContinuousEpiduralInfusionAcutePain.pdf

In summary, epidurals must be removed within 5 days of insertion. There should be at least 12 hours from the last dose of prophylactic LMWH before an epidural is removed. INR should be <1.5.

Emergency advice – Contact haematology registrar or consultant via switchboard. There is a haematology registrar on for referrals between 9am and 5pm each day, with consultant support, thereafter there is an on call registrar and a consultant who covers general haematological problems.

Appendix 1: Safe administration time intervals for perioperative anticoagulant and antiplatelet medicines⁸

| Drug | Acceptable time after administration to perform block | Administration of drug whilst spinal or epidural catheter in place | Acceptable time after block/catheter removal before drug can be given |
|-------------------------------------|---|--|--|
| Heparins | | | |
| UFH subcutaneously (sc) prophylaxis | 4 hours or normal APTTR | Caution ¹ | 1 hour |
| UFH intravenous (iv) treatment | 4 hours or normal APTTR | Caution ¹ | 4 hours ² |
| LMWH sc prophylaxis | 12 hours | Caution ¹ | 4 hours ² |
| LMWH sc treatment | 24 hours | Not recommended | 4 hours ² |
| Heparin alternatives | | | |
| Danaparoid | Avoid (consider anti- Xa levels) | Not recommended | 6 hours |
| Bivalirudin | Avoid ³ | Not recommended | 6 hours |
| Argatroban | Avoid ³ | Not recommended | 6 hours |
| Fondaparinux | 96 hours (consider | Not recommended | 6-12 hours |
| prophylaxis | anti-Xa levels) | | |
| Fondaparinux treatment | Avoid (consider anti- Xa levels) | Not recommended | 12 hours |
| Antiplatelet medication | | | |
| NSAIDs | No additional | Continue | Continue |
| 110/1120 | precautions | Continuo | Continuo |
| Aspirin | No additional precautions | Continue | Continue |
| Clopidogrel | 7 days | Not recommended | 6 hours |
| Prasugrel | 7 days | Not recommended | 6 hours |
| Ticagrelor | 7 days | Not recommended | 6 hours |
| Tirofiban | 8 hours | Not recommended | 6 hours |
| Eptifibatide | 8 hours | Not recommended | 6 hours |
| Abciximab | 48 hours | Not recommended | 6 hours |
| Dipyridamole | No additional precautions | Continue | 6 hours |
| | | | |

| Oral anticoagulants | | | |
|---|---|--|-------------------------------|
| Warfarin Rivaroxaban CrCl >30ml/min Dabigatran | 5 days or INR <1.5 60 hours ⁴ | Not recommended Not recommended | After removal 6 hours |
| CrCl >80ml/min CrCl 50-80ml/min CrCl 30-50ml/min Apixaban | 60 hours ⁴ 72 hours 96 hours 60 hours ⁴ | Not recommended Not recommended Not recommended Not recommended | 6 hours 6 hours 6 hours |
| Thrombolytic drugs Alteplase, anistreplase, reteplase, streptokinase | 2 days ⁵ | Not recommended | 10 days |

Notes:

- Caution is advised in the use of UFH due to the variability in response and difficulty controlling levels. Whilst caution is advised when considering prophylactic LMWH with an epidural in situ this is standard practice presuming there are no specific concerns that would contraindicate its use;
- 2.) UFH and LMWH should be avoided for 6 hours following traumatic spinal or epidural insertion;
- 3.) Association of Anaesthetists of Great Britain and Ireland (AAGBI) suggests that central neuraxial blockade can be performed following bivalirudin and argatroban after 10 and 4 hours respectively with a normal APTTR, however epidural insertion is not generally recommended given the likely necessity to resume these medications following surgery;
- 4.) Guidance varies from AAGBI regarding the DOACs and how long they should safely be stopped for preoperatively. For consistency 60 hours is recommended from last dose to safe insertion of central neuraxial blockade. 48 hours is acceptable for most types of surgery where no central neuraxial blockade is anticipated;
- 5.) If normal fibrinogen. All thrombolytic agents have a short half-life. The guidance from the AAGBI document suggests central neuraxial blockade is contraindicated for 10 days following administration of thrombolytics but we are unable to find evidence to support this. However thrombolysis is contraindicated for 10 days following central neuraxial blockade.

Appendix 2: Sub-specialty agreed arrangements

Breast, burns and plastics, maxillofacial, colorectal, upper gastrointestinal and general surgery

No specific advice beyond guidance above. Stop aspirin on day of surgery.

Liver

Liver biopsy, TIPSS, ERCP:

| Drug | Action |
|-------------------------------|---|
| Aspirin, dipyridamole, NSAIDs | Stop 7 days preprocedure |
| Clopidogrel | Stop 10 days preprocedure ¹ |
| Warfarin | Stop 5 days preprocedure and start LMWH if necessary; INR <2 for transjugular biopsy, <1.3 for percutaneous biopsy. |

1.) This is an amendment to the Trust liver biopsy guideline which will be altered in line with this guideline.

Neurosurgery

The below is a summary of the guidance agreed between the neurosurgeons and anaesthetists.

For neuroradiology procedures discuss with the responsible neuroradiologist before stopping or commencing any anticoagulant or antiplatelet medication.

| Drug | Action |
|--------------|--|
| Aspirin | Stop 7 days preoperatively. If high risk discuss with anaesthetist. |
| Dipyridamole | Stop 24 hours preoperatively. |
| Clopidogrel | Stop 7 days preoperatively. |
| NSAIDs | Stop 5 days preoperatively. |
| | Exception is microdiscectomy – discuss with surgeon. |
| Warfarin | Stop preoperatively with referral to bridging clinic if required (see |
| | appendix 3). INR must be normal for operation. |
| DOACs | Stop At least 48 hours preoperatively unless eGFR |
| | <30ml/min/1.73m ² , in which case stop for 72 hours. Dabigatran may |
| | need to be stopped for longer (as per table on page 7). |

Ophthalmology

Cataract surgery

Two large studies have shown no increased risk of complications following cataract surgery in patients taking anticoagulants. As such patients should continue their usual anticoagulant regimen, within the therapeutic range, checked on the day of surgery. It may be preferable to perform a blunt needle technique such as a subtenon rather than peribulbar block.⁹

Orbital and lid surgery

These are more prone to bleeding and blood tracking into the orbit can cause compartment syndrome and acute visual loss. As such patients may need to stop or take a reduced anticoagulation regimen.

Retinal and glaucoma surgery

These have an increased risk of intra-ocular haemorrhage and will need to be assessed on a case-by-case basis by the consultant surgeon.

Pain management

| Low risk | Intermediate risk | High risk |
|---|--|--|
| Peripheral nerve blocks Peripheral joints and musculoskeletal injections Trigger point injections Sacroiliac joint injections | Interlaminar ESI Transforaminal ESI Facets /MBBI Radiofrequency ablations Intradiscal procedures Paravertebral blocks Sympathetic Blocks (stellate ganglion , thoracic, splanchnic, coeliac, lumbar hypogastric, ganglion impar) Peripheral nerve stimulations trials or implants IPG placement/ ITP replacement Sacroiliac join injections | Spinal Cord Stimulator trial and implant Intrathecal catheter and pump implant Vertebral augmentation (vertebroplasty and kyphoplasty) Epiduroscopy and epidural decompression |

For low risk procedures all medicines can be continued perioperatively. For intermediate and high risk procedures stop medications as per guidance on pages 6-7 unless listed below.

| Drug | Action |
|---------------|--|
| Dipyridamole | Stop 2 days pre-procedure. |
| Acenocoumarol | Stop 3 days pre-procedure. Normal INR. |

Renal

Major procedures:

| Drug | Action |
|--------------|--|
| Aspirin | Stop 24 hours preoperatively unless differing instruction from consultant. |
| Dipyridamole | Stop 24 hours preoperatively. |
| Clopidogrel | Stop 7 days preoperatively. |
| Warfarin | Stop 5 days preoperatively +/- LMWH cover. Withhold LMWH the night before procedure. |

Renal biopsy:

| Drug | Action |
|--------------|--|
| | |
| Aspirin | Stop 7 days preprocedure unless differing instruction from consultant. |
| Dipyridamole | Stop 24 hours preprocedure unless differing instruction from |
| | consultant. |
| Clopidogrel | Stop 7 days preprocedure. |
| Warfarin | Stop 5 days pre-procedure +/- LMWH cover. INR must be <1.4. Last |
| | dose of LMWH must be at least 24 hours prior to biopsy. |

Urology

Stop aspirin/clopidogrel for 7 days before all major procedures and prostate biopsies.

List of major procedures: artificial urinary sphincter insertion, bladder biopsy, bladder neck incision, cystoscopy and biopsy, any cystectomy procedure, reimplantation of ureter, neobladder formation, nephrectomy, Nesbitt's procedure, orchidectomy, parastomal hernia repair, percutaneous nephrolithotomy (PCNL), pyeloplasty, prostatectomy, renal ablation, renal stone fragmentation, retroperitoneal lymph node dissection, transurethral resection of bladder tumour (TURBT), transurethral resection of prostate (TURP), ureteric stone removal, uretogram, uretoscopy, urethrectomy, urethroplasty, urinary diversion, vesicovaginal fistula repair.

Trauma and orthopaedics

There is specific guidance available pertaining to fractured neck of femur in patients depending on the proposed operative method of fixation.

Vascular

If in any doubt preoperative clinic will speak to the consultant surgeon directly.

Drug-eluting cardiac stent within the last 12 months or bare metal stent within the last three months: do not stop aspirin or clopidogrel. Speak to consultant surgeon who liaise with relevant specilaties.

Otherwise, the following guidance is accepted:

| Drug | Action |
|-------------------|--|
| | |
| Aspirin | Do not stop. |
| Clopidogrel | In general, do not stop. If sole agent before open abdominal |
| | aortic aneurysm(AAA) switch to aspirin 7 days pre-operatively |
| | (not endovascular aneurysm repair (EVAR)). |
| Dual antiplatelet | Do not stop either for carotid endartectomy. If for open AAA |
| therapy | continue aspirin only and stop clopidogrel for 7 days. |
| Dipyridamole | If sole agent, stop on day of surgery only. |
| Warfarin | Stop for 5 days and consider referral to bridging clinic if |
| | appropriate (discuss with surgeon if in doubt – see appendix 3). |

Appendix 3: Referral to anticoagulation bridging clinic.

All referrals to bridging clinic within UHB are performed via PICS. A minimum of one week is required between referral and surgery in order to accommodate patient admission if necessary. Where less than one week is available, please phone extension 2481 or 2479 to speak to the anticoagulation nurses whom may be able to provide further advice and arrange bridging therapy.

By following these step-by-step guidelines you should successfully submit a referral:

- 1. Log onto PICS
- 2. Click on "Pat Srch"
- 3. Enter patient hospital number
- 4. Click on "Open patient record without creating any form of admission"
- 5. Click on "Pat Admin"
- 6. Click on "Allergies"
- 7. Edit details then confirm
- 8. Click on "Observations"
- 9. Click on "Height/Weight"
- 10. Click on "**Now**" (right hand side of screen) and enter height and weight
- 11. Click on "Requests"
- 12. Click on "Nurse Specialists" then "New"
- 13. Select "Anticoagulant Team"
- 14. Select "Anticoagulant Bridging Therapy Referral"
- 15. Complete request. Include if a central neuraxial blockade is intended;
- 16. The screen page should indicate the referral has been submitted.

The anticoagulant team will then scan their response/action plan onto Clinical Portal once confirmed. It can be found under "Correspondence".

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