MIL

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This Medicines Information Leaflet is produced locally to optimise the use of medicines by encouraging prescribing that is safe, clinically appropriate and cost-effective to the NHS.

Elective Surgery and Invasive Procedures in Patients Taking Warfarin or a Direct Oral Anticoagulant (DOAC)

The management of patients who are receiving oral anticoagulation with warfarin or a Direct Oral Anticoagulant (DOAC e.g. dabigatran, rivaroxaban, apixaban, edoxaban) who require surgery or are undergoing a procedure depends on the underlying thrombotic risk, the intended surgical intervention, and the risk of bleeding associated with it. This MIL covers the management of patients on warfarin or a DOAC undergoing elective procedures, grouped into three categories: major surgery (excluding vascular surgery), minor surgery and endoscopy.

Note: Patients within 3 months of acute venous thromboembolism (VTE) are at high risk of recurrent VTE if anticoagulation is stopped; it is estimated that cessation of anticoagulation in the first month after an acute VTE is associated with a 40% one-month risk of recurrent VTE, and 10% for the subsequent two months. Therefore, wherever possible elective surgery should be delayed until 3 months after an acute VTE. If this is not possible then please speak with haematology (bleep 5529).

1) WARFARIN

a. Major surgery or procedure which requires the INR to be normalised

(i) Pre-operation

For patients on warfarin the pre-operative assessment team must liaise with the patient's anticoagulation service (bleep 1857 for Oxfordshire patients). Warfarin should be stopped 5 days before surgery.

The main decision is whether to give bridging therapy, with full treatment doses of low molecular weight heparin (LMWH) or, less commonly with unfractionated heparin (UFH) once the INR is subtherapeutic. Patients on warfarin for mechanical heart valves (MHV), atrial fibrillation (AF) or for treatment or prevention of venous thromboembolism (VTE) are considered for bridging therapy if they are regarded as at high risk of thrombosis (see table 1). The dose of dalteparin recommended for bridging is outlined in table 2.

All patients who do not require bridging with full treatment dose heparin peri-operatively should be risk assessed and given prophylactic dose LMWH as appropriate.

Table 1: Consider bridging with full treatment dose heparin in patients who stop warfarin if thrombotic risk is high

	Consider bridging with full treatment dose heparin in:
VTE	Patients with a VTE within previous 3 months. Very high risk patients such as patients with a previous VTE whilst on therapeutic anticoagulation who now have a target INR of 3.5.
AF	Patients with a previous stroke/TIA in last three months. Patients with a previous stroke/TIA and three or more of the following risk factors: • Congestive cardiac failure • Hypertension (greater than 140/90 mmHg or on medication) • Age over 75 years • Diabetes mellitus
MHV	All Mechanical Heart Valve patients except those with a bileaflet aortic valve and no other risk factors (AF, prior stroke or TIA, hypertension, diabetes, congestive cardiac failure or age over 75 years).

Table 2: Dose of dalteparin for bridging therapy

Body weight (kg)	Dose of dalteparin (units) (pre-filled syringe)
Less than 46	7,500 once daily
46-56	10,000 once daily
57-68	12,500 once daily
69-82	15,000 once daily
83-98	18,000 once daily
99-112	10,000 twice daily
113-137	12,500 twice daily
138-165	15,000 twice daily
166 or more	18,000 twice daily

There is no need to monitor the INR in patients who are at home for the 5 days before surgery. The last dose of warfarin should be taken on the evening of day -6. LMWH is started on the morning of day -3 and is continued until day -1 (i.e. 24 hours before surgery). If the surgery poses a high risk of bleeding, this final dose of LMWH on day -1 should only be half the full anticoagulant dose. **N.B.** according to Oxfordshire Shared Care guidelines, supply of LMWH for patients who need bridging at home should come from the hospital. This should be discussed and arranged during the pre-operative assessment.
In patients who are in hospital in the run up to surgery and who are receiving bridging anticoagulation with therapeutic dose UFH, heparin should be stopped 4-6 hours before surgery (discuss timing with the operating surgeon). Refer to MIL vol.5 no.6 "Guidelines on when to use and how to monitor unfractionated heparin in adults" for full guidance on the use of UFH.

In all patients whose warfarin has been stopped 5 days before surgery, the INR should be measured on the day before surgery, allowing correction with oral phytomenadione (vitamin K) if it is greater than or equal to 1.5 (suggested dose 2mg). If correction with phytomenadione is required, the INR should be re-checked on the morning of surgery.

(ii) Post- operation/procedure

In patients undergoing a procedure which carries a high risk of bleeding, the perioperative anticoagulation depends on a balance between the risk of bleeding and the risk of thrombosis.

Following major surgery, or procedure with high bleeding risk, therapeutic anticoagulation with LMWH should not be started until at least 48 hours post procedure. Consider prophylactic dose LMWH after surgery once haemostasis has been secured until therapeutic anticoagulation can be reintroduced. **Instruction for the provision of post-operative heparin is the responsibility of the operating surgeon and should be documented in the patient notes.**

Warfarin can be resumed, at the normal maintenance dose, the evening of surgery or the next day if there is adequate haemostasis, following discussion with the operating surgeon.

b. Minor surgery or procedure with low bleeding risk

For some operations the surgeon may advise that the INR need only be reduced (e.g. to 1.5-2) for the procedure in which case bridging anticoagulation may not be required. In these cases, the surgical team should liaise with the anticoagulation service in good time to make necessary dose adjustments and arrange an INR test the day before surgery as described above.

Some procedures, such as joint injections and cataract surgery, can be carried out without interrupting warfarin therapy. However, the person performing the procedure may advise that the INR is reduced to 1.5-2.

c. Gastrointestinal (GI) endoscopy in patients on warfarin

In general, low risk diagnostic procedures including mucosal biopsy can be performed when the INR is up to and including 3 without altering anticoagulation. For therapeutic procedures, the risk of post-procedure bleeding is higher and reduction of anticoagulation is preferred. However, there are no absolute rules and the risks and benefits should be discussed with the patient prior to the procedure and an individual decision made.

If warfarin is stopped, it is safe to reinstate anticoagulation on the evening of the procedure unless the endoscopist advises otherwise.

The risk of thromboembolism and risk of bleeding after a procedure can be divided into high and low, see **table 3**. The recommendations for action following risk assessment are summarised below:

High Risk Procedure
Warfarin should be discontinued 5 days before the procedure. Bridging therapy with heparin (UFH or LMWH) should be considered for high risk conditions whilst the INR is subtherapeutic. No bridging is needed if low risk condition.

Low Risk Procedure
No change in anticoagulation is recommended unless the INR is greater than 3 either due to over-anticoagulation or a previously desired higher target range.

Table 3: Risk evaluation for GI endoscopic procedures

Procedure	Condition
High Risk Procedures Polypectomy ERCP with sphincterotomy Ampullectomy EMR/ESD Dilation of strictures Therapy of varices PEG EUS with FNA Oesophageal, enteral or colonic stenting	**High Risk Conditions** Prosthetic metal heart valve in mitral position Prosthetic heart valve and AF AF and mitral stenosis Less than 3 months after VTE
Low Risk Procedures Diagnostic procedures +/- biopsy Biliary or pancreatic stenting Device-assisted enteroscopy without polypectomy	**Low Risk Conditions** Prosthetic metal heart valve in aortic position Xenograft heart valve AF without valvular disease Greater than 3months after VTE

2) DOACs

The approach to the peri-operative or peri-procedure management of patients on DOACs is based on an approximate calculation of the half-life of the drug and so its persistence in the circulation, taking into account renal function. This is combined with consideration of the bleeding risk of the proposed procedure and a clinical evaluation of the patient's individual risk factors for thrombosis and bleeding. Current strategies for elective surgery do not routinely include measurement of either non-specific or specific coagulation parameters to assist in quantification of DOAC levels.

Due to their short half-lives bridging with heparin is not required. Suggested periods for discontinuation are in table 4. Note: eGFR is a reasonable guide to GFR in most patients. However, in patients at extremes of body weight a GFR should be should be calculated using the Cockcroft-Gault formula.

Table 4: Discontinuation of DOACs for elective procedures

Renal Function eGFR (ml/min)	Low bleeding risk procedure	High bleeding risk procedure
Dabigatran		
80 or more	24 hours	48 hours
50 to 79	24-48 hours	48-72 hours
30 to 49	48-72 hours	96 hours
Dabigatran is not licensed for use with an eGFR below 30ml/min		
Apixaban, Rivaroxaban and Edoxaban		
30 or more	24 hours	48 hours
15-29	48 hours	72 hours
Apixaban, rivaroxaban and edoxaban are not licensed for use with an eGFR below 15ml/min		

Following low bleeding risk procedures, treatment dose anticoagulation can be recommenced once haemostasis is secured, usually at 24 hours.

Following major surgery, or procedure with high bleeding risk, DOACs should not be re-introduced at full dose until at least 48 hours post procedure.

In patients with a high thrombosis risk it is appropriate to give **prophylactic** dose LMWH until it is safe to switch the patient back onto a DOAC: When using prophylactic LMWH, it should usually be administered 6-12 hours post-surgery provided haemostasis is secure. For high bleeding risk surgery (such as spinal and cranial surgery) prophylactic dalteparin should be delayed for 24-48 hours. LMWH and DOAC should not overlap; they should be switched directly by giving the DOAC when the next dose of LMWH would have been due.

References

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