GUIDELINES ON PERIOPERATIVE MANAGEMENT OF ANTICOAGULANT AND ANTIPLATELET AGENTS

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Clinical Excellence Commission
Board Chair: Associate Professor Brian McCaughan, AM
Chief Executive: Ms. Carrie Marr

Any enquiries about or comments on this publication should be directed to:
Clinical Excellence Commission
Locked Bag 8
Haymarket NSW 1240
Phone: (02) 9269 5500
Email: cec-medicationsafety@health.nsw.gov.au

CONTENTS

INTRODUCTION

This clinical guideline is intended to assist clinicians with the inpatient and outpatient management of adult patients (over 16 years of age) undergoing procedures* who are taking anticoagulant or antiplatelet therapy.

This guideline outlines a standardised approach for:

- Elective procedures - pre-procedure assessment
- Elective procedures - perioperative management of:
    - patients taking antiplatelets
    - patients taking oral anticoagulants who can have therapy continued in the perioperative period
    - patients taking oral anticoagulants who can have anticoagulant therapy withheld prior to surgery without bridging therapy
    - patients taking oral anticoagulants who require bridging therapy
    - patients taking anticoagulants or antiplatelets for whom a neuraxial procedure is planned.
- Reversal of anticoagulant therapy for urgent surgery.

Information in this guideline should be used in conjunction with Therapeutic Goods Administration approved Product Information, local protocols (endorsed by local Drug and Therapeutic Committee) and specialist advice. This clinical guideline was developed in conjunction with a multi-disciplinary Anticoagulant Medicines Working Party**. Where indicated, consensus recommendations in the guideline are based on expert opinion from within the Working Party.

Note: The terms oral direct thrombin inhibitor and factor Xa inhibitors are used instead of 'Non-Vitamin K Antagonist Oral Anticoagulant' (NOAC) or 'Direct Oral Anticoagulant' (DOAC) in this document.

Bridging therapy

Bridging therapy in this document refers to the administration of a therapeutic dose of a short-acting anticoagulant, typically low molecular weight heparin (LMWH), during the interruption of a longer-acting anticoagulant, typically warfarin[1]. Bridging therapy does not refer to the administration of a venous thromboembolism (VTE) prophylactic dose of an anticoagulant during the post-operative period.

This guideline provides guidance on bridging with enoxaparin (LMWH) or unfractionated heparin. Refer to local guidelines for information on bridging with other LMWH medicines including daltaparin or nadroparin.

Should a delay in surgery be considered?

It is important to note that patients who require elective surgery within the first three months following an episode of VTE are likely to benefit from delaying surgery, even if the delay is only for a few weeks. Other circumstances where a delay in surgery should be considered include post stent placement; after recent cerebrovascular accident (CVA) or prosthetic valve insertion.

*The term 'procedure' also refers to surgical procedures.
**The Anticoagulant Medicines Working Party members included; a Director of Clinical Governance, nurses, pharmacists, medical specialists (a cardiologist, anaesthestist, surgeon, general practitioner and hematologists), and representatives from the NSW Therapeutic Advisory Group and the National Prescribing Service.

2 PRE-PROCEDURE ASSESSMENT

A number of factors need to be taken into consideration during the pre-procedure assessment including:

- the surgeon's and the general practitioner's or prescribing physician's preference
- other medications including those with an antiplatelet action and other over the counter products such as fish oils
- other patient related bleeding factors, for example, platelet count, haemoglobin level, previous medical history.

For most surgical procedures, anticoagulants are usually stopped due to the bleeding risk. However, there are some procedures for which the risk of bleeding is not significant and anticoagulation can be continued.

For patients assessed as having a high risk for bleeding and a high risk for thromboembolism, decisions about anticoagulation require both experience and a detailed knowledge of the planned procedure. These decisions should not be made by junior medical officers. Decisions about perioperative anticoagulation in this circumstance should be made by or referred to the Admitting Surgeon unless there are explicit local delegation arrangements in place. (For example, cardiothoracic and vascular surgical units will usually have locally agreed practices under which a senior registrar or post FRACS Fellow would be expected to make these decisions on a routine basis, but even then the locally agreed practices should be explicit, and available either in writing or accessible electronic form).

In contrast to anticoagulants, antiplatelet agents usually can be continued throughout the perioperative period. Seek advice from the specialist managing the antiplatelet agent (see Section 3.3).

2.1 Estimating procedural bleeding risk

The risk of bleeding is best assessed by the surgeon or proceduralist. Table 1 lists common minimal, low and high risk of bleeding procedures (it is not an exhaustive list).

Table 1: Risk of procedural bleeding (2-Day risk of major bleeding)[2]

Minimal bleeding risk procedures	Low bleeding risk procedures (2-day risk of major bleed <2%)	High bleeding risk procedures (2-day risk of major bleed ≥2%)
• Minor dermatologic procedures (excision of basal and squamous cell skin cancers, actinic keratoses, and premalignant or cancerous skin nevi) • Cataract procedures • Minor dental procedures (dental extractions, restorations, prosthetics, endodontics), dental cleanings, fillings • Pacemaker or cardioverter-defibrillator device implantation[α]	• Arthroscopy • Cutaneous/lymph node biopsies • Shoulder/foot/hand surgery • Coronary angiography • Gastrointestinal endoscopy +/- biopsy • Abdominal hysterectomy • Laparoscopic cholecystectomy • Abdominal hernia repair • Haemorrhoidal surgery • Bronchoscopy +/- biopsy • Epidural injections with INR <1.2	• Major surgery with extensive tissue injury • Cancer surgery • Major orthopaedic surgery • Reconstructive plastic surgery • Urologic or gastrointestinal surgery • Transurethral prostate resection, bladder resection, or tumour ablation • Nephrectomy, kidney biopsy • Colonic polyp resection[β] • Bowel resection • Percutaneous endoscopic gastrostomy placement, endoscopic retrograde cholangiopancreatography • Surgery in highly vascular organs (kidneys, liver, spleen) • Cardiac, intracranial or spinal surgery • Any major operation (procedure duration of >45 min)

[α]For oral direct thrombin inhibitor or factor Xa inhibitor therapy: Interruption of therapy is currently recommended[3, 4].
For warfarin: Associated with pocket haematoma, but randomized controlled trial Level 1 evidence reveals that procedures can be performed without oral anticoagulation interruption.
[β]The size of the polyp influences the risk of bleeding. It may be appropriate to categorise polyps less than 1 cm in size as low-risk for bleeding.

2.2 Estimating risk of thromboembolism

The risk of thromboembolism is best assessed by the prescribing physician. Table 2 lists the risk of thromboembolism for certain conditions. The $CHADS_2$ score referred to in Table 2 is used to estimate the annual risk of stroke in a patient with non-valvular atrial fibrillation, not taking an anticoagulant. The $CHADS_2$ score, rather than the CHA_2DS_2VASc score, is used as $CHADS_2$ was used to stratify stroke-risk in the landmark study which assessed the risk of bleeding and thromboembolism in patients receiving perioperative bridging therapy compared to having anticoagulant therapy withheld[1].

Table 2: Risk of thromboembolism[5]

	Low	Moderate	High
Mechanical heart valve	Bileaflet aortic valve prosthesis without AF and no other risk factors for stroke	Bileaflet aortic valve prosthesis and one or more of the following risk factors: • AF, prior stroke or TIA[α] • hypertension • diabetes • congestive heart failure • age >75 years	• Any mitral valve prosthesis • Any caged-ball or tilting disc aortic valve prosthesis • Recent (within 6 months) stroke or TIA
Atrial fibrillation (AF)	$CHADS_2$ score of 0 to 2 (assuming no prior stroke or TIA) (Stroke risk stratification with the $CHADS_2$ – adjusted stroke rate 1.9% - 4% per annum[6])	$CHADS_2$ score of 3 or 4 (Stroke risk stratification with the $CHADS_2$ – adjusted stroke rate 5.9% - 8.5% per annum[6])	• $CHADS_2$ score of 5 or 6 • Recent (within 3 months) stroke or TIA • Rheumatic valvular heart disease (Stroke risk stratification with the $CHADS_2$ – adjusted stroke rate 12.5% - 8.2% per annum[6])
VTE[∞]	VTE greater than 12 months previous and no other risk factors	• VTE that occurred 3-12 months ago • Non-severe thrombophilia (e.g. heterozygous factor V Leiden or prothrombin gene mutation) • Recurrent VTE • Active cancer (treated within 6 months or palliative)	• Recent (within 3 months) VTE • Severe thrombophilia (e.g. deficiency of protein C, protein S, or antithrombin; antiphospholipid antibodies; multiple abnormalities)

[α]Transient ischemic attack (TIA)
[∞]Patients who require surgery within the first three months following an episode of VTE are likely to benefit from delaying elective surgery, even if the delay is only for a few weeks.

Reprinted with minor adaptation from Chest, Vol 141, Doutekits J D, Spyropoulos A C, Spencer F A, Mayr M, Jaffer A K et al, Perioperative management of antithrombotic therapy. Antithrombotic therapy and prevention of thrombosis, 9th ed: Douketis et al American College of Chest Physicians. Evidence-based clinical practice guidelines, pp e326S-e350S, 2012 with permission from Elsevier

3 PERIOPERATIVE MANAGEMENT OF ANTICOAGULANT AND ANTIPLATELET AGENTS

3.1 Perioperative management of WARFARIN

The pre-procedure management of warfarin is dependent on estimating procedural bleeding risk (see Figure1). While the risk of bleeding is best assessed by the surgeon or proceduralist, the specialist managing the anticoagulant therapy or prescriber should also be consulted.

3.1.1 Patients for whom WARFARIN can be continued

Patients who are having selected minimal or low bleeding risk procedures for example endoscopy in high thrombotic risk patients (see Table 1 for guidance) may not require warfarin therapy to be withheld[7]. For patients undergoing a procedure who are taking warfarin, it is important to confirm that the International Normalised Ratio (INR) is not supratherapeutic at the time of the procedure. Clinicians should be aware of potential drug interactions with anticoagulant therapy if antibiotic cover is required for the procedure. Clinicians should also be aware of any effects of fasting or reduced oral intake on anticoagulant therapy.

3.1.2 Patients for whom WARFARIN therapy can be withheld prior to surgery with no bridging therapy required

Specialist advice should be sought when warfarin therapy is stopped prior to surgery. Patients who are assessed as HIGH risk of bleeding (see Table 1) and LOW or MODERATE risk of thromboembolism (see Table 2) may have their warfarin therapy withheld preoperatively. The risk of bleeding is best assessed by the surgeon or proceduralist. Bridging therapy (pre-procedure) is not required for these patients (see definition of bridging therapy).

Warfarin should be withheld for patients who are assessed as LOW or MODERATE risk of thromboembolism (see Table 2) for FIVE FULL DAYS before the procedure. Surgery can proceed safely if the INR is <1.5 on the day of surgery. To avoid cancellations because the INR is above this level, check the INR on the day before the procedure so that vitamin K_1 can be administered if needed[7] (see 3.5).

Table 3: Withholding warfarin pre-procedure for patients not requiring bridging therapy

	6 days prior to surgery	5 days prior to surgery	4 days prior to surgery	3 days prior to surgery	2 days prior to surgery	1 day prior to surgery	Morning of Surgery
Warfarin	Take last dose of warfarin	X No warfarin	X No warfarin	X No warfarin	X No warfarin	X No warfarin	X No warfarin
INR test	X	X	X	X	X	Check if INR <1.5	

Recommencing WARFARIN for patients for whom WARFARIN therapy was withheld prior to surgery with no bridging therapy

The treating surgeon should advise when warfarin can be recommenced. Generally, when there is adequate haemostasis, warfarin is recommenced at the maintenance dose 12 to 24 hours post-procedure[7].

VTE prophylaxis should be considered for these patients post-procedure until the INR is therapeutic.

3.1.3 Patients on WARFARIN who require bridging therapy

Bridging therapy is required for patients treated with warfarin for whom:

1. Interruption of warfarin is required (i.e. the risk of haemorrhage during the perioperative period outweighs the risk of thromboembolism)

AND

2. There is a high risk of thromboembolism (see Table 2).

Bridging with an intravenous unfractionated heparin infusion

Bridging with an intravenous unfractionated heparin infusion should be reserved for only those patients for whom bridging with LMWH is contraindicated, for example, severe renal impairment or when rapid offset of anticoagulant effect is required [8]. When indicated, bridging with an intravenous unfractionated heparin infusion should be according to the local intravenous unfractionated heparin protocol.

Pre-procedure

The intravenous unfractionated heparin infusion should be ceased 6 hours prior to the procedure [assuming the Activated Partial Thromboplastin Time (aPTT) is within the therapeutic range]. Check that the aPTT is within the normal range. If the aPTT is above the therapeutic range, a longer delay may be required before the procedure.

Post-procedure

General guidance for patients with a very high risk of thromboembolism (i.e. patients with a prosthetic heart valve) is:

- recommence the intravenous unfractionated heparin infusion (without bolus) 6 to 8 hours postoperatively depending on surgical assessment.
- for patients with a high bleeding risk recommence the intravenous unfractionated heparin infusion after 24 to 48 hours postoperatively (depending on surgical assessment).

Bridging with therapeutic dose LMWH (enoxaparin)

The following guide may be used for providing bridging therapy using a therapeutic dose enoxaparin for patients who require their warfarin therapy to be interrupted and will then be at a high risk of thromboembolism. There is no evidence to date available to support using dabigatran (direct thrombin inhibitor) or apixaban or rivaroxaban (factor Xa inhibitors) as a bridging agent.

Pre-procedure

Discontinue warfarin 5 full days prior to surgery (see Table 4). Check the INR, and commence recommended dose of enoxaparin (see Table 5) when INR is ≤ 2 (≤ 2.5 for mechanical valve). LMWH is continued until 24 hours before the procedure. Consider halving the last dose of LMWH prior to procedures with a high bleeding risk[7].

Table 4: Withholding warfarin and commencing enoxaparin pre-procedure for patients requiring bridging therapy

	6 days prior to surgery	5 days prior to surgery	4 days prior to surgery	3 days prior to surgery	2 days prior to surgery	1 day prior to surgery	Morning of Surgery
Warfarin	Take last dose of warfarin	X No warfarin	X No warfarin	X No warfarin	X No warfarin	X No warfarin	X No warfarin
INR test	X	X	Check INR			Either 1 day prior, or morning of surgery: Check if INR < 1.5	
Enoxaparin	X No enoxaparin	X No enoxaparin	Commence enoxaparin when INR is ≤ 2			Cease enoxaparin 24 hours before procedure	

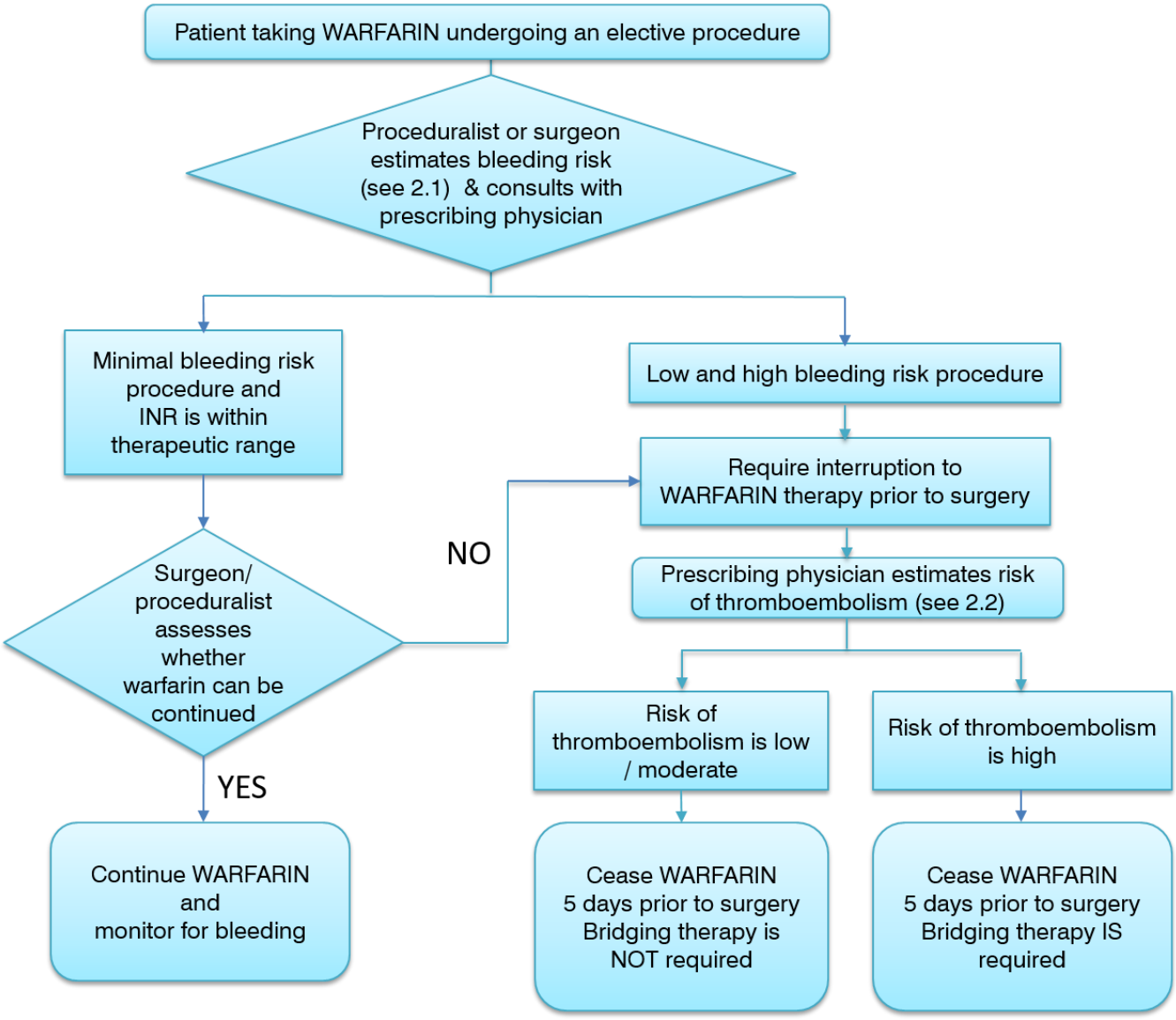
Table 5: Enoxaparin treatment dose[9]

CrCl	Dose*
Patient with CrCl <30 mL/min	Seek haematologist or renal physician advice 1 mg/kg subcutaneous injection once daily
Patient with CrCl ≥30 mL/min	1 mg/kg subcutaneous injection twice daily *or* 1.5 mg/kg once daily

*Dose adjustments for extremes of body weight and required monitoring parameters should be made according to local protocols.

Surgery can proceed safely if the INR is <1.5 on the day of surgery. To avoid cancellations because the INR is above this level, check the INR on the day before surgery so that vitamin K_1 can be administered if required[7] (see 3.5).

Figure 1: Pre-procedure warfarin management*



* Warfarin will need to be stopped for most patients having low bleeding risk procedures

Post-procedure

The treating surgeon and treating physician should advise when anticoagulant therapy can be recommenced. Bleeding risk can be minimised after major procedures by adjusting the time when anticoagulant is resumed[7]. Following high bleeding risk procedures, therapeutic LMWH should be delayed for 48 to 72 hours or substituted with prophylactic dose LMWH[7].

Warfarin can be restarted on the evening of surgery at the previous maintenance dose if there is adequate surgical haemostasis. Continue LMWH or intravenous unfractionated heparin infusion until the target INR is reached.

3.2 Perioperative management of dabigatran (direct thrombin inhibitor), apixaban and rivaroxaban (factor Xa inhibitors)

Withholding of oral direct thrombin inhibitor [dabigatran (Pradaxa®) or factor Xa inhibitor [apixaban (Eliquis®) and rivaroxaban (Xarelto®)] therapy for patients who are having selected minimal or low bleeding risk procedures (see Table 1) may not be required. The treating surgeon should advise whether oral direct thrombin inhibitor or factor Xa inhibitor therapy needs to be withheld. If the decision is made to withhold therapy, it should be withheld according to the guidelines (see Tables 6 - 8). Bridging therapy is generally not required for patients receiving oral direct thrombin inhibitor or factor Xa inhibitor therapy.

Further information regarding management of oral direct thrombin inhibitors or factor Xa inhibitors can be found in the Clinical Excellence Commission Non-Vitamin K Antogonist Oral Anticoagulant (NOAC) Guidelines (referred to as oral direct thrombin inhibitor and factor Xa inhibitor in this document)

Table 6: Timing for ceasing dabigatran (Pradaxa®) prior to surgery[10-13]

Dabigatran (Pradaxa®) (110 or 150 mg twice a day)	Low bleeding risk surgery	High bleeding risk surgery
Normal renal function (CrCl ≥80 mL/min)	Last dose 24 hours before surgery	Last dose 48 hours before surgery
Mildly impaired renal function (CrCl 50 - 80 mL/min)	Last dose 24–48 hours before surgery	Last dose 48–72 hours before surgery
Moderately impaired renal function (CrCl 30 - 49 mL/min)	Last dose 48 – 72 hours before surgery	Last dose 96 hours (4 days) before surgery
CrCl <30 mL/min	Seek specialist advice. Dabigatran is contraindicated. Stop at least 5 days before high-risk surgery	

Table 7: Timing for ceasing apixaban (Eliquis®) prior to surgery[12-14]

Apixaban (Eliquis®) (2.5 mg or 5 mg twice a day)	Low bleeding risk surgery	High bleeding risk surgery
Normal/ mildly impaired renal function (CrCl >50 mL/min)	Last dose 24 hours before surgery	Last dose 48–72 hours before surgery
Moderately impaired renal function (CrCl 30 - 50 mL/min)	Last dose 48 hours before surgery	Last dose 72 hours before surgery
CrCl <30 mL/min	Seek specialist advice	

Table 8: Timing for ceasing rivaroxaban (Xarelto®) prior to surgery [12, 13, 15]

Rivaroxaban (Xarelto®) (15 mg or 20 mg once a day)	Low bleeding risk surgery	High bleeding risk surgery
Normal/ mildly impaired renal function (CrCl >50 mL/min)	Last dose 24 hours before surgery	Last dose 48–72 hours before surgery
Moderately impaired renal function (CrCl 30 - 50 mL/min)	Last dose 48 hours before surgery	Last dose 72 hours before surgery
CrCl <30 mL/min	Seek specialist advice	

Post-procedure

The treating surgeon and treating physician should advise when to recommence oral direct thrombin inhibitor or factor Xa inhibitor therapy after surgery. The anticoagulant effect will be present within 2 to 3 hours of the first dose. Table 9 provides guidance on when therapeutic dose therapy should be recommenced post-operatively (also refer to Table 1 to determine bleeding risk).

Table 9: Recommencing oral direct thrombin inhibitors or factor Xa inhibitors after a procedure[12, 13, 16]

Risk of procedural bleeding (2-Day risk of major bleed)	When to recommence oral direct thrombin inhibitors or factor Xa inhibitors
Low bleeding risk (2-day risk of major bleed 0% - 2%)	Start or resume 24 hours after surgery
High bleeding risk (2-day risk of major bleed 2% - 4%)	Do not resume therapeutic dosing until 48 to 72 hours after surgery Consider alternative VTE prophylaxis in the interim

3.3 Perioperative management of ANTIPLATELET agents

Specialist advice should be sought from the surgeon and the specialist managing the antiplatelet agents regarding management in the perioperative period. Patients receiving antiplatelet agents alone do not require bridging therapy. Patients on combination antiplatelet therapy are a high risk group and require specialist input from the surgeon and the specialist managing the antiplatelet agents.

Patients with a moderate or high risk of cardiovascular event

For patients with a moderate or high risk of thromboembolism, specialist advice should be sought from the surgeon and the specialist managing the antiplatelet agents.

Patients with a low risk of cardiovascular event

Specialist advice should be sought from the surgeon and prescribing physician for patients undergoing high-bleeding risk procedures including spinal, intracranial, extra-ocular, transurethral resection of the prostate or major plastic reconstructive procedures[17] (bleeding risk for antiplatelet therapy is classified differently than for anticoagulant therapy). In some circumstances, in patients undergoing these high bleeding risk procedures, aspirin may be continued in patients taking dual antiplatelet therapy. If antiplatelet agents are to be ceased, they should be ceased according to the timeframes outlined in Table 10.

Generally, for patients with a low risk of thromboembolism and a minimal/ low risk of procedural bleeding, aspirin can be continued. For patients taking dual antiplatelet therapy, generally aspirin can be continued however other antiplatelet agents should be ceased according to Table 10.

Table 10: Recommended time interval between discontinuation of antiplatelet agents prior to procedure (if required)

Antiplatelet agent	When to cease antiplatelet therapy (if required)
aspirin	At least 5 days prior
clopidogrel	At least 7 days prior
prasugrel	At least 7 days prior
ticagrelor	At least 5 days prior
ticlopidine	At least 14 days prior

Post-procedure

The treating surgeon should advise when antiplatelet agents can be recommenced. Generally antiplatelet agents should be recommenced as soon as possible following the surgery or procedure.

3.4 Perioperative management of anticoagulant and antiplatelet agents for patients requiring neuraxial procedures

Neuraxial procedures include lumbar puncture and insertion or removal of spinal or epidural catheter. In general, neuraxial procedures for therapeutically anticoagulated patients is not recommended. Specialist anaesthetic advice should be sought for patients receiving anticoagulant or antiplatelet therapy who require neuraxial procedures.

The risk of epidural or spinal haematoma is greater with traumatic or repeated spinal/epidural puncture. The risk of epidural or spinal haematoma is increased with the use of indwelling catheters, and these should be avoided in patients requiring therapeutic anticoagulation.

Warfarin and heparins

Table 11 and Table 12 provide guidance on the recommended time interval between discontinuation and therapeutic (Table 11) and prophylactic (Table 12) anticoagulation.

Table 11: Management of therapeutic heparin and warfarin therapy during neuraxial procedures*[18]

	Before catheter insertion	While epidural catheter in place	Prior to catheter removal	After catheter removal
IV UNFRACTIONATED HEPARIN infusion	Withhold intravenous UNFRACTIONATED HEPARIN infusion for at least 6 hours PRIOR to CATHETER INSERTION Check that the aPTT is within the normal range	Do not administer intravenous UNFRACTIONATED HEPARIN until 1 hour AFTER epidural CATHETER INSERTION (longer if a 'bloody' tap)	Withhold intravenous UNFRACTIONATED HEPARIN infusion for at least 6 hours PRIOR to CATHETER REMOVAL Check that the aPTT is within the normal range	Do not administer intravenous UNFRACTIONATED HEPARIN until 1 hour AFTER CATHETER REMOVAL. In the case of traumatic puncture delay recommencing the intravenous UNFRACTIONATED HEPARIN infusion for at least 24 hours (if possible)
Therapeutic dose LMWH	Withhold therapeutic dose LMWH at least 24 hours PRIOR to CATHETER INSERTION Longer delays are required for patients with creatinine clearance < 30 mL/minute	Do not administer LMWH until 12 hours AFTER epiduraL CATHETER INSERTION	Withhold therapeutic dose LMWH at least 24 hours prior to catheter REMOVAL Longer delays are required for patients with creatinine clearance < 30 mL/minute	Recommence LMWH after a delay of at least 4 hours following catheter REMOVAL In the case of traumatic puncture delay recommencing LMWH for at least 24 hours
Warfarin	Warfarin should be withheld or reversed to achieve INR <1.5 prior to procedure	CONTRAINDICATED	Ensure INR less than 1.5	Do not administer warfarin until 4 hours after catheter REMOVAL. May need alternative anticoagulation following procedure

*This table is based on Horlocker et al (2018) and the expert opinion from within the Working Party. Timings and directions may differ slightly from the Product Information.

Table 12: Management of prophylactic heparin therapy during neuraxial procedures*[18]

Medicine	Before catheter insertion*	While epidural catheter in place	Prior to catheter removal*	After catheter removal**
Subcutaneous UNFRACTIONATED HEPARIN injections (daily dose less than 10,000 units)	Withhold subcutaneous UNFRACTIONATED HEPARIN injections for at least 6 hours PRIOR to CATHETER INSERTION	Do not administer subcutaneous UNFRACTIONATED HEPARIN until 1 hour AFTER CATHETER INSERTION	Withhold subcutaneous UNFRACTIONATED HEPARIN injections for at least 4 to 6 hours PRIOR to CATHETER REMOVAL	Recommence subcutaneous UNFRACTIONATED HEPARIN injections after a delay of least 6 hours FOLLOWING CATHETER REMOVAL
LMWH	Withhold LMWH at for least 12 hours PRIOR to CATHETER INSERTION (longer delays are required for patients with creatinine clearance < 30 mL/minute)	Do not administer LMWH until 12 hours AFTER CATHETER INSERTION	Withhold LMWH for at least 12 hours PRIOR to CATHETER REMOVAL (longer delays are required for patients with creatinine clearance < 30 mL/minute)	Recommence LMWH after a delay of at least 4 hours FOLLOWING CATHETER REMOVAL

*This table is based on Horlocker et al (2018) and the expert opinion from within the Working Party. Timings and directions may differ slightly from the Product Information.

**A longer delay is required if there are multiple punctures or traumatic insertion of spinal or epidural catheter.

Seek specialist advice if you need to anticoagulated a patient who has undergone a neuroaxial procedure.

Dabigatran (direct thrombin inhibitor), apixaban and rivaroxaban (factor Xa inhibitors)

There is limited safety data on neuraxial procedures and oral direct thrombin inhibitors (dabigatran) or factor Xa inhibitors (apixaban and rivaroxaban). Specialist medical advice should be sought for patients receiving an oral direct thrombin inhibitor or factor Xa inhibitor who require a neuraxial procedure.

Therapeutic dose

Spinal or epidural anesthesia is contraindicated in patients receiving the therapeutic dose of an oral direct thrombin inhibitor or factor Xa inhibitor. If a decision has been made to cease therapeutic dose oral direct thrombin inhibitor or factor Xa inhibitor therapy prior to surgery to enable planned epidural or spinal anaesthesia, therapy should be ceased according to perioperative guidelines (Tables 6, 7 and 8). If therapy has not been ceased for sufficient time to predict absence of anticoagulant effect then epidural or spinal anesthesia should be avoided unless laboratory testing establishes the absence of anticoagulant effect (see Table 13).

Table 13: Effect of oral direct thrombin inhibitors or factor Xa inhibitors on routinely performed coagulation assays[19]

Effect	Dabigatran	Rivaroxaban	Apixaban
Significant anticoagulant effect unlikely	aPTT and thrombin time (TT) normal	PT* normal	Normal PT* **DOES NOT** exclude presence of therapeutic apixaban
Anticoagulant effect present	TT prolonged aPTT prolonged	PT* prolonged	PT* prolonged or normal
Specific assays to quantify drug presence	Dilute thrombin clotting time (Hemoclot assay)	Modified Anti Xa assay specific for rivaroxaban	Modified Anti Xa assay specific for apixaban

*PT sensitivity to oral direct thrombin inhibitors or factor Xa inhibitors will vary according to local laboratory reagents. In some laboratories, PT will be insensitive to oral direct thrombin inhibitors or factor Xa inhibitors. Check with local laboratory.

Adapted with permission from The Royal Australian College of General Practitioners from Brieger D, Curnow J. Anticoagulation: A GP primer on the new oral anticoagulants. Aust Fam Physician 2014;43(5):254–59. Available at www.racgp.org.au/afp/2014/may/anticoagulation

VTE prophylaxis dose

There is limited data on the safety of prophylactic dose oral direct thrombin inhibitors or factor Xa inhibitors use whilst a patient has an epidural catheter in situ. Prophylactic dose administration is not recommended for patients who have an epidural catheter in situ.

Table 14 provides general guidance regarding timing of VTE prophylactic oral direct thrombin inhibitors or factor Xa inhibitors doses in relation to epidural or spinal anaesthesia. Longer periods apply for patients with renal impairment. The recommendations in this table should be used in consultation with specialist medical advice.

Table 14: Recommended time interval between discontinuation of VTE PROPHYLACTIC oral direct thrombin inhibitor or factor Xa inhibitor therapy in relation to neuraxial procedures in patients without reduced renal function[16, 20]

Timing of VTE prophylactic dose	Dabigatran (Pradaxa®) 220 mg or 150 mg daily	Apixaban (Eliquis®) 2.5 mg twice daily	Rivaroxaban (Xarelto®) 10 mg daily
Last **prophylactic** dose prior to spinal or epidural catheter insertion	48 hours	24 hours	24-48 hours
Last **prophylactic** dose prior to spinal or epidural catheter removal	48 hours	24 hours	24-48 hours
Next **prophylactic** dose post catheter insertion (if indwelling epidural catheter in-situ)	Not recommended		
Next **prophylactic** dose after epidural catheter removal*	At least 6 hours*		

*A longer delay is required if there are multiple punctures or traumatic insertion of spinal or epidural catheter.

Nonsteroidal anti-inflammatory drugs (NSAID) and aspirin

NSAIDs including aspirin alone do not significantly increase the risk of spinal haematoma but should be regarded as a risk factor if combined with other anticoagulants[21]. Neuraxial procedures should be avoided in patients receiving NSAIDS (including aspirin) along with another anticoagulant. COX-2 selective agents have less antiplatelet action and are considered safe.

Antiplatelet agents (other than NSAIDs or aspirin)

If a neuraxial procedure is considered absolutely necessary, antiplatelet agents (other than NSAIDs or aspirin) should be ceased in accordance with Table 15. Antiplatelet agents should not be resumed until the catheter is removed (see Table 15).

Table 15: Recommended time interval between discontinuation and recommencement of antiplatelet agents in relation to neuraxial procedures[21]

Antiplatelet agent	When to cease antiplatelet therapy	When to resume antiplatelet therapy
clopidogrel	At least 5 days prior	Resume after catheter removal
prasugrel	At least 7 days prior	Recommence 6 hours after catheter removal
ticagrelor	At least 5 days prior	Recommence 6 hours after catheter removal
ticlopidine	At least 14 days prior	Resume after catheter removal

The concurrent use of herbal medications (such as garlic, ginko or ginseng) with other antithrombotic drugs may increase bleeding risk.

3.5 Reversal of anticoagulant therapy for URGENT SURGERY

WARFARIN

Patients who are having a minimal and selected low bleeding risk procedures (see Table 1) may not require warfarin therapy to be withheld[7]. For patients undergoing a procedure who are taking warfarin, it is important to confirm that the INR is not above the therapeutic range at the time of the procedure (see Figure 2).

Specialist hematology advice is required for patients receiving warfarin (with an INR ≥1.5) who require urgent surgery. Surgery can proceed safely if INR is less than 1.5.

For patients who require semi-urgent reversal of warfarin, (for example, the day prior to the procedure) warfarin should be withheld and vitamin K_1 administered. The recommended dose of Vitamin K_1 for warfarin reversal is 3 mg via intravenous injection[7].

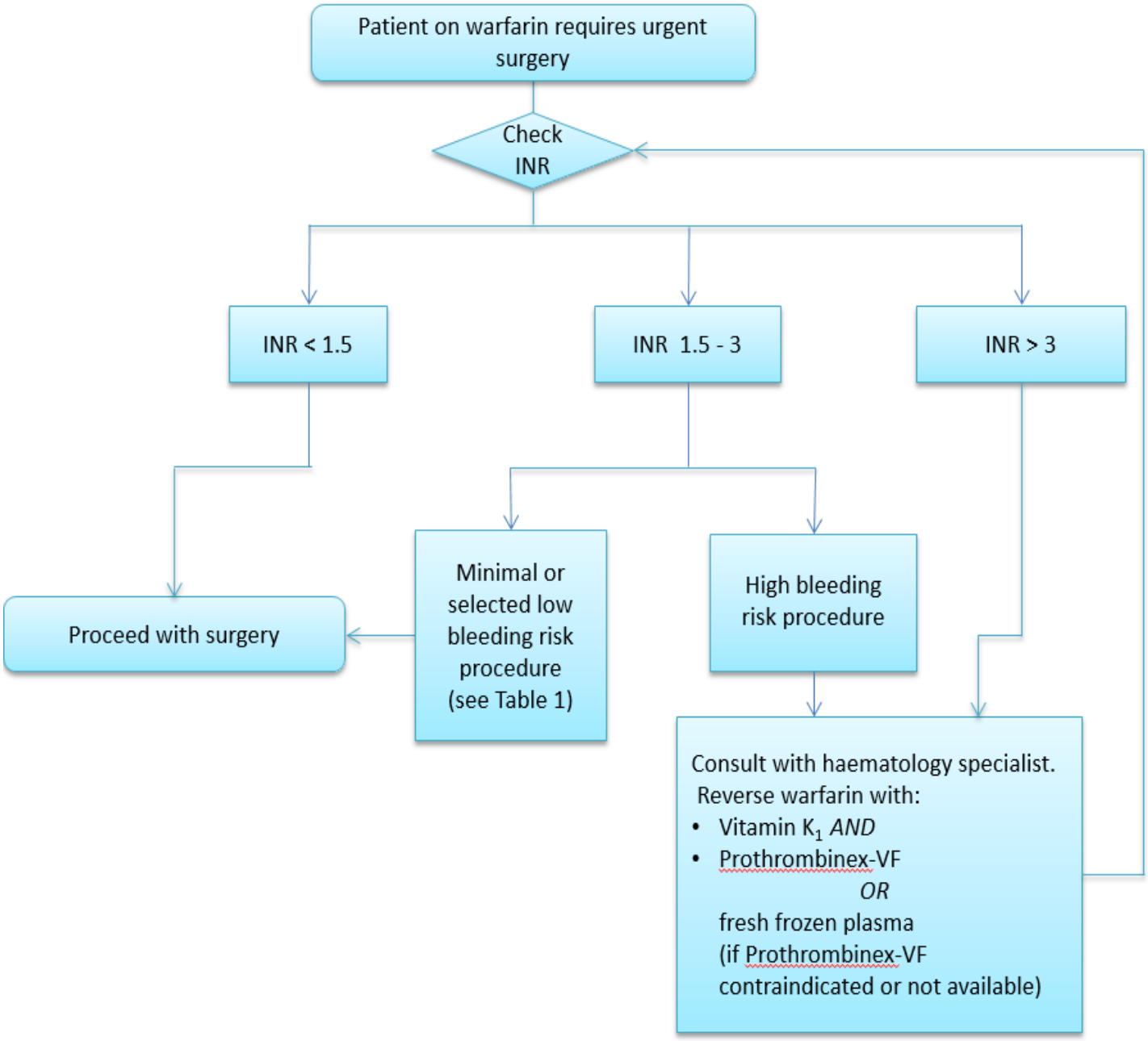
If immediate reversal is required, in the case of urgent surgery, Prothrombinex-VF or plasma products along with vitamin K_1should be administered. The rapid reversal effect of Prothrombinex-VF on an elevated INR occurs within 15 minutes however, the duration of effect is limited to a similar degree as the half-lives of endogenous clotting factors. Vitamin K_1 should be administered with Prothrombinex-VF to sustain the desired reversal effect[7].

Table 16: Recommended Prothrombinex-VF doses to reverse warfarin therapy according to initial and target INR[7]

	Initial INR 1.5 – 2.5	Initial INR 2.6 – 3.5	Initial INR 3.6 – 10	Initial INR >10
Target INR: 0.9 – 1.3	30 units/kg	35 units/kg	50 units/kg	50 units/kg
Target INR: 1.4 - 2	15 units/kg	25 units/kg	30 units/kg	40 units/kg

If Prothrombinex-VF is not available, use fresh frozen plasma (FFP) 10 – 15mL/kg[7] for warfarin reversal.

Figure 2: Warfarin reversal for URGENT SURGERY flowchart



Oral direct thrombin inhibitors or factor Xa inhibitors

At the time of publication, reversal agents for the factor Xa inhibitors (apixaban and rivaroxaban) were **not** available.

Further information on managing bleeding (for patients taking an oral direct thrombin inhibitor or factor Xa inhibitor) is available in the CEC NOAC Guidelines.

DABIGATRAN (PRADAXA®) REVERSAL

Idarucizumab (monoclonal antibody that reverses effects of dabigatran) was registered with Therapeutic Goods Administration in May 2016.

Indications

Idarucizumab is indicated for when rapid reversal of the anticoagulant effects of dabigatran is required for emergency surgery/ urgent procedures and in life-threatening or uncontrolled bleeding[22].

An analysis of dabigatran reversal with idarucizumab in patients with serious bleeding or who required an urgent procedure, demonstrated that idarucizumab completely reversed the anticoagulant effect of dabigatran within minutes[23, 24]. Though the anticoagulant effect is reversed, achieving haemostasis will be dependent on identifying and treating the source of bleeding.

In mild or moderate bleeding, for example patients presenting with a non-life threatening bleed or in need of non-urgent surgery or invasive procedure, discontinuation of dabigatran and administration of appropriate supportive care is usually sufficient.

Drug interactions

No formal interaction studies with idarucizumab and other medicines have been conducted. Clinically relevant interactions with other medicines are considered unlikely.

Monitoring

The following laboratory tests should be conducted before idarucizumab administration and 30 minutes after idarucizumab administration:

- aPTT
- PT
- Fibrinogen
- TT.

Idarucizumab is only indicated if the TT is prolonged. A normal TT rules out the presence of dabigatran. The TT is extremely sensitive, even to clinically insignificant levels of dabigatran. Repeat doses of idarucizumab should not be based on repeat TT results in isolation.

Dosage and administration

The recommended dose of IDARUCIZUMAB is 5 g (2 x 2.5 g/ 50 mL). Administer intravenously as two consecutive infusions over 5 to 10 minutes each or as a bolus injection. No dose adjustment is required for renal impairment.

Restarting dabigatran

Reversing dabigatran exposes patients to the thrombotic risk of their underlying disease. Resumption of anticoagulant therapy should be considered as soon as medically appropriate. Specialist advice should be

sought. Dependent on patient circumstances, treatment can be initiated 24 hours after administration of idarucizumab.

Idarucizumab may not be available in all facilities. Clinicians should verify availability with their relevant Drug and Therapeutics Committee and Pharmacy Department.

An Idarucizumab information sheet is available on the Clinical Excellence Commission High-Risk Medicines webpage.

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ABBREVIATIONS / DEFINITIONS

Abbreviation	Term
AF	Atrial fibrillation
aPTT	Activated Partial Thromboplastin Time
Bridging	Bridging anticoagulation involves the administration of a short-acting anticoagulant, typically a low molecular weight heparin (LMWH), during the interruption of a longer-acting anticoagulant, typically warfarin.
CrCl	Creatinine clearance (estimated using the Cockcroft-Gault equation)
DVT	Deep vein thrombosis
FBC	Full blood count
INR	International normalised ratio
LMWH	Low molecular weight heparin
NOAC	Non-vitamin K antagonist oral anticoagulant
PT	Prothrombin time
TIA	Transient ischaemic attack
TT	Thrombin time
VTE	Venous thromboembolism

APPENDICES

Patient Communication Forms

1. Management of Warfarin Before and After Medical Procedures or Surgery (No Bridging)
2. Management of Warfarin Before and After Medical Procedures or Surgery for patients requiring bridging therapy
3. Management of Dabigatran (Pradaxa®) Before and After Medical Procedures or Surgery
4. Management of Apixaban (Eliquis®) Before and After Medical Procedures or Surgery
5. Management of Rivaroxaban (Xarelto®) Before and After Medical Procedures or Surgery

MANAGEMENT OF WARFARIN BEFORE AND AFTER MEDICAL PROCEDURES OR SURGERY (NO BRIDGING)

This form should be completed by your doctor. It provides instructions on when to take your warfarin if you are having a procedure or surgery.

Date of procedure: _____

Procedure: _____

Indication(s) for anticoagulation: _____

MRN:

Name:

DOB:

Usual warfarin brand: ☐ Coumadin ☐ Marevan Usual warfarin dose: _____ Target INR:_____

Bleeding risk:

☐ MINIMAL ☐ LOW ☐ HIGH

Consulted with specialist performing the procedure: ☐ YES ☐ NO

Comments:_____

Thrombotic (clotting) risk:

☐ LOW ☐ MODERATE ☐ HIGH

Consulted with specialist managing anticoagulation: ☐ YES ☐ NO

Comments: _____

Show this form to the doctor at any appointments **BEFORE** your procedure. Bring this form to your procedure.

When to take warfarin BEFORE your procedure:

Number of days before surgery	6	5	4	3	2	1	Morning of procedure
Date							
INR							
WARFARIN	Take last dose of warfarin	X No warfarin	X No warfarin	X No warfarin	X No warfarin	X No warfarin	X No warfarin

If you require further information please contact: _____on_____

Doctor name: _____ Signature: _____

Designation: _____ Phone Contact: _____ Date: _____

Taking warfarin AFTER your procedure

Date of procedure: _____

Procedure: _____

MRN:

Name:

DOB:

Complete this form with your surgeon or proceduralist **AFTER** your procedure.

When to take warfarin AFTER your procedure:

Number of days after surgery	Day of procedure	1	2	3	4	5	6
Date							
INR							
WARFARIN DOSE							

Then, continue to take your warfarin as normal from _____.

Your next INR test is due on _____.

Show this form to your doctor during any appointments straight **AFTER** your procedure.

If you require further information please contact: _____on_____.

Instructions if you notice any signs of bleeding AFTER your procedure

Signs of bleeding may include:_____

Please contact _____on_____ if you notice any of these signs.

If the bleeding is severe, go straight to your nearest Hospital Emergency Department.
Tell them you are taking WARFARIN

Doctor name: _____ Signature: _____

Designation: _____ Phone Contact: _____ Date: _____

For further information please refer to the CEC Guidelines for perioperative management of anticoagulant and antiplatelet agents.

Acknowledgement
The Clinical Excellence Commission acknowledges the members of the Anticoagulant Medicines Working Party who contributed to the development of this document.

Management of warfarin before or after medical procedures or surgery (no bridging)
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MANAGEMENT OF WARFARIN BEFORE AND AFTER MEDICAL PROCEDURES OR SURGERY FOR PATIENTS REQUIRING BRIDGING THERAPY

This form should be completed by your doctor. It provides instructions on when to take your warfarin and inject enoxaparin (Clexane®) if you are having a procedure or surgery.

Date of procedure: _____

Procedure: _____

Indication(s) for anticoagulation: _____

MRN:

Name:

DOB:

Usual warfarin brand: ☐ Coumadin ☐ Marevan Usual warfarin dose: _____ Target INR: _____

Bleeding risk:

☐ MINIMAL ☐ LOW ☐ HIGH

Consulted with specialist performing the procedure: ☐ YES ☐ NO

Comments: _____

Thrombotic (clotting) risk:

☐ LOW ☐ MODERATE ☐ HIGH

Consulted with specialist managing anticoagulation: ☐ YES ☐ NO

Comments: _____

Show this form to the doctor at any appointments **BEFORE** your procedure. Bring this form to your procedure.

When to take warfarin and inject enoxaparin BEFORE your procedure:

Number of days before surgery	6	5	4	3	2	1	Morning of procedure
Date							
INR							
Warfarin	Take last dose of warfarin	X No warfarin	X No warfarin	X No warfarin	X No warfarin	X No warfarin	X No warfarin
Enoxaparin (Clexane®) injection dose	X No enoxaparin	X No enoxaparin	Time Dose	Time Dose	Time Dose	Time Dose	X No enoxaparin

If you require further information please contact: _____ on _____

Doctor name: _____ Signature: _____

Designation: _____ Phone Contact: _____ Date: _____

Taking warfarin AFTER your procedure

Date of procedure: _____

Procedure: _____

MRN:

Name:

DOB:

Complete this form with your surgeon or proceduralist **AFTER** your procedure (before you are discharged home)

When to take warfarin and inject enoxaparin AFTER your procedure:

Number of days after surgery	Day of procedure	1	2	3	4	5	6
Date							
INR							
Warfarin Dose							
Enoxaparin (clexane®) injection	Time	Time	Time	Time	Time	Time	Time
	Dose	Dose	Dose	Dose	Dose	Dose	Dose

Then, continue to take your warfarin as normal from _____. Your next INR test is due on _____

Show this form to your doctor during any appointments straight **AFTER** your procedure.

If you require further information please contact: _____on_____

Instructions if you notice any signs of bleeding AFTER your procedure

Signs of bleeding may include: _____

Please contact _____on_____ if you notice any of these signs.

If the bleeding is severe, go straight to your nearest Hospital Emergency Department.
Tell them you are taking WARFARIN

Doctor name: _____ Signature: _____

Designation: _____ Phone Contact: _____ Date: _____

For further information please refer to the CEC Guidelines for perioperative management of anticoagulant and antiplatelet agents

Acknowledgement
The Clinical Excellence Commission acknowledges the members of the Anticoagulant Medicines Working Party who contributed to the development of this document.

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MANAGEMENT OF DABIGATRAN (PRADAXA®) BEFORE AND AFTER A MEDICAL PROCEDURE OR SURGERY

This form should be completed by your doctor. It provides instructions on when to take your dabigatran (Pradaxa®) if you are having a procedure or surgery.

Date of procedure: _____

Procedure: _____

Indication(s) for anticoagulation: _____

MRN:

Name:

DOB:

Usual DABIGATRAN dose: _____ Calculated CrCl (mL/min) (kidney function): _____

Bleeding risk:

☐ MINIMAL ☐ LOW ☐ HIGH

Consulted with specialist performing the procedure: ☐ YES ☐ NO

Comments:_____

Thrombotic (clotting) risk:

☐ LOW ☐ MODERATE ☐ HIGH

Consulted with specialist managing anticoagulation: ☐ YES ☐ NO

Comments:_____

Show this form to the doctor at any appointments **BEFORE** your procedure. Bring this form to your procedure.

When to take DABIGATRAN BEFORE your procedure

Continue to take your DABIGATRAN as usual until _____

Number of days before surgery	4	3	2	1	Day of procedure
Date					
MORNING dose				None	None
EVENING dose				None	None

If you require further information please contact: _____on_____

Doctor name: _____ Signature:_____

Designation: _____ Phone contact: _____ Date: _____

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Taking DABIGATRAN AFTER your procedure

Date of procedure: _____

Procedure: _____

MRN:

Name:

DOB:

Complete this form with your surgeon or proceduralist **AFTER** your procedure (before you are discharged home)

When to take DABIGATRAN AFTER your procedure:

Number of days after procedure	Day of procedure	1	2	3	4	5	6
Date							
MORNING dose	None						
EVENING dose							

Then, continue to take your DABIGATRAN as normal from _____

Show this form to your doctor during any appointments straight **AFTER** your procedure.

If you require further information please contact: _____on_____

Instructions if you notice any signs of bleeding AFTER your procedure

Signs of bleeding may include:_____

Please contact_____on_____ if you notice any of these signs.

If the bleeding is severe, go straight to your nearest Hospital Emergency Department.
Tell them you are taking DABIGATRAN

Doctor name: _____ Signature: _____

Designation: _____ Phone Contact: _____ Date: _____

For information on managing DABIGATRAN refer to the CEC NOAC Guidelines http://bit.ly/2q4ObP5

Acknowledgement
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Management of DABIGATRAN (Pradaxa®) before and after a medical procedure or surgery
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MANAGEMENT OF APIXABAN (ELIQUIS®) BEFORE AND AFTER MEDICAL PROCEDURES OR SURGERY

This form should be completed by your doctor. It provides instructions on when to take your apixaban (Eliquis®) if you are having a procedure or surgery.

Date of procedure: _____

Procedure: _____

Indication(s) for anticoagulation: _____

MRN:

Name:

DOB:

Usual APIXABAN dose: _____ Calculated CrCl (mL/min) (kidney function): _____

Bleeding risk:

☐ MINIMAL ☐ LOW ☐ HIGH

Consulted with specialist performing the procedure: ☐ YES ☐ NO

Comments:_____

Thrombotic (clotting) risk:

☐ LOW ☐ MODERATE ☐ HIGH

Consulted with specialist managing anticoagulation: ☐ YES ☐ NO

Comments:_____

Show this form to the doctor at any appointments **BEFORE** your procedure. Bring this form to your procedure.

When to take APIXABAN BEFORE your procedure

Continue to take your APIXABAN as usual until ____/____/____

Number of days before surgery	4	3	2	1	Day of procedure
Date					
MORNING dose				None	None
EVENING dose				None	None

If you require further information please contact: _____on_____

Doctor name: _____ Signature: _____

Designation: _____ Phone Contact: _____ Date: _____

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Taking APIXABAN AFTER your procedure

Date of procedure: _____

Procedure: _____

MRN:

Name:

DOB:

Complete this form with your surgeon or proceduralist **AFTER** your procedure.

When to take APIXABAN AFTER your procedure:

Number of days after procedure	Day of procedure	1	2	3	4	5	6
Date							
MORNING Dose	None						
EVENING Dose	None						

Then, continue to take your APIXABAN as normal from ____/____/____

Show this form to your doctor during any appointments straight AFTER your procedure.

If you require further information please contact: _____on_____

Instructions if you notice any signs of bleeding AFTER your procedure

Signs of bleeding may include:_____

Please contact_____on_____ if you notice any of these signs.

If the bleeding is severe, go straight to your nearest Hospital Emergency Department.
Tell them you are taking APIXABAN

Doctor name: _____ Signature: _____

Designation: _____ Phone Contact: _____ Date: _____

For information on managing APIXABAN refer to the CEC NOAC Guidelines Updated July 2017 http://bit.ly/2q4ObP5

Acknowledgement
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Management of apixaban (Eliquis®) before and after medical procedures or surgery
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MANAGEMENT OF RIVAROXABAN (XARELTO®) BEFORE AND AFTER MEDICAL PROCEDURES OR SURGERY

This form should be completed by your doctor. It provides instructions on when to take your rivaroxaban (Xarelto®) if you are having a procedure or surgery.

Date of procedure: _____

Procedure: _____

Indication(s) for anticoagulation: _____

MRN:

Name:

DOB:

Usual RIVAROXABAN dose: _____ Calculated CrCl (mL/min) (kidney function): _____

Bleeding risk:

☐ MINIMAL ☐ LOW ☐ HIGH

Consulted with specialist performing the procedure: ☐ YES ☐ NO

Comments: _____

Thrombotic (clotting) risk:

☐ LOW ☐ MODERATE ☐ HIGH

Consulted with specialist managing anticoagulation: ☐ YES ☐ NO

Comments: _____

Show this form to the doctor at any appointments **BEFORE** your procedure. Bring this form to your procedure.

When to take RIVAROXABAN BEFORE your procedure

Continue to take your RIVAROXABAN as usual until ____/____/____

Number of days before surgery	4	3	2	1	Day of procedure
Date					
MORNING Dose					None
EVENING dose				None	None

If you require further information please contact: _____on_____

Doctor name: _____ Signature: _____

Designation: _____ Phone Contact: _____ Date: _____

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Taking RIVAROXABAN AFTER your procedure

Date of procedure: _____

Procedure: _____

MRN:

Name:

DOB:

Complete this form with your surgeon or proceduralist **AFTER** your procedure.

When to take RIVAROXABAN AFTER your procedure:

Number of days after procedure	Day of procedure	1	2	3	4	5	6
Date							
MORNING dose	None						
EVENING dose	None						

Then, continue to take your RIVAROXABAN as normal from ____/____/____

Show this form to your doctor during any appointments straight **AFTER** your procedure.

If you require further information please contact: _____on_____

Instructions if you notice any signs of bleeding AFTER your procedure

Signs of bleeding may include:_____

Please contact_____on_____ if you notice any of these signs.

If the bleeding is severe, go straight to your nearest Hospital Emergency Department.
Tell them you are taking RIVAROXABAN

Doctor name: _____ Signature: _____

Designation: _____ Phone Contact: _____ Date: _____

For information on managing RIVAROXABAN refer to the CEC NOAC Guidelines http://bit.ly/2q4ObP5

Acknowledgement
The Clinical Excellence Commission acknowledges the members of the Anticoagulant Medicines Working Party who contributed to the development of this document.

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Clinical Excellence Commission
Locked Bag 8
Haymarket NSW 1240
Phone: (02) 9269 5500
Email: CEC-info@health.nsw.gov.au
Web: www.cec.health.nsw.gov.au

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