



Warfarin Therapy – Management During Invasive Procedures and Surgery

Effective Date: April 1, 2015

Scope

This guideline provides recommendations for the management of warfarin therapy in adults aged ≥ 19 years requiring invasive procedures and surgery.

Perioperative management of non-vitamin K antagonist oral anticoagulants can be found in [BCGuidelines.ca – Use of NOACs in Non-Valvular Atrial Fibrillation](#). Non-perioperative management of warfarin is covered in [BCGuidelines.ca – Warfarin Therapy Management](#).

Key Recommendations

- Warfarin discontinuation prior to invasive procedures is necessary for all interventional procedures except for minor skin procedures, routine dental work, cataract surgery, endoscopies without biopsy, and percutaneous venous access.
- For elective procedures, warfarin should be stopped for 5 to 6 days prior to the procedure to allow gradual normalization of the international normalized ratio (INR).
- For urgent procedures, use of prothrombin complex concentrate is highly effective in rapidly reversing warfarin anticoagulant activity and has a duration of action of ~ 6 hours.
- The use of bridging heparin therapy is dependent on the risk of thrombosis.
- Discuss the risk of bleeding with the surgeon and anesthesiologist to determine optimal timing for resuming warfarin and bridging heparin therapy after surgery.

Risks

The management of warfarin therapy in patients undergoing surgery or other invasive procedures involves a fine balance between the risk of hemorrhage if the procedure was performed while on warfarin, and the risk of thrombosis if warfarin was discontinued. The thrombotic risk in the perioperative period depends on pre-existing conditions, the time since the last episode of thrombosis, and the thrombotic effect of surgery.¹⁻⁸

The risk of hemorrhage in the perioperative period depends on the patient's age, associated medical conditions, type of procedure, approach, site, type of incision and closure, and the method of administration of anesthesia and analgesia. It is recommended that the anesthesiologist and the surgeon be consulted in determining the hemorrhagic risk.

Preoperative management of warfarin therapy consists of timely discontinuation of warfarin and replacement (known as "bridging") with therapeutic low molecular weight heparin (LMWH) or unfractionated heparin if the risk of thrombosis is considered to be sufficiently high. Almost all patients will achieve an international normalized ratio (INR) of < 1.5 within 4 – 5 days of stopping warfarin,⁹ although patients with a higher (2.5 – 3.5) target INR and the elderly (> 70 years) will require a longer period of warfarin withdrawal before surgery. Patients with a high risk of thromboembolism or stroke may benefit from bridging with heparin during the preoperative period, either as outpatients (LMWH subcutaneously) or inpatients (unfractionated heparin intravenously) by shortening the duration of subtherapeutic anticoagulation.

Postoperative management of warfarin therapy consists of re-initiation of anticoagulation. Postoperative anticoagulation increases the rate of major bleeding.³ Typically, warfarin can resume the evening of or next day after the procedure because the anticoagulant activity is not established for several days. Restarting warfarin may be delayed in neurosurgical patients, those receiving epidural analgesia and in patients who are bleeding. For patients at high risk of thrombosis, LMWH by injection is given concurrently with warfarin and the overlap is maintained until a therapeutic INR has been reached. LMWH used postoperatively may allow earlier discharge of the patient compared with using unfractionated heparin.

If urgent or emergent procedures are to be undertaken in < 4-5 days and warfarin reversal is required, it may be satisfactory to give 1-2 mg of vitamin K orally in order to expedite the reversal process. When reversal of anticoagulation is required within 6 hours, intravenous vitamin K and prothrombin complex concentrate (PCC) (e.g., Octaplex®, Beriplex®) is highly effective and is recommended over frozen plasma infusion.

Management

► Therapeutic Measures for Reversal of Warfarin Therapy

Vitamin K

- Intravenous (IV) delivery is the fastest and most reliable way to obtain the effect of vitamin K.
- Intramuscular (IM) or subcutaneous delivery should be avoided.
- If the procedure is in more than 24 hours, there is no difference between using IV and oral (PO).
- Useful for postoperative periods as well.
- Excessive dose of vitamin K can lead to difficulty with re-anticoagulation.
- Effect on INR is observed after 8 – 12 hours, depending on route of administration.
- Recommended doses:
 - Oral 1 – 2 mg, or
 - IV 5 mg in 50cc normal saline infused over 30 minutes.

Virally Inactivated Plasma-Derived Prothrombin Complex Concentrate

- Use only in consultation with specialist.
- Preferred product for rapid reversal of warfarin when available.
- Duration of action is ~6 hours, typically only one dose is needed.
- Virally inactivated plasma-derived concentrate containing factors II, VII, IX, X and Protein C and Protein S.
- Must be used in conjunction with IV vitamin K.
- Indicated for immediate INR reversal in patients:
 - with active, serious bleeding, and/or
 - who require surgery within next 6 hours.
- Contains heparin and is contraindicated in patients with heparin induced thrombocytopenia and liver insufficiency (see product monograph).
- May be associated with clinically important thrombosis.

Frozen Plasma (FP)

- Short duration of action at ~4 hours.
- Indicated for rapid reversal when PCC not available.
- Risk of infectious agent transmission.
- Available in large centres; rural centres can have FP shipped quickly from nearby larger centres as needed.

► Management of Perioperative Anticoagulation

1) Acceptable INR for surgery

- Discuss with surgeon and anesthesiologist what the goal INR should be before surgery.
- Baseline INR is recommended in every case and this will guide further therapy.
- An INR < 1.5 is generally acceptable except for neurosurgery, ocular surgery and procedures requiring spinal anesthesia or epidural analgesia.¹

2) Risk of bleeding

- In general, the type of procedure determines the risk of bleeding and how long anticoagulation must be withheld post-operatively.
- Discontinuation of warfarin is essential for procedures (refer to Table 1) associated with a high risk of bleeding.
- Discontinuation of warfarin is usually not necessary for procedures (refer to Table 1) associated with a low risk of bleeding.
- Assess with surgeon and anesthesiologist what the risk of bleeding from the procedure.

Table 1. Procedures associated with high and low risk for bleeding

Higher Risk Procedures for Bleeding	Lower Risk Procedures for Bleeding
<ul style="list-style-type: none"> • Procedures that the body cavity is entered (e.g., open thoracic, abdominal or pelvic surgery) • Percutaneous needle procedures in non-compressible sites, including organ biopsies • Any type of prostatic surgery • Surgery sites where minor bleeding can cause significant morbidity (e.g., central nervous system and intraocular procedures) • Major arthroplasty surgery (e.g., hip or knee replacement). 	<ul style="list-style-type: none"> • Percutaneous needle procedures in readily compressible sites (e.g., peripheral venous access) • Many skin procedures • Routine dental procedures (e.g., hygiene, simple extractions, restorations, endodontics, prosthetics)⁶ • Endoscopy without biopsy • Cataract surgery

3) Risk of thrombosis and need for peri-procedural bridging therapy

- Assess the preoperative risk of thrombosis from pre-existing conditions (refer to Table 2) before the procedure.
- Assess the postoperative risk of thrombosis from the procedure with the anesthesiologist and surgeon.

Table 2. Pre-existing conditions associated with higher and lower risk of thrombosis

Higher Risk Conditions	Lower Risk Conditions
<ul style="list-style-type: none"> • Mechanical mitral valve and old model aortic prosthesis (i.e., ball, Bjork-Shiley, Lillehei-Kaster) • Atrial fibrillation plus either history of stroke/TIA, or ≥ 3 additional risk factors^{2,4} for cardioembolic events* • DVT/PE occurring within past 3 months • DVT/PE in patients with active cancer • Hypercoagulable state with recent thrombotic episode, recurrent thrombosis or history of life-threatening thrombosis 	<ul style="list-style-type: none"> • Newer model mechanical aortic valve prostheses and any tissue valves • Atrial fibrillation without additional risk factors* for stroke/TIA • DVT/PE occurring more than 3 months ago • Hypercoagulable state without recent thrombotic episode, recurrent thrombosis or history of life-threatening thrombosis

Abbreviations: DVT = deep vein thrombosis; PE = pulmonary embolism; TIA = transient ischemic attack.

Footnote: *Risk Factors include recent cardiac failure, hypertension, age > 75 years, and diabetes. For more information, refer to BCGuidelines.ca – Atrial Fibrillation – Diagnosis and Management.

4) Management based on risk of thrombosis

For *low risk* of thrombosis (including risk associated with preoperative and postoperative):

- i) Discontinue warfarin 5 days prior to surgery. Therefore, give last dose on day 6, to achieve 5 warfarin-free days if day of surgery = day 0.
- ii) Check INR the day before procedure to ensure it is lower than the goal INR (< 1.5 for most procedures). If INR is higher than goal INR, discuss with physician performing procedure.
- iii) Restart warfarin at preoperative dose as soon as hemostasis is assured and only after epidural catheters are removed post-surgery.
- iv) Recheck INR within one week after starting warfarin at the last stable dose and resume regular monitoring and dose adjustment. Warfarin doses may change postoperatively if there were significant changes in medication (especially use of antibiotics) or nutrition.
- v) Patients can receive prophylactic doses of unfractionated heparin or LMWH for thromboprophylaxis until the INR is therapeutic.

For *high risk* of thrombosis (including risk associated with preoperative and postoperative):

- i) Discontinue warfarin at least 5 days prior to surgery. Therefore, give last dose on day 6 to achieve 5 warfarin-free days if day of surgery = day 0. Unless target INR is 3.0 (range 2.5 to 3.5) stop 6 days prior. Therefore, give last dose on day 7 to achieve 6 warfarin-free days if day of surgery = day 0.
- ii) If indicated, give therapeutic dose of LMWH on day 4, day 3, and day 2 in consultation with a haematologist at the closest referral centre/major hospital or thrombosis clinic.
- iii) Last dose of LMWH is generally not given any later than 24 hours before the procedure. Exact timing of the last LMWH dose will depend on the type and dose of LMWH and risk of thrombosis.
- iv) Check INR the day before procedure to ensure it is below the goal INR (< 1.5 for most procedures). If INR is higher than goal INR, discuss with physician performing the procedure.
- v) In the absence of an indicated procedure-specific thromboprophylactic regimen, start prophylactic dose LMWH 12 – 24 hours after surgery/procedure provided hemostasis is assured. Consider escalation to therapeutic dose of LMWH starting postoperative day 3, if there are no bleeding concerns. Discuss dose and timing of postoperative LMWH with surgeon.
- vi) Restart warfarin at preoperative dose as soon as hemostasis is assured and only after epidural catheters are removed post-surgery.
- vii) Continue LMWH until the INR is in therapeutic range.

To help the patient with this process, provide them with an *Associated Document: Anticoagulation Before & After Surgery – Patient Record Sheet*.

5) Timing of surgery/procedure

- Whenever possible, surgery in a chronically anticoagulated patient should be undertaken on an elective basis to allow for planned anticoagulant reversal.
- In patients receiving a fixed duration of anticoagulation (e.g., 3 months), consider delaying invasive procedures until after the completion of anticoagulation.
- For when **urgent or emergent surgery/procedure** is required and warfarin reversal is indicated (See *Appendix A: Flow Chart for Warfarin Reversal*), perform a baseline INR and proceed as follows:

Surgery/procedure to be done in < 24 hours

- i) Discontinue warfarin and administer IV vitamin K.
- ii) If surgery will be performed within 6 hours PCC is recommended (if not available then give FP).
- iii) Check INR immediately after product infusion and prior to surgery to document correction. If INR not corrected, consider repeat administration of PCC or FP in consultation with specialist.

Surgery/procedure to be done in 24 – 96 hours

- i) Discontinue warfarin and administer IV or PO vitamin K.
 - ii) Check INR in 24 hours.
 - iii) If INR is not corrected after a dose of vitamin K, give another dose of IV vitamin K and recheck INR in 12 hours.
 - iv) If INR is not corrected after 2 doses of vitamin K, consider other conditions that may elevate INR (e.g., disseminated intravascular coagulopathy, liver disease).
 - v) Check INR immediately prior to surgery to document correction.
- For when an **elective surgery** is required and with planned anticoagulant reversal proceed as follows:
 - i) Patient should be 5 or 6 days warfarin-free prior to surgery depending on therapeutic INR range.
 - ii) Consider need for LMWH bridging therapy (see *Management based on risk of thrombosis* above).
 - iii) Check INR one day prior to surgery or on day of surgery if possible, especially with high risk bleeding procedures.

6) Type of anesthesia

- Local and general anesthesia can be safely administered to a patient on warfarin.
- Neuraxial blocks (e.g., epidural analgesia, spinal anesthesia and retrobulbar blocks) should not be performed on patients on warfarin.
- In patients with epidural catheters:
 - i) Prophylactic dosing of LMWH is okay with an epidural in place;
 - ii) Do not give a therapeutic level dosing of LMWH with an epidural in place;
 - iii) Catheter should not be removed within 12 hours after a dose of LMWH;
 - iv) Do not start warfarin until epidural catheter is removed; and
 - v) Do not give LMWH until after 2 hours of catheter removal.

Resources

► References

1. Horlocker TT, Wedel DJ, Rowlingson JC, et al. Regional anesthesia in the patient receiving antithrombotic or thrombolytic Therapy: American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines, 3rd ed. *Reg Anesth Pain Med.* 2010;35:64-101.
2. Douketis JD, Spyropoulos AC, Spencer FA, et al. Perioperative management of antithrombotic therapy: Antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest* 2012;141:e326S-e350S.
3. Kearon C, Hirsh J. Management of anticoagulation before and after elective surgery. *N Engl J Med.* 1997;336:1506-1511.
4. Douketis JD. Perioperative management of patients who are receiving warfarin therapy: An evidence-based and practical approach. *Blood* 2011;117:5044-5049.
5. Ansell J, Hirsh J, Hylek E, et al. Pharmacology and management of the vitamin K antagonist: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines, 8th ed.. *Chest.* 2008;133:1235-1315.
6. Jacobs LG, Nusbaum N. Perioperative management and reversal of antithrombotic therapy. *Clin Geriatr Med.* 2001;17:189-202,ix.
7. Spandorfer J. The management of anticoagulation before and after procedures. *Med Clin North Am.* 2001;85:1109-16,v.
8. Brigden ML. Oral anticoagulant therapy: practical aspects of management. *Postgrad Med.* 1996; 6:81-84,87-89,93-94 passim.
9. White RH, McKittrick T, Hutchinson R, et al. Temporary discontinuation of warfarin therapy: Changes in the international normalized ratio. *Ann Intern Med.* 1995;122:40-42.

► Resources

- Thrombosis Canada, thrombosiscanada.ca

► Appendices

- Appendix A: Flowchart for Warfarin Reversal

► Associated Documents

The following documents accompany this guideline:

- BCGuidelines.ca – *Warfarin Therapy Management*
- Anticoagulation Before & After Surgery – Patient Record Sheet

This guideline is based on scientific evidence current as of the Effective Date.

This guideline was developed by the Guidelines and Protocols Advisory Committee, approved by the British Columbia Medical Association, and adopted by the Medical Services Commission.

THE GUIDELINES AND PROTOCOLS ADVISORY COMMITTEE

The principles of the Guidelines and Protocols Advisory Committee are to:

- encourage appropriate responses to common medical situations
- recommend actions that are sufficient and efficient, neither excessive nor deficient
- permit exceptions when justified by clinical circumstances

Contact Information:

Guidelines and Protocols Advisory Committee
PO Box 9642 STN PROV GOVT
Victoria BC V8W 9P1

Email: hlth.guidelines@gov.bc.ca

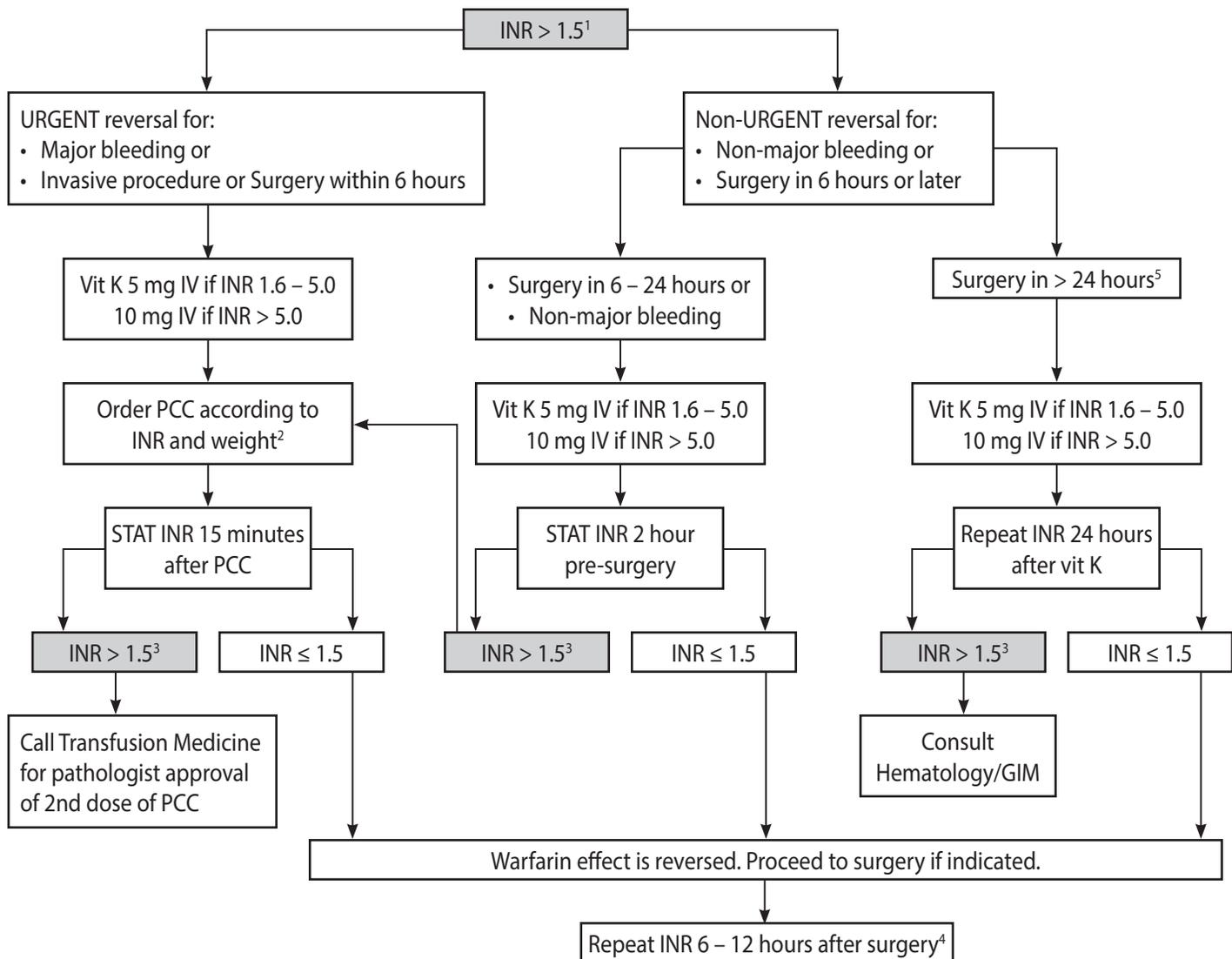
Website: www.BCGuidelines.ca

Disclaimer

The Clinical Practice Guidelines (the “Guidelines”) have been developed by the Guidelines and Protocols Advisory Committee on behalf of the Medical Services Commission. The Guidelines are intended to give an understanding of a clinical problem, and outline one or more preferred approaches to the investigation and management of the problem. The Guidelines are not intended as a substitute for the advice or professional judgment of a health care professional, nor are they intended to be the only approach to the management of clinical problem. **We cannot respond to patients or patient advocates requesting advice on issues related to medical conditions. If you need medical advice, please contact a health care professional.**



Appendix A: Flow Chart for Warfarin Reversal



Abbreviations: GIM =General Internal Medicine; INR = International Normalized Ratio; IV = Intravenous; LMWH = low molecular weight heparin; PCC = prothrombin complex concentrate; VTE = Venous thromboembolism; vit = vitamin.

Footnotes:

- 1) This algorithm is recommended for Warfarin reversal **only** and should not be used for reversal of other anticoagulants.
- 2) **Do not** give frozen plasma **in addition** to PCC. If indicated, transfuse red cells (for severe anemia) or platelets (e.g., platelet count < 50 x 10⁹/L or patient on antiplatelet therapy).
- 3) If INR is greater than 1.5 after one dose of vitamin K or one dose of PCC, contact Transfusion Medicine and/or consult Hematology for further assistance.
- 4) Half-life of PCC is approximately 6 hours therefore, should reassess the need for repeat PCC infusion (e.g., if surgery is ongoing, INR > 1.5 and patient is still bleeding) at 6 – 12 hr after surgery or PCC infusion.
- 5) In patients with high or very high risk of stroke (e.g., atrial fibrillation with CHADS2 score ≥ 3, previous stroke, mechanical heart valve), thrombosis (e.g., VTE within past 3 months, cancer-associated thrombosis, antiphospholipid antibody syndrome), consider need for bridging therapy with LMWH if surgery is expected to occur later than 24 hours after INR reversal.



Anticoagulation Before & After Surgery – Patient Record Sheet

Patient Name: _____ Patient Weight: _____ kg

Surgeon Name: _____ Warfarin dose: _____ mg

Type of Procedure: _____ LMWH: _____

Date	# Days before/ after Surgery	Please take your warfarin and LMWH injection as instructed below:	Blood Testing
	7	 aspirin, clopidogrel (Plavix®), ticlopidine (Ticlid®) if asked by your surgeon	
	6	LAST DOSE OF WARFARIN BEFORE SURGERY	
	5	 warfarin. Do not take any more warfarin before surgery.	INR
	4	No LMWH. No warfarin.	
	3	LMWH _____ units at 8 am. No warfarin.	
	2	LMWH _____ units at 8 am. No warfarin.	
	1	No LMWH. No warfarin.	INR
	Surgery	Warfarin ____ mg at bedtime if you have no bleeding	
	+1	LMWH _____ units at 8 am AND Warfarin ____ mg at supper	
	+2	LMWH _____ units at 8 am AND Warfarin ____ mg at supper	
	+3	LMWH _____ units at 8 am AND Warfarin ____ mg at supper	INR,CBC
	+4	LMWH _____ units at 8 am AND Warfarin ____ mg at supper	
	+5	LMWH _____ units at 8 am AND Warfarin ____ mg at supper	INR,CBC
	+6	Continue warfarin and LMWH (if needed) as instructed by your doctor.	

If you have any questions or experience serious bleeding, call your doctor: _____

MD Signature: _____ Date: _____