

Guidelines for the Management of Warfarin During Invasive Procedures (Adult Surgical Patients (non-pregnant))

These guidelines provide recommendations for patients on long-term warfarin (or other vitamin K antagonists) who require an **elective** procedure for which an INR less than 1.5 is required. Patients on these oral anticoagulants requiring **emergency** procedures may require rapid anticoagulant reversal and should be discussed with a clinical haematologist on a case-by case basis.

Certain procedures **may** be performed without interruption of anticoagulation (with INR less than 3.0), including: minor dental, ophthalmological and dermatological surgery; joint injections; diagnostic angiography or pacemaker insertion; and low risk endoscopic procedures (e.g. diagnostic procedure +/- biopsy, biliary or pancreatic stenting). Refer to the relevant specialist or departmental guidelines.

Management of perioperative anticoagulation varies according to the balance between **thrombosis risk** (baseline risk plus additional thrombotic risk from the procedure) and **bleeding risk** (baseline risk of patient on anticoagulant plus additional risk from the procedure or other factors, including spinal/epidural anaesthesia).

Reintroduction of prophylactic or therapeutic anticoagulation following an invasive procedure must be based on the assessment of surgical site bleeding risk: a period **without any anticoagulation** may be required to avoid excessive or critical site bleeding. Procedures with a very high operative bleeding risk or involving use of spinal/epidural anaesthesia may follow these protocols but post-procedural anticoagulation may need to be individualised and should be discussed between the responsible surgeon and haematologist.

It is important that the risks of the procedure are discussed with the patient and a plan agreed upon. A senior member of the team is best placed to evaluate the risks, discuss them and formulate a plan. The templates in this document provide a way for the outcomes of these discussions to be clearly documented for all members of the team involved in the patient's care.

Procedures under spinal or epidural anaesthesia require specific consideration: refer to GHNHSFT Policy <u>A2165</u> ('Anticoagulants, Antiplatelets and spinal/epidural Anaesthesia). Neuraxial procedures including catheter insertion should not be performed if INR greater than or equal to 1.5; within 12 hours of prophylactic dose low molecular weight heparin (LMWH); or within 24 hours of treatment dose LMWH. Doses of LMWH can be administered a minimum of 4 hours after catheter removal (in the presence of adequate haemostasis).

Perform a patient risk assessment using Table 1 then select from the LOWER (Protocol A) or HIGHER (Protocol B) risk protocol. These templates may require modification for patients considered to have a very high bleeding risk, patients with renal impairment or to accommodate neuraxial procedures as recommended above.

Prescribing information for LMWH is contained in Appendix 1 and Appendix 2.

Patients apart from the below (Table 1) can generally be managed by stopping warfarin 5 days before elective surgery, as appropriate. These LOWER thrombotic risk patients (Protocol A), should then be risk assessed and provided with prophylactic LWMH post-operatively as outlined in Appendix 1.

Table 1 When to consider bridging with treatment dose LMWH in patients who stop warfarin

Consider bridging with full treatment dose LMWH i.e. Protocol B (HIGHER thrombotic risk), for:			
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			
Patients with a previous stroke/TIA in the last 3 months			
 Patients with a previous stroke/TIA and three of more of the following risk factors Congestive cardiac failure 			
 Hypertension (either BP greater than 140/90 mmHg or on antihypertensive treatment) 			
Age over 75 years			
Diabetes mellitus			
All Mechanical Heart Valve patients except those with a bileaflet aortic valve and no other risk			
factors e.g. previous stroke/TIA, atrial fibrillation or reduced left ventricular ejection fraction			



Anticoagulant Bridging Protocol for Invasive Procedures and Surgery Protocol A: LOWER THROMBOTIC RISK				
Name:				
Date of birth:				
Hospital number:				
Procedure:		Date of Procedure:		
Surgeon:		Indication for anticoagulation:		
Anaesthetist:		Target INR:		
Patient weight	kg			
Creatinine Clearance mL/min (see Appendix 1 for dosing information)				

		Date	Management	(See Appendix 1 for dosing information and delete as appropriate)
Day -5	day	dd/mm/yy	stop warfarin (last dose	on Day -6). No pre-operative anticoagulation required.
Day -4	day	dd/mm/yy	no warfarin	
Day -3	day	dd/mm/yy	no warfarin	
Day -2	day	dd/mm/yy	no warfarin	
Day -1	day	dd/mm/yy	no warfarin. If feasible,	check INR and consider Vitamin K 1mg orally if INR greater or equal
			to 1.5	
Op day	day	dd/mm/yy	no warfarin. Check INR	less than 1.5 on admission
			Providing haemostasis is	s secure, and at the discretion of the responsible surgeon, start
			prophylactic dose	mg Low Molecular Weight Heparin (LMWH)
			subcutaneously once da	ily, 6-12 hours post-operatively
Day +1	day	dd/mm/yy	providing haemostasis is	s secure
			give prophylactic dose . greater or equal to 2 for	mg ONCE daily LMWH subcutaneously until INR two consecutive days <u>and</u> restart warfarin at <u>usual maintenance</u>
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- for procedures under spinal or epidural anaesthesia refer to GHNHSFT Policy <u>A2165</u>
- check platelet count every 2 days after starting LMWH to exclude heparin induced thrombocytopenia
- ensure anticoagulation follow up arranged on discharge from hospital

Risks of procedure discussed with patient and above management plan agreed	Risks of	procedure	discussed w	ith patient	and above	management	plan agreed
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LAST DOSE OF WARFARIN ON -	Authorising Senior Clinician		
		(sign)	(print)
	Position		
	Date		



Anticoagulant Bridging Protocol for Invasive Procedures and Surgery <u>Protocol B: HIGHER THROMBOTIC RISK (As per risk factors in Table 1)</u>

Name:

		Date	Management	(See Appendix 1 and 2 and delete as appropriate)
Day -5	day	dd/mm/yy	stop warfarin (last dose on Day -6)	
Day -4	day	dd/mm/yy	no warfarin	
Day -3	day	dd/mm/yy	no warfarin give therapeutic dosemg subcutaneously (SC)	ONCE a day at 8am Low Molecular Weight (LMWH)
Day -2	day	dd/mm/yy	no warfarin give therapeutic dosemg	ONCE a day at 8am LMWH SC
Day -1	day	dd/mm/yy	no warfarin give therapeutic dosemg (Reduce to 1mg/kg if high bleeding The last dose of therapeutic LMWH	ONCE a day at 8am LMWH SC risk surgery or planned spinal/epidural anaesthesia) should be at least 24 hours before surgery.
Op day	day	dd/mm/yy	no warfarin. Check INR less than 1. Providing haemostasis is secure, an prophylactic dose	5 pre-operatively d at the discretion of the responsible surgeon, restart ng LMWH subcutaneously ONCE daily 6-12 hours post-
Day +1	day	dd/mm/yy	operatively providing haemostasis is secure, if I continue prophylactic dose	high bleeding risk or spinal/epidural anaesthesia mg ONCE daily LMWH <u>OR</u> if non-high-risk
Day +2	day	dd/mm/yy	bleeding give therapeutic dose LM ^N <u>6pm</u> (no loading doses) give therapeutic dose LMWH until concern over bleeding, continue pr	WH <u>and</u> restart warfarin at <u>usual maintenance dose at</u> INR greater or equal to 2 for two consecutive days. If any ophylactic dose LMWH until bleeding concern resolved,
			then increase to therapeutic dose a	is described.

- for procedures under spinal or epidural anaesthesia refer to GHNHSFT Policy A2165
- check platelet count every 2 days after starting LMWH to exclude heparin induced thrombocytopenia
- ensure anticoagulation follow up arranged on discharge from hospital

Risks of procedure discussed with patient and above management plan agreed

LAST DOSE OF WARFARIN ON -	Authorising Senior Clinician	(sign)	(print)
	Position		
	Date		



Appendix 1- Dosing Guidelines for PROPHYLACTIC dosing (in Adult Surgical Patients (non-pregnant))

Body weight, renal function (calculated as creatinine clearance [CrCl] using Cockcroft-Gault equation – eGFR should <u>not</u> be used as it is not equivalent) and individual contraindications/bleeding risk factors should be checked before prescribing.

A CrCl calculator is available via: Creatinine Clearance (Cockcroft-Gault Equation) (mdcalc.com)[†]

Patients with creatinine clearance over 30ml/min (via subcutaneous injection)

Weight less than 50kg	Enoxaparin 20mg ONCE daily
Weight greater than or equal to 50kg	Enoxaparin 40mg ONCE daily

Patients with creatinine clearance less than 30ml/min, including dialysis* (via subcutaneous injection)

All patients	Enoxaparin 20mg ONCE daily

- + MDCalc is not a registered medical device. Healthcare professionals must exercise their own clinical judgement when using this tool to calculate creatinine clearance.
- Following EU harmonisation of the Summary of Product Characteristics in 2017, enoxaparin is no longer licensed for use if CrCl is
 <15ml/min. However, the local nephrologists consider this acceptable practice, given the difficulties with alternative approaches and the extensive local experience with enoxaparin in this group of patients.



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Appendix 2- Dosing Guidelines for THERAPEUTIC dosing (in Adult Surgical Patients (non-pregnant))

For therapeutic dosing, the dose of enoxaparin is based on body weight. Patients must therefore be weighed to ensure an accurate dose of enoxaparin is prescribed, and the weight documented. Renal function must also be checked prior to prescribing (calculated as creatinine clearance [CrCl] using <u>Cockcroft-Gault equation</u>[†] – eGFR should <u>not</u> be used as it is not equivalent). Patients with CrCl less than 30ml/min should receive a reduced dose of enoxaparin – see below section on renal impairment.

Inhixa[®] (enoxaparin biosimilar) is supplied as pre-filled syringes of 20mg, 40mg, 60mg, 80mg, 100mg, 120mg and 150mg. Standard doses are rounded to the nearest syringe size.

In this peri-operative cohort of patients the standard dosing of 1.5mg/kg OD SC (CrCl >30ml/min) should be used. As per Protocol B consideration should be given to reducing to 1mg/kg in high bleed risk procedures.

Standard dosing of Inhixa [®] for treatment of VTE in CrCl >30ml/min: 1.5mg/kg OD SC			
40-47kg	60mg OD		
48-59kg	80mg OD		
60-73kg	100mg OD		
74-88kg	120mg OD		
89-109kg	150mg OD		
110-125kg	180mg OD (100mg + 80mg)		
126-150kg	1.5mg/kg split dose (dose divided BD and rounded		
	to nearest syringe size. This may lead to		
	asymmetric dosing)		
Over 150kg	Discuss with haematology		

Renal Impairment

For patients with severe renal impairment (CrCl less than 30ml/min) the dose of enoxaparin for the treatment of VTE is 1mg/kg once daily SC*. The dose should be rounded to the nearest 10mg for ease of administration, as follows:

Weight range	Renal dose	Additional Administration Information			
45-54kg	50mg OD	0.	5ml from 60mg syringe		
55-64kg	60mg OD		-		
65-74kg	70mg OD	0.	7ml from 80mg syringe		
75-84kg	80mg OD	-			
85-94kg	90mg OD	0.9ml from 100mg syringe			
95-104kg	100mg OD	-			
105-114kg	110mg OD	60mg + 0.5ml (50mg) from 60mg syringe			
115-124kg	120mg OD	-			
125-134kg	130mg OD	80mg + 0.5ml (50mg) from 60mg syrin			
135-144kg	140mg OD	80mg + 60mg			
145-154kg	150mg OD	-			

Doses greater than 150mg will also require multiple syringes to be used. The dose is not capped.

When using partial syringes, be aware that the 60mg, 80mg and 100mg syringes are 100mg/ml strength, but the 120mg and 150mg syringes are a higher 150mg/ml strength.

References

Warfarin. September 2019. UK Clinical Pharmacy Association Handbook of Perioperative Medicines. Accessed: <u>https://periop-handbook.ukclinicalpharmacy.org/drug/warfarin/</u>

Venous thromboembolism in over 16s: reducing the risk of hospital-acquired deep vein thrombosis or pulmonary embolism (NG89). 13 August 2019. National Institute for Health and Care Excellence (NICE). Accessed: <u>https://www.nice.org.uk/guidance/ng89/resources/venous-thromboembolism-in-over-16s-reducing-the-risk-of-hospitalacquired-deep-vein-thrombosis-or-pulmonary-embolism-pdf-1837703092165</u>

Keeling D, Campbell Tait R, Watson H on behalf of the British Committee for Standards in Haematology. Perioperative management of anticoagulation and antiplatelet therapy. British Journal of Haematology. 2016; 175:602-612

Summary of Product Characteristics for Inhixa[®]. Last updated on eMC 10th March 2022. Electronic Medicines Compendium Inhixa 4,000 IU (40 mg)/0.4 mL solution for injection - Summary of Product Characteristics (SmPC) - (emc)

Keeling D, Baglin T et al on behalf of the British Committee for Standards in Haematology. Guidelines on oral anticoagulation with warfarin. 14 June 2011. <u>https://doi.org/10.1111/j.1365-2141.2011.08753.x</u>

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