

Warfarin in Inpatients - Full Clinical Guideline - DERBY
(To be used with the anticoagulant prescription and referral chart)

Reference no.: CG-T/2014/136

1. Introduction

Several thousand people in Southern Derbyshire are taking warfarin which is a vitamin K dependant oral anticoagulant.. Many are admitted to hospital with acute illness or for planned procedures.

2. Aim and Purpose

To ensure the safe management of in-patients who are taking warfarin.

3. Definitions, Keywords

PT=Prothrombin time. INR = International Normalized Ratio (this is the blood test which monitors the effect of warfarin on the blood and is used to adjust the dose of warfarin).

LMWH = Low molecular weight heparin. This is given subcutaneously and has a half life of 3 – 4 hours. It is dosed by body weight with adjustments for renal impairment.

4.

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A. Patients admitted on warfarin

Anticoagulation is a balance of risks and benefits i.e. treatment or prevention of thromboembolism versus bleeding. On admission to hospital the balance of risks may shift towards bleeding as intercurrent illness and medication change are major causes of high INR. Interventional procedures and surgery may mean warfarin needs to be stopped or reversed. If the patient is bleeding and/or the INR is high the warfarin effect may need to be reversed quickly or immediately.

- **Careful consideration should be given in all acute admissions as to whether warfarin should be continued or stopped. Discuss with Registrar or Consultant in your specialty.**
- **If warfarin continues: Do a daily INR until a Registrar or Consultant document in the notes that the patient is stable and the INR can be done less frequently.**
- **INR results must be checked and written on the anticoagulant prescription and referral chart before warfarin is prescribed or given.**

B. Reversing the warfarin effect.

If a decision is made to reverse the warfarin effect consider:

- a) How quickly you want to achieve this: simply stopping the warfarin takes 5 days, oral vitamin K 24 hours, IV vitamin K 6 – 12 hours.
- b) Will the patient need on-going thromboprophylaxis (see Trust VTE Risk assessment Form)
- c) A minority of patient on long term warfarin will need 'bridging' with therapeutic heparin (see section 6)

Stop warfarin:

- Do daily INR.
- Takes 5 days for the INR to return to normal.
- Recheck INR the day before any surgery/interventional procedure.
- If INR > 1.5 give vitamin K as below.
- If patient is unwell or debilitated the INR may not fall when warfarin is stopped.

Oral Vitamin K (2mg):

- Takes 24 hours to work.
- Check INR at 24 hours

IV vitamin K (2mg or 5mg):

- Takes 6 - 12 hours to work.
- Check INR at 6 – 12 hours

C. Immediate Reversal of Warfarin: Octaplex and IV vitamin K 5mg

- **Life or limb threatening bleeding including head injury (see below, section 4).**
- **Emergency Surgery which can't wait 6 - 12 hours for IV vitamin K to work (Octaplex must NOT be used to reverse warfarin for elective procedures)**

Give Octaplex as per protocol (Octaplex to reverse prolonged INR due to Vitamin K antagonist CG-T/2014/076).

Give 5mg vitamin K IV as soon as possible (Octaplex works immediately but will wear off if Vitamin K is not given).

D. Head injury

- **All patients on warfarin with a head injury however minor should have their INR measured.**
- **Patients on warfarin are more likely to have an intracerebral bleed with more minor injury and there should be a lower threshold for CT scanning.**
- **Patients on warfarin with facial or scalp laceration, bruising, persistent headache, amnesia, loss of consciousness or reduced Glasgow Coma Scale should have a head CT scan immediately.**
- **Patients on warfarin with a strong suspicion of intracerebral haematoma after a clear head injury should have their INR reversed with Octaplex immediately and before the CT scan and INR results are available.**

E. Management of Over Anticoagulation for Inpatients on Warfarin

Current INR	Action	Next INR
3.1 – 6.0 (TR 2-3)	Reduce dose or stop and restart when INR <5.0	Daily
4.1 – 6.0 (TR 3-4)		
6.0 – 8.0	Stop warfarin	Daily
If Minor Bleeding , risk of bleeding ¹ and/or just started Warfarin	Consider Vitamin K 2 mg oral/IV	Daily
>8.0	Stop warfarin Give Vitamin K 2 mg IV/oral (if INR >12.0 give 4 mg oral or 5mg IV).	Daily
Major Bleed INR >1.8	Stop warfarin Give Vitamin K 5 mg IV Give Octaplex ²	30 minutes post Octaplex then daily

¹ Risk of bleeding e.g. age > 70, cerebral arterial disease, uncontrolled hypertension, previous h/o bleeding, postoperative, renal failure.

²Guideline: Octaplex for the reversal of prolonged INR due to warfarin in life or limb threatening haemorrhage. CG-T/2014/076, see guidelines and policies on the Trust Intranet.

All patients who have warfarin effect reversed should receive appropriate thromboprophylaxis unless contraindicated (see departmental/directorate thromboprophylaxis protocol).

Occasionally patients at very high risk of thrombosis may need 'bridging' with therapeutic heparin – see below.

F. PERIOPERATIVE MANAGEMENT OF WARFARIN: ELECTIVE PROCEDURES

Not all procedures require warfarin to be stopped e.g:

- Dental extraction
- Cataract surgery
- Some minor gynaecological surgery
- Some endoscopy

= *see departmental protocols.*

If warfarin needs to be stopped the risk and consequences of thrombosis have to be weighed against the risks and consequences of bleeding if prophylactic or therapeutic LMWH/UFH is substituted.

In the majority of patients stopping warfarin, THERAPEUTIC ANTICOAGULATION WITH LMWH/UFH (CALLED 'BRIDGING') IS NOT NECESSARY as it does not reduce the risk of thrombosis and carries a significant risk of bleeding.

If bridging with therapeutic LMWH/UFH is deemed necessary LMWH should be used in preference to UFH in most patients (in individual very high risk cases Unfractionated Heparin can be considered – Consultant decision). Prophylactic doses should be used in the first 48 hours postoperatively at least.

See the different categories below. See the following page for details of perioperative management.

VTE

VTE ≥ 3 months previously: Give prophylactic enoxaparin as per Trust VTE guidelines, continuing until the INR is therapeutic.

VTE < 3 months : **Consider** bridging with therapeutic enoxaparin.

Very high risk patients such as patients with a previous VTE whilst on therapeutic anticoagulation who now have a target INR of 3-5: **Consider** bridging with therapeutic enoxaparin

Atrial Fibrillation

Low risk AF i.e. No prior history of CVA/TIA (CHADS2 ≤ 4): Do not bridge with therapeutic enoxaparin. If thromboprophylaxis for VTE is indicated give prophylactic enoxaparin as per VTE guidelines

High risk AF i.e. AF plus CVA/TIA within the previous 3 months; or AF with previous CVA/TIA at any time plus 3 out of 4 of the following risk factors: CCF, diabetes, hypertension (140/90 on medication), age > 75 years: **Consider** bridging with therapeutic enoxaparin

Mechanical Heart Valve

Bileaflet Mechanical Aortic valve with no other risk factors: give prophylactic enoxaparin if required for VTE thromboprophylaxis.

All other mechanical heart valve patients: **Consider** bridging with therapeutic enoxaparin

∞CHADS2 = CCF, Hypertension, Diabetes, Age ≥75 [score 1 each], Stroke [score 2]

**Perioperative Management of Warfarin
SCHEDULE A**

This protocol is suitable if the warfarin needs to be stopped and at least one of the following applies:

VTE \geq 3months ago

Low risk AF and VTE thromboprophylaxis is needed.

Bileaflet Mechanical Aortic valve with no other risk factors and VTE thromboprophylaxis is needed.

Treatment protocol:

- Hydration, mobilisation and use of mechanical measures as for usual thromboprophylaxis.
- Stop warfarin 5 days preop.
- Check INR the day before surgery. If INR \geq 1.5 give 2mg vitamin K IV.
- Omit enoxaparin on morning of procedure.
- If neuraxial anaesthesia is planned ensure the INR is normal and at least 12 hours has elapsed since the last prophylactic enoxaparin dose– anaesthetist decision.
- If thromboprophylaxis is needed give Enoxaparin 6 – 12 hours postop (morning list 18.00, afternoon list 22.00) provided haemostasis is secure and at least 4 hours after insertion/removal of epidural catheter (discuss with the anaesthetist).
- Restart warfarin at usual maintenance dose (NOT a loading dose) on first postop day.
- Continue prophylactic enoxaparin until the INR is therapeutic
- Refer to outpatient anticoagulation service on discharge (tel 89419, dhft.anticoagulationclin@nhs.net)

Prophylactic enoxaparin dose adjustment for weight:

Less than 50kg	– 20mg once daily subcutaneously
50– 100 kg	– 40mg once daily subcutaneously
100 – 150kg	– 60mg once daily subcutaneously
Greater than 150kg	– 80mg once daily subcutaneously

Dose adjustment for renal impairment:

eGFR 10 - < 30 give Enoxaparin 20mg S/C OD

eGFR < 10 give Unfractionated Heparin 5000 iu TDS S/C

NB: For patients with BMIs of <18.5 kg/m² or >30 kg/m² calculate a creatinine clearance using the Cockcroft Gault formula (discuss with pharmacy).

**Perioperative Management of Warfarin
SCHEDULE B**

This protocol is can be considered if the warfarin needs to be stopped and at least one of the following applies:

VTE < 3 months ago

Very high risk patients such as patients with a previous VTE whilst on therapeutic anticoagulation who now have a target INR of 3-5.

Mechanical Heart Valve patients except those with Bileaflet Mechanical aortic valve and no other risk factors.

Treatment protocol:

- Hydration, mobilisation and use of mechanical measures as for usual thromboprophylaxis.
- Stop warfarin 5 days pre-op.
- Commence Enoxaparin 3 days pre-operatively at 1 mg/kg twice daily (08.00 and 18.00), providing normal renal function (GFR \geq 30ml/min, see below for dose adjustment in renal impairment)
- Check INR the day before surgery. If INR \geq 1.5 give 2mg vitamin K IV. Recheck INR before surgery.
- **Omit Enoxaparin the evening before and the morning of the operation.**
- If spinal/epidural anaesthesia planned ensure normal INR and at least 24 hours post enoxaparin – anaesthetist decision.
- Restart **prophylactic** enoxaparin 6 – 12 hours post-op (e.g morning list 18.00, afternoon list 22.00) provided haemostasis is secure and at least 4 hours after insertion/removal of epidural catheter (discuss with the anaesthetist). See below for weight adjusted enoxaparin dose.
- Give prophylactic enoxaparin at 18.00 on the first and second postop day.
- Restart warfarin at usual maintenance dose (NOT a loading dose) on the first postop day after reassessment and exclusion of post op bleeding complications.
- Increase enoxaparin to 1 mg /kg twice daily on the second or third postop day after assessment of bleeding risk and exclusion of post op bleeding complications. For high bleeding risk procedures the increase to a therapeutic dose may be delayed further – discuss with surgeon.
- Continue therapeutic enoxaparin until the INR is within the therapeutic range.
- Refer to outpatient anticoagulation service on discharge (tel 89419, dhft.anticoagulationclin@nhs.net)

Prophylactic enoxaparin dose adjustment for weight:

Less than 50kg – 20mg once daily subcutaneously
 50 – 100 kg – 40mg once daily subcutaneously
 100– 150kg – 60mg once daily subcutaneously
 Greater than 150kg – 80mg once daily subcutaneously

Dose adjustment for renal impairment:

eGFR 10 to < 30; reduce to 1mg/kg OD and monitor antiXa.
 eGFR < 10 use unfractionated heparin instead.

_ NB: for BMI < 18.5 or > 30kg/m² calculate Creatinine Clearance using Cockcroft Gault Formula (discuss with pharmacy).

G. Restarting Warfarin.

If warfarin is stopped temporarily (for whatever reason) restart at the patient's **usual maintenance dose** when appropriate. Continue thromboprophylaxis until the INR is > 2.0.

In some situations the patient may be more sensitive to warfarin due to intercurrent illness or medication. It may be appropriate to give a lower dose than maintenance, or omit warfarin altogether. In the latter case give thromboprophylaxis according to directorate or departmental protocol.

H. Starting Warfarin (see appendix 3 for induction regimes)

All patients: do baseline PT, APTT, LFT, U and E.

Discuss the risks and benefits of anticoagulation. Give the patient an OAT booklet.

- There is a significant risk of over-anticoagulation when older patients are given loading doses.
- Traditional loading doses of warfarin (e.g.10mg, 10mg, 5mg) are only suitable for rapid induction of anticoagulation in younger patients (< 60) who are receiving therapeutic heparin for an acute thrombo-embolism.
- See below for the correct induction regime for your patient and indication.

For patients with recent acute thromboembolism

who are older(>60 years)and/or with bleeding risk factors (e.g. base line INR > 1.2, abnormal LFTs, moderate to severe congestive cardiac failure, on drugs known to potentiate warfarin, body weight <45 kg, **or high risk Atrial Fibrillation:**

- 5mg mg daily for 4 days – **Tait 5mg induction** (see appendix 1 for details)

For younger patients (≤60 yrs) with acute VTE and none of the above risk factors use the standard Fennerty protocol starting with 10mg.

- Fennerty regime – **Fennerty 10 mg induction** (appendix 1 for details)

I. Discharge

- ALL people discharged on warfarin must be referred to the RDH out-patient anticoagulation service.
- When completing the discharge summary the 'warfarin – discharge only' option must be chosen. This results in the patients details being included in a daily report to the anticoagulation team.
- To contact the anticoagulation team phone 89419 or email dhft.anticoagulationclinic@nhs.net

5. References (including any links to NICE Guidance etc.)

- ▯ Guidelines on oral anticoagulation with warfarin - 4th edition: British Committee for Standards in Haematology.
- ▯ Peri-operative management of anticoagulation and antiplatelet therapy
David Keeling, R. Campbell Tait, and Henry Watson, on behalf of the British Committee of Standards for Haematology
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6. Documentation Controls

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Appendices

Appendix 1. WARFARIN INDUCTION REGIMES

Tait (5mg induction regime) R.C Tait & A. Sellick;B.J. Haem, 1998, 101: 450-454.

For acute VTE in older people (>60 years); or with the following risk factors; or Atrial Fibrillation:

- Base line of INR > 1.2
 - Abnormal LFTs
 - Moderate to severe congestive cardiac failure
 - Patients on drugs known to potentiate warfarin
 - Body weight <45 kg
1. Check baseline INR. Providing this less than or equal to 1.3 AND patient not taking amiodarone
 2. Give 5mg Warfarin at 6pm for 4 days (Mon-Thu) then check INR on day 5 (Fri)
 3. Amend dose for evening of day 5 based on the result and recheck on day 8 (Mon)
 4. After day 8 test, amend dose and recheck in a further 4 (Fri) or 7 (Mon) days, thereafter following normal practice.

INR on Day 5 of warfarin therapy	Warfarin dose for days 5 - 7	INR on Day 8 of warfarin therapy	Warfarin dose from day 8 onwards
1.7 or less	5mg	1.7 or less 1.8 – 2.4 2.5 – 3.0 >3.0	6mg 5mg 4mg 3mg for 4 days
1.8 – 2.2	4mg	1.7 or less 1.8 – 2.4 2.5 – 3.0 3.1 – 3.5 >3.5	5mg 4mg 3.5mg 3mg for 4 days 2.5mg for 4 days
2.3 – 2.7	3mg	1.7 or less 1.8 – 2.4 2.5 – 3.0 3.1 – 3.5 >3.5	4mg 3.5mg 3mg 2.5mg for 4 days 2mg for 4 days
2.8 – 3.2	2mg	1.7 or less 1.8 – 2.4 2.5 – 3.0 3.1 - 3.5 >3.5	3mg 2.5mg 2mg 1.5mg for 4 days 1mg for 4 days
3.3 – 3.7	1mg	1.7 or less 1.8 – 2.4 2.5 – 3.0 3.1 – 3.5 >3.5	2mg 1.5mg 1mg 0.5mg for 4 days omit for 4 days
3.8 or more	0mg	<2.0 2.0 – 2.9 3.0 – 3.5	1.5mg for 4 days 1mg for 4 days 0.5mg for 4 days

Fennerty (10mg induction regime) Fennerty et al, Br Med J (1988) 297:1285-5

Recommended for younger, fitter patients with acute venous thromboembolism whose age is less than 60 years and with no bleeding risk factors e.g base line INR > 1.2, abnormal LFTs, moderate to severe congestive cardiac failure, patients on drugs known to potentiate warfarin, body weight <45 kg, postoperative.

Day	INR*	Warfarin dose (mg)
1.	< 1.4	10
2.	< 1.8	10
	1.8	1
	> 1.8	0.5
	< 2.0	10
3.	2.0 - 2.1	5
	2.2 - 2.3	4.5
	2.4 - 2.5	4
	2.6 - 2.7	3.5
	2.8 - 2.9	3
	3.0 - 3.1	2.5
	3.2 - 3.3	2
	3.4	1.5
	3.5	1
	3.6 - 4.0	0.5
	> 4.0	0
	4.	< 1.4
1.4		8
1.5		7.5
1.6 - 1.7		7
1.8		6.5
1.9		6
2.0 - 2.1		5.5
2.2 - 2.3		5
2.4 - 2.6		4.5
2.7 - 3.0		4
3.1 - 3.5		3.5
3.6 - 4.0		3
4.1 - 4.5		Miss out next day's dose then give 2mg
> 4.5		Miss out 2 days doses then give 1 mg