Warfarin Initiation and dosage adjustments

BSUH suggested loading regimes for warfarin (doses to be given once daily at 2pm for up to three consecutive days)

Patients between 20-65 years and greater 60kg with no additional factors increasing sensitivity to warfarin (see below):

- Day 1: 8mg
- Day 2: 8mg
- Day 3: Check INR. If <2, give 8mg. If INR >2, consider switching to maintenance dose (see table below)

Patients with one or more of the following factors increasing sensitivity to warfarin:

Age > 65years, low body weight (less than or equal to 60kg), concurrent interacting drugs e.g amiodarone or some antibiotics e.g. clarithromycin (see BNF for full list), low serum albumin

Patients with raised baseline INR (>1.3) require further investigation prior to starting oral anticoagulation – contact haematology

- Day 1: 6mg
- Day 2: 6mg
- Day 3: Check INR. If <2, give 6mg. if INR >2, consider switching to maintenance dose (see table below)

In-patient dosing of warfarin is to be completed by the day team before the end of shift. It is unsafe practice for the on-call team to prescribe warfarin to patients they are not familiar with. Warfarin should be prescribed daily at 2pm whilst patient is in hospital. This moves to 6pm on discharge in line with community practice.

For loading regimes of other vitamin k antagonists e.g. acenocoumarol or phenindione, please consult the BNF as these differ from warfarin.

Author Clare Proudfoot, Lead Anticoagulation Pharmacist, checked by Dr B Marson, Cons Haematologist and H Hayllar Thrombosis Nurse Specialist. Approved by Medicines Governance Group July 2020, review date July 2023

Maintenance dose calculation

As a precaution, it is recommended that the INR is initially checked after two loading doses on day 3 – if the INR is below 2, continue with loading protocol but if the INR is above 2, review the loading dose to prevent over-anticoagulation and consider switching to maintenance dose.

The maintenance dose of warfarin is calculated by taking the INR on **day 4 after three loading doses** by using the chart below.

INR after 3 doses	Predicted fraction of daily loading dose
4.0+	omit dose, repeat INR next day
3.0+	1/4
2.5+	1/3
2.0+	1/2
1.6+	2/3
Less than 1.6	Full dose

2/3

Example 1: Patient is loaded on 8mg each day for three days and the INR on day 4 is 2.1. The maintenance dose of warfarin is 4mg (½ of daily loading dose)

Example 2: Patient is loaded on 6mg on day 1 and 6mg on day 2. On day 3 the INR is 2.8. Instead of continuing with the 3rd loading dose, switch to maintenance dose of 2mg (⅓ of daily loading dose)

Warfarin and Dosage Adjustments

Initially increases in warfarin dose may result in small changes in INR, however with higher doses, small adjustments may lead to much bigger changes in INR (as the production of different coagulation factors are reduced). So if a patient is just outside of the range, *an adjustment of ½-1mg* may be all that is needed. Below are some general guidelines on dosage adjustment in over-anticoagulated patients:

Target INR range 2-3

INR	Action
3.0 - 3.2	decrease dose if consistently high by up to 10%
3.3 –3.9	decrease dose by up to 15%
4.0 – 4.5	miss 1 day and decrease dose by up to 20%
4.6 - 4.9	miss 2 days and decrease dose by up to 20%
5.0 – 5.5 no bleeding	miss 3 days and decrease dose by up to 20-25%
5.0 – 5.5 minor bleeding	miss 3 days and decrease dose by up to 20-25% Consider vitamin k* 1-2.5mg po using IV preparation orally
5.6 – 5.9 no bleeding	miss 4 days and decrease dose by up to 20-25%
5.6 – 5.9 minor bleeding	miss 4 days and decrease dose by up to 20-25% Consider vitamin k* 1-2.5mg po using IV preparation orally
6.0-8.0 no bleeding	Stop warfarin. Restart when INR<3 at a reduced dose of up to 25%
6.0-8.0 minor bleeding	stop warfarin. Consider vitamin K* 1-2.5mg po using the IV preparation orally. Restart warfarin when INR<3 at a reduced dose of up to 25%
>8.0	stop warfarin and see guidance below “management of INR >8”

Target INR range 3-4

INR	Action
4.0 – 4.5	Decrease dose by 20% if consistently high
4.6 - 4.9	miss 1 days and decrease dose by up to 20% if consistently high
5.0 – 5.5 no bleeding	miss 2 days and decrease dose by up to 20-25%
5.0 – 5.5 minor bleeding	miss 2 days and decrease dose by up to 20-25% Consider vitamin k* 1-2.5mg po using IV preparation orally
5.6 – 5.9 no bleeding	miss 3 days and decrease dose by up to 20-25%
5.6 – 5.9 minor bleeding	miss 3 days and decrease dose by up to 20-25% Consider vitamin k* 1-2.5mg po using IV preparation orally
6.0-8.0 no bleeding	Stop warfarin. Restart when INR<4 at a reduced dose of up to 25%
6.0-8.0 minor bleeding	stop warfarin. Consider vitamin K* 1-2.5mg po using the IV prep orally. Restart when INR<3 at a reduced dose of up to 25%
>8.0	stop warfarin and see guidance below “management of INR>8”

Management of INR>8

Stop warfarin till INR in therapeutic range.
Give vitamin K* 1-5mg orally (effective within 24 hours) using the IV preparation orally OR vitamin K* 1- 3mg by slow IV
Repeat dose of vitamin K if INR still too high after 24 hours.

See below for management if patient is bleeding

* Doses of vitamin K
When considering using Vitamin K always use lower dose in higher thrombotic risk groups and higher dose in lower thrombotic risk groups:

Higher thrombotic risk (consider lower dose vitamin k)	lower thrombotic risk group (consider higher dose vitamin k)
VTE within 3 months	VTE > 3 months previously
AF with CVA/TIA/embolism within 3 months or rheumatic mitral disease	Recurrent VTE on life-long warfarin with target INR 2-3
Non AF cardiac source embolism within 1 month	AF without high risk criteria
Mitral or aortic mechanical heart valve	
Recurrent VTE on life-long warfarin with target INR 3-4	
Antiphospholipid syndrome, Antithrombin deficiency	

Management of non-major bleeding

- Stop warfarin temporarily
- Consider giving vitamin K

Management of major bleeding

e.g. intracerebral haemorrhage or GI bleed requiring transfusion

- Stop warfarin
- Give vitamin K 5mg by slow IV injection over at least 30 seconds, usually by slow IV injection over 3-5 minutes
- Give prothrombin complex - contact Transfusion lab in pathology

In terms of anticoagulation reversal, **major bleeding** can be defined as limb or life-threatening bleeding with an INR> 1.3 that requires complete reversal as soon as possible (ie quicker than the onset of action of vitamin k which is 6 hours post dose).

Prothrombin complex will completely reverse warfarin-induced anticoagulation within 10 minutes but has a short half-life of approximately 6 hours therefore vitamin K must be used in conjunction for sustained reversal. Fresh frozen plasma produces suboptimal anticoagulation reversal and should only be used if prothrombin complex is not available.

If a patient is on warfarin and intracranial haemorrhage is suspected, give prothrombin complex urgently on clinical grounds without delay.

Reduction of anticoagulant effect

Planned Reduction

For elective surgery refer to Bridging Guidelines
Patients should be restarted on usual warfarin dose as soon as risk of surgical bleeding has resolved as per bridging guidelines.

Non-emergency surgery should be re-scheduled if the INR is too high
For further guidance on reduction of the effects of warfarin, please contact the on-call haematologist.

Emergency Reduction

Emergency anticoagulation reversal in patients with major bleeding should be managed with prothrombin complex and 5mg intravenous vitamin K. Contact Transfusion lab in pathology.

Emergency surgery for patients on warfarin

If surgery can be delayed for 6-12 hours, the INR can be corrected using intravenous vitamin K 1mg-3mg
Emergency surgery requiring reversal of warfarin within 1 hour

Give prothrombin complex - contact Transfusion lab in pathology
Give Vitamin K 5mg IV over at least 30 seconds, usually administered by slow IV injection over 3-5 minutes

Oral anticoagulation in-patient monitoring

Warfarin achieves its anticoagulant effect in approximately 72hrs, and when stopped, the effect declines over 24-48hrs. Alternate day monitoring is usually sufficient, as a change in dose is not likely to be reflected in the INR within 24hrs.

For stabilised in-patients, twice weekly monitoring may be sufficient, whilst more frequent monitoring will be required with changes in clinical status, changes to medication or until stabilised.

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Discharging patients on warfarin

See the Safer Warfarin Discharge document which explains the process for referral and discharging patients on warfarin

- INR must be checked within 4 days of hospital discharge for all patients
- Patients should not be discharged if INR >5

Patient must be told their warfarin dose on discharge
All warfarin tablets are labelled "take as directed according to INR" for discharge. Patients receive a box of 1mg and a box of 3mg packs of warfarin.
All patients must be told verbally their correct dose on discharge to avoid misunderstandings with the two strengths provided and the yellow dosage card (available on some wards) or yellow dosing book must be completed and given to patients at discharge.

All newly initiated patients must be given written and verbal information on their oral anticoagulant. A pharmacist should be contacted to counsel the patient at discharge if possible. The National Patient Safety Agency oral anticoagulation therapy pack including the "yellow book" should be given to all new patients prior to discharge and a healthcare professional should ensure that the patient understands all written information contained. The oral anticoagulation counselling checklist should be used to ensure that all essential points are covered.
Please prescribe dose of warfarin on discharge summary, ensuring it is clear that this dose is only until the next INR test after which the dose may change.

Click here for Counselling Checklist for Oral Anticoagulants Click here for warfarin SmPC

Guidance on completing anticoagulation referrals on Panda
Please ensure all relevant information is completed to ensure safe ongoing dosing and monitoring of your patients:

- The indication for anticoagulation
- Duration of anticoagulation
- Date of DVT / PE /Stroke
- Weight
- Last INR and dose
- INR range - if different from standard, please provide details on rationale
- Name of the referring consultant

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Important-warfarin management services differ across Sussex and other counties - please read the anticoagulation referral form carefully to ensure that all patients receive appropriate follow up on discharge from hospital.

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