

Warfarin Guidelines for Primary Care

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This guideline applies to patients who require warfarin as an anticoagulant. It aims to standardise anticoagulant management across Tees in line with national guidelines and alerts and in so doing minimise morbidity and mortality from thrombosis or haemorrhage.

This guideline should be read in conjunction with the British Committee for Standards in Haematology guidelines¹ on oral anticoagulation and National Patient Safety Agency (NPSA) Alert – ‘Actions that make anticoagulation safer’².

When making the decision to commence a patient on warfarin consideration must be given to the risks of both thrombosis and haemorrhage.

Exclusions

- Pregnancy
- Allergy to warfarin
- Patients with acute thrombosis and active cancer

Contra-indications to Warfarin Therapy

There are few absolute contra-indications, the decision to prescribe warfarin should be based on the balance of risk versus benefit for each individual and must be reviewed on a regular basis not less than annually.

The following contraindications should be considered:³

- Haemorrhagic stroke or intracranial haemorrhage
- Uncontrolled hypertension (> 180/100 mmHg)
- Thrombocytopenia (<100 or <80 x10⁹/L in high risk patients)
- Significant impaired renal or hepatic function
- Excess or erratic alcohol intake
- Clinically significant bleeding (e.g. GI bleeding, haematuria)
- Risk of clinically significant bleeding (e.g. within 72 hours of major surgery with risk of severe bleeding, within 48 hours postpartum, history of GI haemorrhage or haematuria in previous 6 months)
- Drugs where interactions may lead to a significantly increased risk of bleeding (refer to British National Formulary (BNF) current edition, e.g. regular use of NSAIDS)
- Poor compliance
- Dementia
- Pregnancy (*absolute contraindication in the first trimester-stop before 6th week of pregnancy. Risk of placental, foetal or neonatal haemorrhage in the last few weeks of pregnancy or at delivery*)

Caution:

- Recurrent falls and fits

Blood Tests Required Prior To Initiation of Warfarin ³

A coagulation screen, full blood count and liver and renal function tests should be performed. If abnormal, this may be a contraindication to initiation of anticoagulants or will require increased vigilance.

N.B. A coagulation screen includes a prothrombin time (PTT) and an activated partial thrombin time (APTT) (both reported as ratios - PTR and APTR) and should be used as a baseline non-specific screen. An INR is indicated for monitoring oral vitamin K antagonists and is not a replacement for a coagulation screen. The PTR and INR will not always be equivalent. It is advisable to request a coagulation screen prior to initiating warfarin as this has the advantage of screening for other causes of abnormal coagulation that may only prolong the APTT.

Documentation of Treatment Goals

When starting anticoagulants it is essential to document the goals clearly. The minimum information required is:

Indication for use

Target INR

Duration of treatment

Name of drug and current dose

PRESCRIBING WARFARIN

Patient and carer groups have informed the NPSA that warfarin regimens with the following characteristics would promote safer use²:

Use the least number of tablets each day

Use constant daily dosing and not alternate day dosing

Not require the use of half tablets – patients find it difficult to break tablets in half and instead, when necessary, would rather use 0.5mg tablets

Not all patients will need all strengths of tablets (start with 1mg tablets only)

Avoid prescribing the 0.5mg and 5mg tablet to the same patient. 5mg tablets should only be prescribed where the daily dose is 10mg or more.

Always express doses in **mg** and not as the number of tablets

Warfarin should be taken at the same time each day, preferably around 6 pm

Repeat prescriptions for warfarin should not include explicit dosage instructions – locally the dosing instruction ‘to be taken as directed at the same time each day’ has been promoted

Strength	Colour
0.5 mg	White
1 mg	Brown
3 mg	Blue
5 mg	Pink

Patient Information-key points for education of newly diagnosed patients ²

Alcohol - advise patients not to exceed national guidelines and importantly not to 'binge drink' whilst taking anticoagulants

Diet - Stress importance of eating a well-balanced diet and the importance of trying to take the same amount of foods rich in Vitamin K on a daily basis. It is the change in vitamin K intake that affects the INR result. Foods rich in vitamin K include, green leafy vegetables, coleslaw, chick peas, liver, egg yolks etc and to avoid cranberry juice

Patients should be asked to remind prescribers at each consultation that they are taking warfarin

Other prescribed medicines – advise the patient that additional blood tests may be necessary

Over the counter medicines: advise patient not to take aspirin unless it has been specifically prescribed by the GP and to be aware that some paracetamol 'plus' products contain aspirin. Some herbal remedies interact with warfarin. Advise patients to avoid NSAIDs and importantly to always tell the pharmacist that they are taking anticoagulants

What to do in the event of a missed dose

Symptoms of underdose/overdose and action to take if these occur

What to do if dental treatment/surgery is required

What to do if a surgical procedure is required/indicated

Patient hand-held record

Appropriate patient information must be provided- NPSA patient-held yellow booklet Oral Anticoagulant Therapy²: Important information for patients. GP practices delivering the anticoagulation service are responsible for the purchasing and supply of the yellow booklets and refill monitoring and dose books

The provision of this booklet must be recorded by read code using the following codes .9364 or XaMFK

Important - patients prescribed warfarin should use the hand held monitoring and dose record ('yellow book') and ensure that it is accessible to any health care professional. NPSA alert recommends that before dispensing, community pharmacists should be assured that the patient is being monitored regularly and the INR is at a safe level

Prescribing of Interacting Medicines

The NPSA recommends that prescribing and dispensing software should include functionality to enable details of the interacting medicines and the request for the patient to arrange additional INR tests to be recorded. This functionality should be utilised, if available, by all organisations involved in prescribing or dispensing of anticoagulants²

If possible, medicines should be selected that do not produce clinically significant interactions. If this is not possible, the prescriber who initiates or discontinues a prescription for an interacting medicine is responsible for ensuring that the patient is informed that an interacting medicine has been commenced or discontinued. They should also tell the patient to arrange an INR test within three to seven days¹ of the start or discontinuation of the interacting medicine. The patient should be instructed to provide details of the change in therapy when the blood sample is taken

Although not documented in the BNF the interaction of warfarin and tramadol can be very variable and in general the use of tramadol with warfarin is NOT recommended

Please refer to the BNF for information relating to medicines interacting with anticoagulants

Warfarin and Aspirin

If a patient is receiving aspirin, unless specifically indicated this should be stopped as warfarin is commenced. Use of antiplatelet agents and oral anticoagulants would normally be on the recommendation of a Hospital Consultant and will increase the bleeding risk. Recommendations from BCSH 2011¹:

Patients receiving an anti-platelet agent as primary prophylaxis for CVD or secondary prevention of stable CVD (GREATER THAN 12 MONTHS AFTER event), PVD or previous ischaemic stroke, on developing an indication for warfarin should stop their antiplatelet

Patients on a single antiplatelet following ACS (<12MONTHS) who require warfarin should continue aspirin therapy until 12 months post ACS

Patients on aspirin and clopidogrel following ACS or stent placement who develop an indication for warfarin should be carefully assessed for bleeding risk and discussed with their cardiologist with a view to introducing warfarin and minimizing the duration of triple therapy

When combined warfarin and single antiplatelet agent are indicated, consideration should be given to use of aspirin given the higher bleeding risk associated with clopidogrel

Discontinuation of Warfarin

Warfarin can be safely discontinued abruptly

INR TESTING

A recognised laboratory service must be used.

Any primary care healthcare provider wishing to use a near-patient INR testing device must ensure that the equipment is regularly checked using both an internal and external quality control.

All members of staff involved in using near patient testing methods should be trained in the use of the equipment and a training log kept.

Each time a patient has their INR tested, the clinician should audit and record the following information (this is not currently carried out by the District Nursing Service):

Has the patient experienced any signs of bleeding or bruising?

Has the patient followed their advised dosage instructions?

Has there been a change in the patient's other medications or dietary habits since their last test?

When the INR Test is carried out by the District Nursing service the test results are available on ICE or if near patient testing is performed the result should be phoned directly to the practice.

Point of Care Coagulometers ⁴

NICE has assessed 2 point-of care Coagulometers to help the NHS decide whether to use these products. They are called CoaguChek XS and InRatio2 PT/INR. Both Coagulometers are recommended for use by people taking long-term anti-blood clotting therapy who have atrial fibrillation or heart valve disease, if they prefer and are able to effectively use this type of monitoring. People (and their carers) who will be using 1 of these devices should be given training, and their doctor should regularly assess self-monitoring.

Call and recall procedures

A systematic call and recall system should be in place, and the GP practice should implement appropriate strategies to ensure non-attendees are targeted and monitored.

If a patient fails to attend a clinic, or is not at home (for a domiciliary visit), the GP practice should schedule a new appointment within one week – the timing of the next appointment should be by agreement, taking into account clinical criteria.

The patient should again be offered a further appointment unless there is information to suggest this is not necessary. The GP practice may decide that continuation of therapy in the absence of monitoring is a risk.

Maximum Recall Periods during MAINTENANCE Therapy⁵

One therapeutic INR	Recall in 4 weeks
Two therapeutic INR	Recall in 6 weeks (max.for prosthetic valve)
Three therapeutic INR	Recall in 8 weeks(apart from prosthetic valve)
Four Therapeutic INR	Recall in 10 weeks(apart from prosthetic valve)
Five therapeutic INR	Recall in 12 weeks(apart from prosthetic valve)

Training

Two BMJ e-learning modules, 'starting patients on anticoagulants' and 'maintaining patients on anticoagulants: how to do it' (www.learning.bmj.com) are available to support clinical staff involved in managing patients on anticoagulants

All healthcare providers, e.g. community hospital ward, general practice, community pharmacy should have in place, a written procedure (standard operating procedure) to support the specific activity and responsibilities of their staff in the anticoagulant care pathway. All relevant staff should be trained in this procedure. The following points may be included in GP practice procedure:

- Venepuncture and dose confirmation
- Housebound arrangements
- Obtaining laboratory results
- Dosing and determining recall
- Informing patient
- Practice documentation
- Safeguards and fail-safes

Use of Medipaks

Use of Medipaks for anticoagulants **should be minimised** as dosage changes using these systems are very difficult, however, oral anticoagulants may still be dispensed into a medipak on a weekly basis after appropriate assessment of risk providing that checks are made to confirm that the tablets in the compliance aid match the latest prescribed dose. The use of such a device will require excellent communication systems to be established between the prescriber and the dispensing community pharmacy.²

If a patient is receiving warfarin in a weekly MDS this information should be written into the yellow monitoring book together with contact details of the dispensing pharmacy. This information should also be added to the patient record on the practice computer system.

Provision of written confirmation of oral anticoagulant dosage for people in care homes, intermediate care, primary care hospitals and patients supported by care workers in their own home.

Verbal dose changes should always be confirmed in writing as soon as possible

A standard proforma has been developed to communicate information relating to warfarin dose changes between prescribers and care settings - a copy is included in Appendix 4. Practices are requested to use the standard proforma or its content on practice headed notepaper to enable all care settings to receive the information in the same format regardless of source

Written procedures used by prescribers should include a section relating to the provision of written confirmation of oral anticoagulant dosage for patients in care homes, intermediate care facilities and primary care hospitals and for patients supported by care workers in their own homes

Anticoagulation Initiation for Patients Suitable For Slow Induction in Primary Care ³

For patients who do not require rapid anticoagulation a low dose loading regimen is safe and achieves therapeutic anticoagulation in the majority of patients within 3-4 weeks (INR>2.0 average dose 3.5mg). This avoids overanticoagulation and bleeding associated with rapid loading

Low dose induction regimens do not require bridging with heparin and are suitable for patients with risk factors for thrombosis such as atrial fibrillation and more rarely LV aneurysm, peripheral vascular disease. They are NOT suitable for patients with an acute thrombosis requiring urgent anticoagulation as these regimens require the use of heparin

In complex cases, Primary Care Practitioners may wish to seek advice from the Haematology department; this will usually require a written referral through the normal channels

This initiation dosing regimen has been used by the Newcastle Hospitals with excellent audit data:

- Start on a Tuesday, Wednesday or Thursday
- Prescribe 1 mg tablets **only**

Starting dose:

Pre-treatment INR/PTR	< 60 years	> 60 years or < 60 years with significant co-morbidity
<= 1.3	2mg daily or 1mg if significant comorbidity	1mg daily
> 1.3	Reject and investigate	

- Monitor INR at weekly intervals

Subsequent weeks:

INR	Action
< / = 1.7	Increase dose by 1mg daily
> 1.7	Same dose

- Once INR is within therapeutic range, monitor and adjust doses according to usual protocol
- If at week 4, the INR is greater than 1.7 but less than 2.0 (i.e. not in target range) increase dose accordingly (see Appendix under Anticoagulation).

Management of Bleeding and OVER Anticoagulation-please see Appendix 2

All patients must be assessed on an individual basis taking into account the potential risk of haemorrhage versus risk of thrombosis. Consider reason for anticoagulation, comorbidity, concomitant use of antiplatelet agents, precipitating cause and whether temporary or permanent and whether there may be issues with compliance

Bleeding may occur when patients are NOT overcoagulated. For those patients who report signs of bleeding at therapeutic range it may still be necessary to reverse anticoagulation and investigate the possibility of an underlying cause

If the INR is out of therapeutic range consideration needs to be given to possible causes and whether these are temporary e.g. drugs, alcohol or permanent e.g. permanent change in other medication, liver disease. Dose reductions need to be considered depending on the most likely cause for a high INR especially if due to permanent reasons

The need for continued anticoagulation should be reviewed in any patient with a significant bleed and in those whose INR is difficult to control

If in doubt, please seek further advice from either the medical on-call team or Haematologist on call or consider admission.

Management of UNDER Anticoagulation-please see Appendix 3

Dose increases **should be used cautiously in all patients who are medically unstable or have significant comorbidity.** It is suggested that practitioners subtract 15% (i.e. 30% – 15% = 15%) from the dose change suggested and importantly consider every patient on an individual basis especially if taking interacting drugs

Consider whether heparin bridging is required if INR below therapeutic range, for high risk patients. Sub-therapeutic high risk patients include:

- DVT/PE patients within the acute phase of treatment (first 6 weeks)
- Mechanical valve prosthesis, particularly first generation valve .Prosthetic mitral valves.
- IVC filter in situ
- Recent arterial embolic event <6 weeks
- If previous life threatening PE
- High risk condition such as inherited natural anticoagulant deficiency (antithrombin, protein C or protein S) or antiphospholipid syndrome

Treatment dose LMWH should be used until INR back in therapeutic range on two consecutive days.

Important: A decision will need to be made on an individual basis and is the responsibility of the person monitoring anticoagulation. Advice may be needed from the appropriate speciality or Haematology.

Appendix 1- Target INR and Duration of Therapy ¹Individual patient characteristics, especially the presence of permanent risk factors, should be taken into account and may result in a longer period of anticoagulation being recommended. In patients with specific comorbidity, and therefore a higher risk of haemorrhage, the minimum duration of treatment is recommended.

Indication	Target INR	Minimum duration
DVT Calf – irrespective of risk factor	2.5	6 weeks (<i>If a diagnostic strategy that identifies isolated calf vein DVT is employed, treatment of such clots can be restricted to 6 weeks</i> ¹⁾)
Proximal DVT or PE – temporary risk factor	2.5	3 months
Proximal DVT or PE – idiopathic or permanent risk factor	2.5	At least 6 months
VTE associated with antiphospholipid syndrome	2.5	Lifelong or at least whilst active disease
Recurrent of VTE after cessation of warfarin	2.5	6months/lifelong dependent on risk factors
Proven recurrence of VTE while on warfarin in therapeutic range	3.5	Lifelong
Cancer with VTE	2.5 if required Therapeutic LMWH is superior to warfarin in treatment of acute VTE	Lifelong or whilst active disease
Atrial Fibrillation	2.5	Lifelong unless for cardioversion
Cardioversion	2.5	Should be in therapeutic range for at least 3 weeks before and 4 weeks after cardioversion
Mural thrombus	2.5	3 months
Mechanical mitral valve	3.0 or 3.5	Lifelong .Target INR depends upon the type of valve
Mechanical aortic valve	2.5 or 3.0	Lifelong .Target INR depends upon the type of valve.
Bioprosthetic (tissue) valve	2.5.if indicated	3-6 months, if required. Not indicated long term
Rheumatic heart disease	2.5	Indefinite
Peripheral arterial thrombosis and grafts`	2.5 Antiplatelet drugs remain 1st line therapy	Long term
Paroxysmal Nocturnal Haemoglobinuria	2.5 For large PNH clones (PNH granulocytes > 50%) and platelets >100. Consider for smaller clones and lower platelet counts dependent on other risk factors for thrombosis and bleeding	Long term(depending on platelet count)

Appendix 2 - Dose Recommendations for OVER Anticoagulation³

TARGET INR 2.5			
INR	Number of days warfarin to be omitted	Repeat INR	Suggested % dose reduction once warfarin restarted** (the dose should be rounded down to nearest 0.5mg: if alternate day dosing, start with lower dose)
3.1 – 3.5	0*	At 2 days unless clinically indicated e.g. minor bleeding or medically unstable then daily	15% - 25% if medically unstable or minor bleeding
3.6 – 4.0	0*	At 2 days unless clinically indicated e.g. minor bleeding or medically unstable then daily	20% - 35% if medically unstable or minor bleeding
4.1 – 5.0	1 day	At 2 days unless clinically indicated e.g. minor bleeding or medically unstable then daily	25% - 40% if medically unstable or minor bleeding
TARGET INR 3.0			
3.6 – 4.0	0*	At 2 days unless clinically indicated e.g. minor bleeding or medically unstable then daily	15% - 25% if medically unstable or minor bleeding
4.1 – 5.0	1 day	At 2 days unless clinically indicated e.g. minor bleeding or medically unstable	20% - 35% if medically unstable or minor bleeding
TARGET INR 3.5			
4.1 – 5.0	0; unless patient medically unstable when omit dose	At 2 days unless clinically indicated e.g. minor bleeding or medically unstable then daily	15% - 25% if medically unstable or minor bleeding
*If patient has significant comorbidity depending on clinical indication for anticoagulation considers omitting 1 day of warfarin e.g. Elderly with lone AF so risk of bleeding is likely to outweigh risk of thrombosis.			
** If the precipitating cause has been identified and removed/stopped (e.g. interacting drugs) up to 15% may be subtracted (i.e. 20% would be 5%)			

INR	Action
5.1-8.0 no bleeding	Stop warfarin ¹ Recheck INR daily – Restart warfarin when INR <5, consider 25% dose reduction
INR>8.0	Stop Warfarin ¹ Consider admission or proceed as follows: Give Vitamin K 2mg orally ¹ (using the iv preparation orally) Recheck INR daily (consider admission if INR cannot be rechecked on a daily basis) Try to identify precipitating cause ¹ If INR still >8 at 24 hours consider repeating dose of Vitamin K – when INR <5, restart warfarin if appropriate Consider 50% dose reduction when restarting
Major bleeding (irrespective of INR) Includes: Intracranial bleed•Retroperitoneal (CT or MRI) •Intra-ocular (NOT conjunctival) •Spontaneous muscle bleed with compartment syndrome •Pericardial •Active bleeding from any orifice plus either BP ≤ 90 mmHg systolic, oliguria or 2 g fall in haemoglobin	• stop Warfarin • ADMIT

Vitamin K Protocol

Konakion MM Paediatric™ (phytomenadione 10mg/ml) 0.2ml ampoules should be used to manage high INRs in the community as per the protocol below. This indication is off-license⁶. This product is licensed for several routes of administration this protocol refers to oral use.

How to administer Vitamin K (Konakion MM Paediatric™ 2mg in 0.2ml) orally:

Check expiry date of ampoule and ensure the product is in date before use

Break ampoule

Using the oral dispenser withdraw the solution to the appropriate mark (0.1ml = 1mg, 0.2ml = 2mg);

Hold dispenser in patient's mouth (at the back of the tongue) and press plunger;

Offer patient a glass of water as the solution has a very bitter taste.

Clinical governance

Ensure the expiry date of Konakion MM Paediatric™ is checked regularly as per practice protocol for checking expiry dates of drugs.

Appendix 3 - Dose Recommendations for UNDER Anticoagulation³

INR	Target INR	Increase dose by % (The dose should be rounded up to nearest 0.5mg –if alternate day dosing start with higher dose)
<1.0 – 1.2	2.5	30%
	3.0	35%
	3.5	40%
1.3 – 1.5	2.5	25%
	3.0	30%
	3.5	35%
1.6 – 1.9	2.5	20%
	3.0	25%
	3.5	30%
2.0 – 2.4	3.0	20%
	3.5	25%
2.5 – 2.9	3.5	20%

Repeat INR 2-3 days later (it will take at least 2 days for any change in dose to have full effect). Please note, if the INR is checked sooner i.e. the next day for any reason DO NOT INCREASE dose any further but wait for increased dose to take full effect

Appendix 4-Information from the Prescriber – Confirmation of Warfarin Dose Changes for Care Homes

Date	
Patient Name	
DOB	
Address	
Carers Details	
Carers Contact Details	

The INR result on (insert date) was recorded as ()

The service users target level is () for (indication)

The warfarin dose should now be (). This replaces the previous dose of ().

(If the previous dose stated is NOT what has been previously administered contact a GP immediately.)

This dose should be taken each day at the same time each day. (Usually at 6pm).

The date of the next INR blood test is ()

Please ensure that the pharmacy supplying your prescription has the details of the INR test prior to dispensing any prescriptions.

Please ensure the care plan is updated and a New MAR is generated with these new instructions attached.

Please ensure you have a copy 'NHS Oral anticoagulant Therapy –Important Information for patients (Yellow Book). If you are unsure of any contents of this guidance or have any concerns about the warfarin therapy for the above named patient please contact the surgery.

Yours Sincerely

Tear off and return

.....

Dear Doctor,

I confirm the dose to be given toismg

This replaces the previous dose ofmg.

Care managers Signature

_____Date:_____

Please post/fax or deliver confirmation of change to GP surgery.

References:

1. British Committee for Standards in Haematology. Guidelines on oral Anticoagulation (warfarin): Fourth edition - 2011. Available at URL: http://www.bcshguidelines.com/documents/warfarin_4th_ed.pdf
 2. National Patient Safety Agency Actions that make anticoagulation therapy safer: NPSA/2007/18
<http://www.nrls.npsa.nhs.uk/EasySiteWeb/getresource.axd?AssetID=60105&type=full&servicetype=Attachment>
 3. South Tees Hospitals NHS Foundation Trust Clinical Guideline document No: CG26 Initiation and Management of Warfarin in Adult Patients Version 2
 4. NICE Diagnostic Guidance (DG14) Atrial fibrillation and heart valve disease: self-monitoring coagulation status using point-of-care Coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor)
<http://www.nice.org.uk/guidance/dg14>
 5. National Enhanced Service Anticoagulation Monitoring
http://www.nhsemployers.org/SiteCollectionDocuments/nes_anti_coagulation_cd_13_0209.pdf
 - 6 Electronic medicines Compendium
<https://www.medicines.org.uk/emc/medicine/1699/SPC/Konakion+MM+Paediatric+2+mg+0.2+ml/>
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