Warfarin in Adults: Guidelines for the use of

Keywords: Oral Anticoagulation, Warfarin

Relevant to: Northumbria Healthcare NHS Foundation Trust

Criteria for use

These guidelines apply to all patients commenced or continuing on warfarin

Exclusions

See contra-indications to treatment (page 2)

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Introduction

Warfarin is an oral vitamin K antagonist used to anticoagulate patients who have venous thrombo-embolism or who are at risk from thrombo-embolic complications because of their disease. It lowers the vitamin K dependent blood clotting factors II, VII, IX and X as well as the vitamin K anticoagulant factors protein C and protein S. It takes 48-72 hours after commencing or changing dose to have an effect on the clotting system. Warfarin effect is measured by the INR (International Normalised Ratio) test. The major side effect is bleeding.

Presentation

WARFARIN TABLETS

500micrograms (white)
1mg (brown)
3mg (blue)
5mg (pink)

Contra-indications to warfarin

ABSOLUTE
- Haemorrhagic stroke
- Excessive alcohol intake with binge drinking
- Oesophageal varices
- Active GI bleeding / peptic ulcer
- Infective endocarditis

RELATIVE
- Pregnancy – warfarin should generally be avoided in pregnancy because of the risk of associated embryopathy, particularly between 6 to 12 weeks of gestation; whenever possible heparin should be substituted. There are occasional exceptions such as patients with mechanical heart valves.
- Increasing age
- Frailty
- Unresolved problem with patient concordance
- Recurrent falls
- History of GI bleeding
- Uncontrolled hypertension
- Liver disease
- Coagulation disorders
- Solid Tumour
**Indication and length of treatment of treatment**

The aim of treatment is to keep the INR in the desired range and prevent any untoward events from occurring. When a patient is to be commenced on warfarin or is admitted on warfarin the indication for warfarin, target INR and length of treatment should be documented in the medical notes. If the length of treatment is uncertain, a review date should be noted.

Current guidelines are outlined below:

<table>
<thead>
<tr>
<th>Indication</th>
<th>INR range (target)</th>
<th>Length of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calf vein thrombosis</td>
<td>2-3 (2.5)</td>
<td>6 weeks</td>
</tr>
<tr>
<td>VTE post surgery/ VTE provoked by non-surgical transient factors</td>
<td>2-3 (2.5)</td>
<td>3 months</td>
</tr>
<tr>
<td>Unprovoked Proximal DVT / PE</td>
<td>2-3 (2.5)</td>
<td>3 months¹</td>
</tr>
<tr>
<td>Recurrent VTE (while not on warfarin)</td>
<td>2-3 (2.5)</td>
<td>Longterm</td>
</tr>
<tr>
<td>Recurrent VTE (while on warfarin at therapeutic levels)</td>
<td>3-4 (3.5)</td>
<td>Longterm</td>
</tr>
<tr>
<td>Anti-phospholipid syndrome (APS)</td>
<td>2-3 (2.5)</td>
<td>Longterm</td>
</tr>
<tr>
<td>Atrial Fibrillation (AF)</td>
<td>2-3 (2.5)</td>
<td>Longterm</td>
</tr>
<tr>
<td>Mechanical Heart Valves</td>
<td>See table below²</td>
<td>Longterm</td>
</tr>
<tr>
<td>Bioprosthetic heart valve</td>
<td>2-3(2.5)</td>
<td>3 months⁴</td>
</tr>
</tbody>
</table>

**Note:**

¹ Patients with unprovoked proximal DVT or PE should be considered for long-term anticoagulation, taking into account information that may help predict risk of reoccurrence versus risk of bleeding in each individual patient.

² Patients undergoing elective cardioversion should be anticoagulated with warfarin for at least 3 weeks prior and 4 weeks post cardioversion with a target INR 2.5. However to minimize cancelled cardioversions due to low INRs a target INR of 3.0 should be set leading up to the procedure.

³ Recommended target INRs for Mechanical Heart Valves

<table>
<thead>
<tr>
<th>Prosthesis</th>
<th>Thrombogenicity</th>
<th>INR target No patient risk factors</th>
<th>INR target Patient Risk factors²²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>2.5</td>
<td>3.0</td>
<td>3.0</td>
</tr>
<tr>
<td>Medium</td>
<td>3.0</td>
<td>3.5</td>
<td>3.5</td>
</tr>
<tr>
<td>High</td>
<td>3.5</td>
<td>3.5</td>
<td>3.5</td>
</tr>
</tbody>
</table>

³Low – Carbomedics(aortic position), Medtronic Hall, St Jude Medical (without silzone)
Medium – Bjork-Shiley, other bileaflet valves;  
High: Starr Edwards, Omniscience, Lillehei-Kaster.

**Patient-related risk factors for thrombosis- Mitral, tricuspid or pulmonary position: previous 
arterial thromboembolism, AF, mitral stenosis, left ventricular ejection fraction <35%, left 
atrial dense spontaneous contrast.

4 patients with bioprosthetic valve and left atrial thrombus at surgery should receive warfarin 
until the clot has resolved. Patients with other prothrombotic risk factors e.g AF should 
receive longterm treatment.

Patients with cancer

Warfarin is generally inferior to therapeutic LMWH for treatment of VTE in patients with a 
solid tumour. Patients with cancer associated VTE should initially be treated for 6 months 
with therapeutic dose of Low Molecular Weight Heparin (LMWH) rather than warfarin.

Patients with cancer related VTE should be consulted with a Haematologist prior to initiation 
of oral anticoagulants.

Initiation of warfarin

The following blood results must be obtained before commencing warfarin. Any 
abnormality must be addressed and investigated appropriately.

- Full blood count (FBC)
- Liver Function tests (LFTs), including albumin
- Urea & electrolytes (U&Es)
- Coagulation screen

Warfarin should not be started if coagulation screen is abnormal until advice is obtained 
from a haematologist.

Ensure the patient is aware of and consents to being prescribed warfarin. They should be 
assessed to ensure the benefits of treatment outweigh the risks. Risks of anticoagulation 
include confusion, inability to understand instructions relating to medication and dose 
alteration, history of falls, excess alcohol consumption.

When initiating warfarin for the treatment of VTE the patient should be prescribed treatment 
dose of LMWH (tinzaparin) alongside warfarin for at least 5 days or until the INR is within 
the therapeutic range whichever is the longer. *(Refer to Trust protocol tinzaparin and 
unfractionated heparin in adults: Guidelines for the use of.)*
Loading dose regimes

Initiation of warfarin should be tailored to each individual requirement. Consideration must always be given to reducing the loading regime for patients with any of the following features:

1. Elderly
2. Low BMI
3. On medication known to potentiate warfarin
4. Previously treated with controlled INR on a low dose of warfarin (<2mg daily).
5. Known liver disease.
6. Known CCF with liver congestion.
7. Abnormal LFT’s and albumin
8. Abnormal clotting screen – contact haematologist.
9. Active cancer

Each patient should be assessed on an individual basis to determine the safest loading dose for initiation. If in doubt contact a member of the anticoagulant team.

Rapid loading regimen

This loading regimen is designed to safely initiate patients to be maintained with an INR range of between 2-3 and is intended for patients who require rapid anticoagulation e.g. VTE. For any other ranges contact a member of the anticoagulant team for initiation advice.

Go through each of the 4 points and score one for each that applies, from the score a loading regimen can be obtained.

1) **Age** – score 1 if patient is over 70

2) **Weight** – score 1 if patient is less than 50kg

3) **Interacting medication** – score 1 if on any of the following
   - Erythromycin, Clarithromycin, Azithromycin
   - Metronidazole, Ciprofloxacin, Doxycycline
   - -azole anti fungals, Co-trimoxazole
   - amiodarone, Prednisolone, fibrates

4) **Disease state** – score 1 if patient has any of the following
   - CCF, Liver disease, Low serum albumin, active cancer
<table>
<thead>
<tr>
<th>Score</th>
<th>0</th>
<th>1</th>
<th>2 or more</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Day 1</strong></td>
<td><strong>Day 2</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10mg</td>
<td>10mg</td>
<td>7 mg</td>
<td>5mg</td>
</tr>
<tr>
<td>7 mg</td>
<td></td>
<td>7 mg</td>
<td></td>
</tr>
<tr>
<td>5 mg</td>
<td></td>
<td>5 mg</td>
<td></td>
</tr>
<tr>
<td><strong>Day 3 INR</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.5 or below</td>
<td>1.6 - 2.1</td>
<td>2.2 - 2.5</td>
<td>2.6- 2.9</td>
</tr>
<tr>
<td>3.0 – 3.3</td>
<td>3.4 -3.5</td>
<td>3.6 – 4.0</td>
<td>&gt;4.0</td>
</tr>
<tr>
<td>10mg</td>
<td>5mg</td>
<td>4mg</td>
<td>3mg</td>
</tr>
<tr>
<td>3mg</td>
<td>2mg</td>
<td>1mg</td>
<td>500micrograms</td>
</tr>
<tr>
<td>500micrograms</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
</tr>
<tr>
<td><strong>Day 4 INR</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.2 or less</td>
<td>1.3 - 1.4</td>
<td>1.5 – 1.7</td>
<td>1.8 - 1.9</td>
</tr>
<tr>
<td>2.0 - 2.3</td>
<td>2.4 - 3.0</td>
<td>3.1 – 4.0</td>
<td>4.1 – 4.5</td>
</tr>
<tr>
<td>4.1 – 4.5</td>
<td>&gt; 4.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10mg</td>
<td>8mg</td>
<td>7mg</td>
<td>5mg</td>
</tr>
<tr>
<td>7mg</td>
<td>6mg</td>
<td>5mg</td>
<td>4mg</td>
</tr>
<tr>
<td>5mg</td>
<td>4mg</td>
<td>3mg</td>
<td>3mg</td>
</tr>
<tr>
<td>3mg</td>
<td>2mg</td>
<td>2mg</td>
<td>miss 1 day then 1mg</td>
</tr>
<tr>
<td>miss 1 day then 2mg</td>
<td>miss 2 days then 1mg</td>
<td>miss 1 day then 1mg</td>
<td>miss 1 day then 1mg</td>
</tr>
</tbody>
</table>

Day 4 INR approximates to the maintenance dose, therefore a day 5 INR is not warranted unless the patient is sub-therapeutic. Advise next INR test after 2-3 days on recommended dosage.

**Management of sub-therapeutic anticoagulation in the first month after acute VTE**

The risk of reoccurrence of VTE has been stated to be 40% within the first month if patients are not anti-coagulated. Sub-therapeutic INR carries the risk of reoccurrence thus bridging therapy with LMWH should be considered if the INR is <1.7 within the first month of an acute VTE.
Slow Loading regime for Atrial Fibrillation (AF)

Fast loading of warfarin carries a risk of over anticoagulation in the initial stages of therapy. Current guidelines now recommend that a slow loading regimen should be used to initiate patients on oral anticoaguants for the indication of AF.

Slow loading should be reserved for use in patients starting warfarin as an outpatient or where initiation occurs the day or day before discharge from hospital.

It should not be used in the in-patient setting without prior consultation with a member of the anticoagulant team to ensure correct procedure and patient education is carried out.

The vast majority of patients in the outpatient setting will be able to be slow loaded via this method, however under certain circumstances e.g. up and coming cardioversion then standard loading regimen described above can be used.

Slow loading should never be used for patients with a new diagnosis of VTE.

Initiating warfarin via a slow loading regimen should be as follows –

- **1mg daily for 7 days unless younger than 65 then 2mg daily**
- **Test INR on day 7**

Day 7 INR should coincide with the patient’s first visit to the anticoagulant clinic.

Refer to the Northern Network of Cardiac Care Guidelines for the Detection and Management of AF

Atrial Fibrillation guidelines

Patient information and education

All new patients should have an ‘Oral Anticoagulant Therapy – Important Information for patients’ pack given to them with their local anticoagulation clinic contact details. Information can be provided by a member of the medical, nursing, pharmacy or anticoagulant team. All new patients should be educated regarding their treatment at the time of initiation of therapy.

Patient commencing on warfarin should understand:

- The nature of the treatment
- The length of treatment
- The need for frequent monitoring of the INR
• The necessity to change dose when required by the INR result
• How to alter their tablets when the dose is changed
• The discipline required to take the tablets at the same time each day
• Risk of haemorrhage and the signs of excess bleeding
• The action required if they have any bleeding
• The need to refrain from binge drinking of alcohol
• The need to make no major changes in diet
• The need to inform medical and dental staff who are treating them in other clinics that they are on warfarin therapy
• The need to inform the anticoagulant clinic when starting on new medication including any over the counter remedies or discontinuing medication
• The need to refrain from taking aspirin and other NSAID treatments unless specifically prescribed by a doctor who is aware of their warfarin therapy
• Where and when their INR will be measured
• Contact details of the anticoagulant clinic

Combination warfarin and anti-platelet therapy

There may be some clinical indications where both anti-platelet and warfarin therapy is indicated. Such combinations are associated with an increased risk of bleeding. If combination therapy is to be used then each patient should be assessed to consider the thrombotic risk versus the bleeding risk. Based on this the following recommendations have been taken from the British Haematology Society Guidelines:

• Patients receiving an anti-platelet agent as primary prophylaxis for CVD who develop an indication for warfarin should stop their anti-platelet agent on obtaining therapeutic INR
• Patients with peripheral artery disease or previous ischaemic stroke on anti-platelet therapy should stop this agent if warfarin is commenced.
• Patients on anti-platelet therapy as secondary prophylaxis with stable IHD should stop their anti-platelet therapy whilst being treated with warfarin.
• Patients on a single anti-platelet agent <12 months following ACS, who require to start warfarin should continue anti-platelet therapy until 12 months post ACS, unless regarded as having a high bleeding risk.
• Patients on dual anti-platelet therapy post ACS or stent placement who develop an indication for warfarin need to be carefully assessed for bleeding risk with a view to introducing warfarin and minimizing duration of triple therapy.
• When a combination of warfarin and single anti-platelet therapy is indicated, aspirin should be considered primarily as higher bleeding rates have been associated with warfarin and clopidogrel rather compared with aspirin and warfarin.
Monitoring Anticoagulation and Adjusting Doses to Maintain Target INR

Inpatients

All patients admitted to hospital on warfarin should have an INR done on admission and/or before the first dose of warfarin is prescribed and administered.

Dose adjustment of warfarin is dependant on many factors and should be titrated to individual patients and circumstances similar to those discussed when loading a patient. INR is likely to be more unstable in inpatients and should be monitored closely, in particular when co-prescribing one or more clinically significant interacting medicines (see below for more information).

All patients should be referred to the anticoagulant service via an in-patient referral form on admission or at the time of initiation of treatment. The anticoagulant team will dose and monitor all patients who are referred to the service upon receipt of an in-patient referral form.

All in-patient INRs and doses should be recorded on the patients medication chart. Warfarin should also be prescribed on the patients medicine administration chart along with the patient’s indication and INR range.

Outpatients

The DAWN AC system is used for documenting results and treatment plans for all outpatients monitored by the anticoagulant service. The DAWNAC system is used to adjust doses of warfarin for some patients. Those patients whose doses cannot be adjusted or the anticoagulant staff would recommend a different dose than that recommended by DAWNAC should have their doses manually adjusted by a member of the anticoagulation service.

Where possible dosing recommendations should use the least number of tablets per day, aim for a constant daily dose, state dose in milligram, and avoid use of half tablets. Dosage recommendations along with patient’s INR and date of next test should always be documented in the patients yellow ‘Oral Anticoagulant Therapy booklet’. An electronic report for each patient including INR, dose and date of next test is sent to each patient’s GP following their clinic attendance.

Co-prescribing Clinically Significant Interacting Medicines

A large number of medicines interact with warfarin and prescribers need to be aware of their effects when co-prescribing. Information sources include the BNF, the Summary of Product Characteristics (SPC), Stockleys Drug Interactions, pharmacy and the anticoagulation service. The anticoagulant service has produced a comprehensive list of medications and their likely interaction with warfarin. This is available on trust intranet.
When selecting medicines known to have major interactions with warfarin, the reason for the choice and the advice given to the patient must be documented in their medical notes. The dose of warfarin may need to be adjusted and their INR will need to be rechecked sooner depending on the interacting medication.

It is the responsibility of the prescriber to identify potentially clinically significant interacting medicines and take appropriate action.

The anticoagulation team should be informed when new medicines are added or changed and can be contacted for advice.

**Referral to the Anticoagulation Service**

A referral form must be completed and forwarded to the anticoagulation service before they can take over monitoring and dosing of patients. Referral forms must clearly state reason for anticoagulation, target INR range and length of treatment. They should be signed and dated. Information about other medication and medical history should also be included on the referral form. Incomplete forms will be returned, which will lead to a delay in obtaining a clinic appointment. Referral forms are available on all wards and can be printed off from trust intranet.

**Discharge of Patients from Hospital**

All patients on warfarin should be given a discharge dose and date and time of next appointment before being discharge. This should be documented in patient yellow anticoagulant booklet as well informing the patient directly. It should also be ensured that all new patients are fully counselled before discharge from hospital. The anticoagulant service must be contacted and have received all the relevant documentation (referral form, copy of in-patient dosing chart, list of all discharge medication) before the patient is discharged.

**Failure to attend Anticoagulation Clinic Appointments**

First failure to attend for INR check will result in the generation of new appointment. The anticoagulation service will contact the GP or supervising consultant should their patient fail to attend anticoagulation clinic appointments on two or more occasions which may lead to the patient being discharged from the service.

**Stopping Warfarin therapy**

When a patient has finished their treatment period or it has been decided that they should not continue with oral anticoagulant therapy, treatment can be stopped abruptly. There is no need to gradually tail the dose off.

If treatment is stopped within the hospital setting, confirmation should be sent to the patient’s GP.

**Annual Clinical Review**
All patients prescribed warfarin should have an annual clinical review to assess for continued clinical appropriateness. It is the responsibility of the GP/supervising consultant to undertake this review.

**Reversal of Warfarin**

Refer to Trust Guidelines:
Warfarin Reversal

**Other oral anticoagulants where INR monitoring is indicated**

Warfarin is the oral anticoagulant of choice and should be used for all patients where one is indicated. However phenindione and acencoumarol are two alternatives which may be indicated for a small number of patients e.g. side effects or allergic reaction from warfarin. Use of these should be discussed with a Consultant Haematologist before prescribing and the anticoagulant team can advise on safe switch over with appropriate equivalent doses.

**Training**

All prescribers and staff involved with anticoagulants whether it is prescribing, dosing, administration or education must complete the relevant anticoagulant training package. Contact a member of the anticoagulant team for any training advice.

**References**

Anticoagulants: Actions that can make anticoagulant therapy safer. NPSA patient safety alert 18.
Northern Network of Cardiac Care Guidelines for the Detection and Management of Atrial Fibrillation (AF) - 2005