All Wales Medicines Strategy Group

Grŵp Strategaeth Meddyginiaethau Cymru Gyfan

Warfarin Monitoring

This resource has been retired (January 2025)

This resource has been retired and is no longer considered an AWMSG-endorsed resource.

The resource underwent an assessment for review in June 2024. At that time members of the All Wales Prescribing Advisory Group (AWPAG) considered it appropriate to retire the resource.

The content contained within the resource was considered to be out of date and, as suitable alternative guidance is available (e.g. AWMSG, SPS and NICE), AWPAG members considered it most appropriate for the resource to be retired at this time.

If you think this resource should be reconsidered for review, please get in touch with AWTTC by emailing AWTTC@wales.nhs.uk.

June 2012

This report has been prepared by the Welsh Analytical Prescribing Support Unit (WAPSU), part of the All Wales Therapeutics and Toxicology Centre (AWTTC), with support from the All Wales Prescribing Advisory Group (AWPAG), and has subsequently been endorsed by the All Wales Medicines Strategy Group (AWMSG).

This resource has now been retired and is no longer considered an AWMSG endorsed resource.

Please direct any queries to AWTTC:

All Wales Therapeutics and Toxicology Centre
University Hospital Llandough
Penlan Road
Llandough
Vale of Glamorgan
CF64 2XX

awttc@wales.nhs.uk
029 2071 6900

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1.0 BACKGROUND

Approximately 1.4% of the population are currently taking anticoagulation therapy at any one time. Following the publication of the National Institute for Health and Clinical Excellence (NICE) clinical guideline CG36, there is clear evidence that treating selected patients with warfarin reduces the risks associated with atrial fibrillation (AF) significantly, thus reducing mortality and morbidity (see Appendix 1)[3,4]. Approximately 60% of patients taking warfarin are being treated for stroke prevention associated with AF. Other common indications include treatment of venous and arterial thromboembolism, as well as prophylaxis after insertion of prosthetic heart valves.

Whilst warfarin is a very effective drug in these conditions, it is associated with significant adverse events, particularly haemorrhage. There is an increased risk of associated morbidity, mortality and hospital admissions. There is a 0.25% risk per annum of fatal haemorrhage, and a 4% chance per annum of significant haemorrhage. These risks increase with co-morbidities, age and international normalised ratios (INRs) over 3, and it is therefore essential to have safeguards in place to prevent harm[2,5]. Similarly, it is important for patients to understand the potential risks and benefits so that they may make an informed choice about management. The haemorrhagic side effects may be related to the INR level, which measures the delay in the clotting of the blood caused by the warfarin. While "normal" INR is 1, the specific range of INR values depends on the disease and the clinical conditions.

Warfarin has a narrow therapeutic index and a long half-life (40 hours), as well as significant interpatient variability; therefore regular INR blood monitoring tests are required to guide dosing.

Warfarin monitoring aims to stabilise the INR within set limits to help prevent serious side effects, while maximising effective treatment. As the INR increases above 3, there is an exponential rise in the risk of haemorrhage[6]. However, if the INR is sub-therapeutic, this is also potentially dangerous as there is an increased thrombotic risk, particularly in the first six weeks of treatment for thromboembolism and long-term in the population with prosthetic heart valves.

The Department of Health Care Closer to Home initiative, in the white paper "*Our health, our care, our say*"[7], also supports management of patients closer to home. Patient choice is important, and many patients prefer to be seen and managed locally to their home, supporting this initiative.

For these reasons, it is essential that personnel involved in dosing patients have a full understanding of the pharmacology of warfarin and potential complications, and that systems are robust in order to minimise risks.

2.0 RECOMMENDED CLARIFICATIONS AND CHANGES TO CURRENT SERVICE PROVISION

2.1 Initiation

- Anticoagulation may be initiated in primary care for AF using a slow-loading regime.
- Other indications, such as prosthetic heart valves and arterial and venous thromboembolism (VTE), are normally initiated and stabilised in secondary care
- Prior to commencing anticoagulation, a risk assessment should be undertaken and documented (see Appendix 2), in addition to baseline INR, clotting screen, full blood count, urea and electrolytes and liver function tests.
- Use a slow-loading regimen for patients who do not require rapid anticoagulation for AF. This is safe and achieves therapeutic anticoagulation within 3–4 weeks for the majority of patients. There are several evidence-based protocols; e.g., prescribe 3 mg warfarin daily for five days, then check INR on the fifth day.
- Practices should ensure that patients' records clearly indicate the location of monitoring. The following read-codes apply:
    - *Anticoagulation monitoring – secondary care {66QC}*
    - *Anticoagulation monitoring – primary care {66QD}*
    - *Self-monitoring of INR {66QE}*
- Avoid warfarin (use low molecular weight heparin [LMWH]) in patients with cancer-associated VTE.

  Patients with active malignancy have a significantly increased risk of bleeding with warfarin. In addition, patients with cancer-associated VTE are at high risk of recurrence, and LMWH has been shown to be more effective than warfarin for the first six months of treatment[8].

  The All Wales Medicines Strategy Group (AWMSG) have recommended that treatment doses of LMWH prescribed for VTE in cancer patients (i.e. patients undergoing cancer therapy or those who have metastatic disease) are suitable for shared care for up to six months of treatment[9].

  Cancer patients requiring anticoagulation for AF[10]: The All Wales Prescribing Advisory Group (AWPAG) Anticoagulation National Audit results suggest that 1–2% of practice populations are taking warfarin, and approximately 60% of these will be for AF. If patients subsequently develop cancer, their risk of thromboembolism and bleeding will change. Given the heterogonous nature of patients with cancer, their risks and benefits for continued anticoagulation should be assessed individually and reviewed periodically.

KEY POINTS

Prior to commencing anticoagulation, undertake and document risk assessment

Use a slow-loading regimen for patients who do not require rapid anticoagulation for AF

Avoid warfarin (use LMWH) in patients with cancer-associated VTE

2.2 Newly diagnosed patients

- Prescribers should have a documented discussion with the patient regarding the risks, benefits and implications of long-term warfarin treatment. Decision aids should be used where possible.; for example: http://www.npc.nhs.uk/therapeutics/cardio/atrial/resources/pda_af.pdf
- Consideration should be given to providing the patient with a warfarin information DVD; e.g. St George's "Living With Warfarin" (available at: http://www.sgul.ac.uk/media/productions-available/productions-available-pdfs/Living%20with%20Warfarin%20Order%20Form.pdf), when starting therapy, and periodically thereafter.

KEY POINTS

Consider providing a warfarin information DVD

Review the need for continuation of therapy regularly and complete annual risk assessment

Dosing practices should use computer dosing software

Review, report and benchmark the success of the practice in maintaining patients within the designated INR range

2.3 Review

- The need for continuation of therapy is reviewed regularly with an annual risk assessment. The following read-code applies:
  - *Annual risk assessment {66Q2}*
- There should be clearly defined commissioning arrangements for an annual medication review (see section 2.7: "Gold standard" annual medication review). This should normally be undertaken in primary care for all patients on the register, and for all levels of enhanced service.
- Dosing practices should use computer dosing software systems. The National Patient Safety Agency (NPSA) states that "*There is evidence that anticoagulant dosing software helps to maintain the INR levels within the therapeutic range, extend the time between INR tests and effectively manage anticoagulant records facilitating service audit*"[2]. Computer dosing has been shown to significantly reduce the risk of bleeding and thromboembolic events and, overall, is a more cost-effective option to manual dosing[11]. The management of non-attenders, recall facility, annual review and audit features, as well as serious incident review, are all important in ensuring delivery of a safe system to patients.

2.4 Quality control

- Level 4 practices (practice-funded phlebotomist or pharmacist, practice sample, practice test, practice dosing) must ensure that there are appropriate internal and external quality control records of near patient testing equipment, as advised by the manufacturer.
- Primary care services providing the National Enhanced Service (NES) for anticoagulation are expected to carry out a clinical audit of the care of patients against the service specification, including untoward incidents. This audit should also review, report and benchmark the success of the practice in maintaining its patients within the designated INR range as part of quality assurance. Suitable measures are under discussion; e.g., percentage time in range for patients established on warfarin for AF.

2.5 Target INR

Table 1. British Society for Haematology (BSH) recommendations[5,12]

Target INR	Condition	Note
2.5	DVT or PE	Includes those associated with antiphospholipid syndrome or for recurrence in patients no longer receiving warfarin)
	AF	
	Cardioversion	Target INR should be achieved at least three weeks before cardioversion and anticoagulation should continue for at least four weeks after the procedure (higher target values, such as an INR of 3, can be used for up to four weeks before the procedure to avoid cancellations due to low INR)
	Dilated cardiomyopathy	
	Mitral stenosis or regurgitation	Patients with either AF, a history of systemic embolism, a left atrial thrombus, or an enlarged left atrium
	Bioprosthetic heart valves in the mitral position (treat for three months), or in patients with a history of systemic embolism (treat for at least three months), or with a left atrial thrombus at surgery (treat until clot resolves), or with other risk factors (e.g. AF or a low ventricular ejection fraction)	
	Acute arterial embolism requiring embolectomy	Consider long-term treatment
	Myocardial infarction	Selected patients only (see BNF)
3.5	Recurrent DVT or PE in patients currently receiving anticoagulation and with an INR above 2	
Mechanical prosthetic heart valves	The recommended target INR depends on the type and location of the valve, and patient-related risk factors	Consider increasing the INR target or adding an antiplatelet drug, if an embolic event occurs whilst anticoagulated at the target INR

AF; atrial fibrillation: DVT: deep vein thrombosis; INR: international normalised ratio; PE: pulmonary embolism

2.6 Duration of therapy

Duration of treatment in patients with AF or prosthetic heart valves is life-long.

Following the publication of the 8th edition American Consensus of Chest Physicians (ACCP) guidance[13], the BSH recommended duration of anticoagulation treatment for VTE has changed (see Table 2).

Table 2. BSH recommended durations of anticoagulant treatment[5]

Condition	Recommended duration	Notes
Proximal DVT or PE with known precipitating factors (e.g. trauma, surgery or pregnancy)	At least three months	Should not need haematological referral to ascertain duration of treatment
Unprovoked proximal DVT or PE	Three months	Patients with unprovoked proximal DVT or PE should be considered for long-term anticoagulation, taking into account information that may help predict risk of recurrence and risk of bleeding in the individual patient. Patients with an unprovoked proximal VTE have an increased recurrence risk of > 10%. Long-term anticoagulation may be appropriate and these patients need specialist referral to discuss the benefits as well as the risks of bleeding, to enable an informed decision[14]. Such patients should be considered for referral to a haematologist.
Calf VTE with known precipitating factors	Six weeks	Should not need haematological referral to ascertain duration of treatment
Idiopathic calf VTE	Three months	Should not need haematological referral to ascertain duration of treatment
DVT: deep vein thrombosis; PE: pulmonary embolism; VTE: venous thromboembolism		

2.7 "Gold standard" annual medication review for patients taking warfarin

This is a consensus recommendation:
Patients prescribed warfarin long-term should be assessed at least annually and have documentation of a "gold standard" annual medication review to identify, document and appropriately action all potential medication-related problems.

KEY POINTS

Hold a face-to-face consultation to assess warfarin use

Complete warfarin risk assessment chart annually

A "gold standard" annual medication review is detailed

For a patient taking warfarin, three components are recommended (some aspects of the review, such as the warfarin risk assessment chart and patient education, may be undertaken by the team; it is the responsibility of the prescriber, normally the general practitioner, to ensure that any delegated components have been actioned):

1. Warfarin risk assessment chart completed annually, "read coded" and actioned.

2. Face-to-face consultation to assess warfarin use, including:
    - Patient's view and understanding of treatment.
    - Annual offer of information relating to warfarin therapy, e.g. St George's DVD, verbal explanation.
    - Clear documentation of indication/duration/target INR and that continued treatment is appropriate.
    - Compliance with monitoring and review of INR control over the preceding 12 months.
    - The patient is asked whether he/she has been advised to stop warfarin for two days or more in the last year. If the interruption in therapy was not due to an elective procedure this question supports the identification of previous high INRs and provides an opportunity to ensure that potential reasons were identified.
    - Note of warfarin-related hospital admissions, bleeding episodes or further thrombosis.

3. Review of all medications. Medication reviews will normally be a face-to-face consultation with a clinician. (Exclusions: the practice holds documentation demonstrating that the patient is under active review by a specialist for all significant repeat medication *and* medications are consistent with national guidance).

In a high quality medication review, the prescriber should demonstrate a systematic approach that questions all the repeat medications and results in demonstrable changes in treatment and/or disease management. The following outcomes should be documented[15]:

1. The patient's chronic condition disease control has been assessed and appropriate laboratory investigations undertaken.
2. Consideration has been given to current evidence and therapeutic advice such as AWMSG and NICE guidance. National indicators will have been addressed.
3. No repeat medications are considered "less suitable for prescribing" as defined by the British National Formulary (BNF) (or locally agreed list) unless documented discussion with the patient.
4. Adverse effects and future risks have been considered.
5. All potential interventions have been undertaken or discussion documented.

PRESCRIBERS ARE REMINDED TO REPEAT INR FIVE DAYS AFTER ANY CHANGES TO MEDICATION

2.8 Audit resources

- AWMSG anticoagulation audit (2008).
  Available at: http://www.wales.nhs.uk/sites3/page.cfm?orgId=371&pid=8341
- NPSA. Actions that can make anticoagulant therapy safer: Alert and other information (2007).
  Available at: http://www.nrls.npsa.nhs.uk/resources/?EntryId45=59814

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13 Kearon C, Kahn SR, Agnelli G et al. Antithrombotic therapy for venous thromboembolic disease. American College of Chest Physicians evidence-based clinical practice guidelines (8th edition). *Chest* 2008; 133 (6 suppl): 454S-545S.

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15 Lewis T. Using the NO TEARS tool for medication review. *BMJ* 2004; 329.

Appendix 1: WeMeReC bulletin: Atrial fibrillation excerpt

To help predict the risk of stroke and aid decisions regarding the most appropriate thromboprophylaxis, several scoring systems have been developed. These are based on different clinical trial cohorts to that used by NICE but produce broadly comparable results. The $CHADS_2$ risk tool (see Box 3) predicts higher rates of stroke in patients with higher scores.[2]

Box 3. $CHADS_2$ scoring system

	Risk factor	Score
C	Congestive HF/left-ventricular dysfunction	1
H	Hypertension	1
A	Age > 75	1
D	Diabetes	1
S	Stroke/TIA/thromboembolism	2

Refinements to these risk stratification schemes continue to be sought. One revised scoring system that is based on modified criteria (CHA_2DS_2-VASc, see Box 4) has shown some improvement in predictive value.[16] This system predicts low event rates in low-risk patients (score 0), but categorises fewer patients with intermediate risk (a score of 1) and more patients with high risk (a score ≥ 2).

Box 4. CHA_2DS_2-VASc scoring system

	Risk factor	Score
C	Congestive HF/left-ventricular dysfunction	1
H	Hypertension	1
A	Age ≥ 75	2
D	Diabetes	1
S	Stroke/TIA/thromboembolism	2
V	Vascular disease (prior myocardial infarction, peripheral artery disease, or aortic plaque)	1
A	Age 65 - 74	1
Sc	Sex category, i.e. female gender	1

When deciding whether long-term warfarin therapy is appropriate, the risk of stroke must be balanced against the risk of bleeding. Communicating these risks can be difficult and using visual aids to help patients understand numerical information can be useful.[17] A set of patient decision aids for atrial fibrillation are available at: www.npci.org.uk/therapeutics/cardio/atrial/resources/pda_af.pdf.

Appendix 2. Risk assessment guidance

This is based on the Aneurin Bevan health board guidance for patients starting anticoagulant therapy: Non-acute anticoagulation of patients with chronic AF [available at http://www.wales.nhs.uk/sitesplus/866/page/40623].

Patient name:
ID:
Date completed:

READ CODES
Initial risk assessment: 66Q1
Annual risk assessment: 66Q2

Before initiating or assessing a patient on anticoagulant therapy, it is essential that the following points are considered. It also provides a useful guide for assessing the appropriateness of continued treatment. These are intended as guidance only. The decision to anticoagulate or continue therapy is the responsibility of the prescribing clinician.

For patients with AF, validated tools (e.g. CHADS score) will help predict the risk of thrombotic stroke. The risk assessment below aims to highlight patients who may be at increased risk of bleeding and complications associated with warfarin use.

Question	Yes	No	Action/Date	Initials
Is the patient > 75 years?				
Does the patient have a history of uncontrolled hypertension (systolic > 180 and diastolic > 100 mmHg)?				
Is there any evidence of alcohol excess?				
Is there any evidence of liver disease? LFTs abnormal?				
FBC, U+Es abnormal?				
Is there any evidence of active bleeding lesions? (i.e. gastrointestinal blood loss, peptic ulcer disease or cerebral haemorrhage)			Contraindicated	
Has the patient any bleeding tendencies? (including coagulation defects and thrombocytopenia)			Discuss with Consultant Haematologist	
Is the patient taking antiplatelet drugs?				
Is there a commitment to use non-steroidal anti-inflammatory drugs and antibiotics?				
Is the patient being investigated for or receiving treatment for cancer? Active VTE + Cancer			LMWH not warfarin	
Is there any evidence of previous trips and falls?				
Is the patient literate?				
If the patient has been previously on anticoagulant therapy, is there any evidence of non-compliance or instability of INR control?			Add % time in range if available	
Is there any evidence of Alzheimers or other cognitive impairment?				
Other considerations, e.g. visual impairment				
Prior to initiation: Prothrombin time = secs Platelets = 10^9/l APTT result = secs INR =				