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NHS Cumbria Clinical Commissioning Group

WARFARIN MANAGEMENT GUIDELINES

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Warfarin Management Guidelines

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Acknowledgement
We would like to acknowledge the work done by Sheffield PCT in developing anticoagulation services and allowing us to use their work in producing this document.

1 Introduction

1.1 Anticoagulants have a narrow therapeutic margin and are safe only if monitored closely. In primary care anti-coagulants are one of the classes of drugs most commonly associated with fatal medication errors.

1.2 When anticoagulants are prescribed on a shared care basis, safe anticoagulant therapy relies on clear communication between the two.

1.3 This document sets out standardised and clinically effective guidelines for the care of patients receiving warfarin that minimises the risks associated with anticoagulation.

1.4 These guidelines should be used by those providers who have been commissioned by Cumbria CCG to provide a level 4 enhanced anticoagulation service.

1.5 The other two oral anticoagulants which require monitoring are nicoumalone (acenocoumarol) and phenindione. Both of these are rarely used, only if patients are allergic to warfarin or are particularly sensitive/resistant to warfarin.

1.6 There are newer oral anticoagulants on the market: currently dabigatran (Pradaxa®) which is a direct thrombin inhibitor and rivaroxaban (Xarelto®) and apixaban (Eliquis®) which are both direct factor X inhibitor. These three drugs are not covered in this guidance as they do not routinely anticoagulant monitoring.

2 National Guidance and Additional Resources

Guidance in this document is produced taking into account:

2.1 Antithrombotics: indications and management. SIGN 129 (August 2012), Edinburgh. Available at: http://www.sign.ac.uk/pdf/SIGN129.pdf

2.2 British Committee for Standards in Haematology. Guidelines on oral anticoagulation (warfarin): Fourth edition – (2011). Available at: http://www.bcshguidelines.com/documents/warfarin_4th_ed.pdf

2.3 Murray et al. INRs and point of care testing. BMJ 2003; 326: 5-6.

2.4 Gillaizeau F et al. Computerized advice on drug dosage to improve prescribing practice. Cochrane Database of Systematic Reviews (2013) Issue 11. Art. No.: CD002894. DOI: 10.1002/14651858.CD002894 (pub3)

2.5 Blann A D, Fitzmaurice D A, Lip GYH. Anticoagulation in hospitals and general practice. BMJ 2003; 326:153-156.

2.6 National Patient Safety Agency – Patient Safety Alert on actions that can make anticoagulant therapy safer, February 2007. Available here

2.7 Atrial fibrillation: the management of atrial fibrillation. NICE. 2014. Available at: http://www.nice.org.uk/guidance/CG180

3 Aim

To offer therapeutic warfarin management to patients in Cumbria who are receiving warfarin therapy, using near patient testing within the local community.

4 Objectives

The objectives are as follows:

- To provide standardised and clinically effective anticoagulation management to patients receiving warfarin therapy whilst minimising the risks associated with anticoagulation
- To identify patients receiving warfarin and offer transfer of care from hospital to primary care clinics for appropriate patients
- To initiate warfarin for suitable patients
- To produce optimum management of INR control
- To educate patients in understanding their treatment, in terms of their condition requiring warfarin, target range for INR, the effects of over and under anticoagulation, diet, lifestyle and drug interactions
- To appropriately manage patients who are over anticoagulated
- To maintain a register of all patients receiving warfarin and have a treatment plan for each patient that is reviewed on a regular basis
- To review the need for continuation of therapy at each visit
- To identify and manage appropriately patients with specific needs i.e. poor compliance, unstable INR control or frequent non-attendees
- To optimise care to patients receiving anticoagulant therapy in terms of accessibility, continuity and waiting times
- To ensure complete and accurate documentation of the clinic process

5 Responsibilities of Cumbria CCG

The role of Cumbria CCG is to ensure that services provided in primary care are in accordance with the service level agreement for the provision of level 4 anticoagulation services including the following;

- Ensuring the NPSA safety alert 18 (Actions that can make anticoagulant therapy safer) March 2007 is implemented in GP Practices
- Develop, update and review the Local Enhanced Service for Anticoagulation in Primary Care as necessary
- Developing Anticoagulation Therapy Guideline, training pack and template Standard Operating Procedures to support GP practices to provide anticoagulation services
- Ensuring anticoagulant guidelines are available for the management of under and over anticoagulation
- Ensuring regular clinical audit is undertaken in line with section 24 of this document
- Monitoring participation of sites in national laboratory quality assurance scheme and monitoring performance (Providers of Level 4 service)

6 Responsibilities of GP Practice

- Notify Cumbria CCG of the level of service agreement they are to provide
- Ensure Cumbria CCG Warfarin Management Guidelines are distributed and available
- To develop Practice Standard Operating Procedures or detailed policies, which are read and signed by all relevant staff and responsibilities of staff are clear and understood
- Ensuring appropriate training is undertaken by all staff involved in anticoagulation and evidence of this training is documented. All competencies must be satisfactory before undertaking the service
- Training on Computerised Decision Support Software (CDSS) is completed prior to implementation, if used
- The appropriate equipment for testing INR and vitamin K is available at the anticoagulation clinic/ GP surgery
- Training on Near Patient Test meters (NPT) must be undertaken before testing can commence
- Ensuring internal and external quality control for the equipment used in anticoagulation is undertaken and results submitted to Cumbria CCG
- Perform and record clinical audit
- Ensure a GP is available at all times when anticoagulation services are offered to patients by the practice
- Ensure reception staff are aware of the importance of patients attending within a specified period so that appointments are not unwittingly delayed without guidance from appropriate clinical staff.

7 Responsibilities of the Patient's GP

Overall responsibility for the care of the patients continues to reside with the registered GP who will be providing prescriptions for anticoagulation therapy, and includes:

- Ensuring that dose recommendations and recall are **guided** by approved written protocols (Appendix 1) or Computerised Decision Support Software (CDSS)
- Ensuring patients receive education regarding anticoagulant therapy (Appendix 2)
- Giving advice on duration and intensity of anticoagulation as guided by initiating clinician
- Being aware of the potential effects of additional therapy given to a patient on anticoagulants, and arranging earlier INR testing as required
- Acting promptly to patients with bleeding problems and/or INR > 8 or who are otherwise considered to be at risk of bleeding
- Dosing decisions should be made by health-care professionals (e.g. GP's, registered Nurses or registered Pharmacists) who have undergone an approved course for practitioners undertaking anticoagulant monitoring in primary care and who are deemed competent under the NPSA competency framework
- Arranging admission to hospital if required
- Issuing warfarin prescriptions
- Ensuring that all patients receive appropriate monitoring, either with primary care anticoagulation service or in secondary care
- To stop anticoagulant when specified duration is complete
- Assessed the patient's ability to take warfarin safely on initiation of therapy, in line with NICE guidance
- Ensuring that patients who do not speak, read or write English or who have communication difficulties (including without limitation hearing, oral or learning impairments) are provided with appropriate assistance. A responsible person or carer should be identified who can assist patient with any dose alterations

8 Responsibilities of Secondary Care

- Able to provide urgent medical advice relating to anticoagulation
- To accept patients who are maybe not suitable for anticoagulation monitoring in primary care (examples listed in section 9.4)
- Ensuring transferring of care from secondary to primary care is seamless in terms of patients anticoagulant therapy
- To provide INR testing from venous samples

9 Target population

9.1 Patients who are currently on warfarin therapy in the primary care.

9.2 Complex high risk patients can be considered for monitoring in secondary care include:

- A known hereditary or acquired bleeding disorder
- Patients with alcohol dependence due to instability in anticoagulation management
- Severe malnourishment due to absorption difficulties
- Mentally ill with no carer support in the community
- Dementia with no carer support in the community
- Liver failure
- Severe renal impairment
- Documented evidence of CNS haemorrhage
- Severe heart failure
- Uncontrolled severe hypertension
- Gastric-intestinal bleeding in the last 6 months
- Pregnancy
- Those on chemotherapy for malignant tumours
- Children under 16 years
- Homozygous protein C deficiency (risk of skin necrosis)

10 Secondary Care Referral process

10.1 A formal referral to primary care must be made from secondary care using the agreed transfer process. The guidelines for the appropriate referral and transfer of patients from secondary care to primary care is given in Appendix 3, and details of the documentation (Appendix 4) needs to be received and completed for:

- Existing warfarin patients who are currently monitored by secondary care
- New warfarin patients initiated by secondary care
- Existing warfarin patients who are currently monitored in primary care who are admitted to and then discharged from secondary care

10.2 Following written agreement from the primary care provider to take responsibility for anticoagulation of an individual patient, a clinic appointment in primary care must be made.

10.3 Patients unable to be seen in primary care before their next hospital-booked clinic appointment will remain with their current arrangement until an appointment can be booked with the GP surgery.

10.4 At the first patient consultation, appropriate anticoagulation documentation (see section 15) should be completed.

11 Actions for those patients excluded from primary care management

11.1 Patients who are not eligible for treatment under an approved primary care anticoagulation service will remain under their present anticoagulation care management system.

11.2 If patients fail to attend their secondary care monitoring appointments then secondary care will contact the patient's registered GP to discuss further. Consideration may need to be made as to the patient's suitability to continue with anticoagulant therapy.

12 Primary Care - Clinic Organisation

12.1 All patients will be seen in person either in a clinic, at a GP's surgery or at home by a Health Professional who has undergone training approved by Cumbria CCG as detailed in section 21.

12.2 Each individual GP practice will organise their own clinics. If there are only a few patients at one practice, monitoring and dosing may be organised at another GP practice.

12.3 It is recommended to test patients INR in the mornings to allow adequate time to obtain a venous sample and to organise treatment if required for patients with a high INR. (see Appendix 7 and 8).

12.4 Each practice will need to ensure adequate cover is arranged to cover illness and holidays by suitably trained personnel.

13 Call and Recall Procedures

13.1 A systematic call and recall system should be in place, and the provider should implement appropriate strategies to ensure non-attendees are identified and monitored.

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

13.3 If the patient again fails to attend, the patient should again be offered a further appointment unless there is information to suggest this is not necessary. The registered GP may decide that continuation of therapy in the absence of monitoring is considered too risky. The patient's registered GP will then be responsible for ensuring that no further prescriptions are raised.

14 Clinical Management

Individual Management Plan

14.1 The patients registered GP in conjunction with the patient should prepare an individual management plan. The plan should outline, as a minimum, the diagnosis, planned duration of treatment and therapeutic range to be achieved.

Clinical Procedures

14.2 All clinical information is recorded in the patient's own GP held lifelong record, including completion of the "significant problem" record indicating that the patient is on warfarin and the indication for anticoagulation. At initial diagnosis and on an annual basis, a comprehensive review of the patient's health needs to be undertaken to include the identification of potential complications. Additionally, regular review of the patient's own monitoring records should be undertaken.

Education of Newly Diagnosed Patients

14.3 All new patients prescribed warfarin must have a counselling checklist (Appendix 2) completed to ensure the patient has received all the appropriate information required. At the first appointment following transfer from secondary care, education should be reinforced (according to a Counselling Checklist - Appendix 2). The counselling should be comprehensive to ensure that patients are fully aware of their treatment and should include:

a. The name of the drug and current dose,
b. The reason they are taking the drug,
c. Therapeutic goal,
d. The anticipated length of treatment,
e. What to do in the event of a missed dose,
f. Symptoms of under/over anticoagulation and action to take if these occur,
g. Drug/drug and drug/food interactions,
h. Clinic arrangements and how to obtain further medicine supplies,
i. What to do if dental treatment/surgery is required,
j. What to do if a surgical procedure is required/indicated,
k. Who to contact regarding any worries or concerns relating to their anticoagulation management.

14.4 Check the patient has received a yellow Anticoagulant pack. This contains a yellow record booklet which they need to show to their GP/health practitioner whenever they seek medical or dental treatment or purchase medicines from a Pharmacy. Patients should be encouraged to carry their yellow credit card style information card with them at all times. It should be ensured that all newly diagnosed patients (and/or their carers and support staff when appropriate) receive appropriate management of, and prevention of, secondary complications of their condition, including the provision of a handheld anticoagulation booklet.

Supplies of the yellow warfarin booklet are available from Stationary Department, Contractor Distribution, LASCA Tel 01772 221308. Order by usual general stationary order form or via website (free of charge)

14.5 The patient needs to present their yellow booklet to the Pharmacist when collecting their prescription of anticoagulant. The patient may be given a print out of their results and new doses from the Computer Decision Support Software (CDSS). The patient needs to take their yellow booklet or the CDSS printout with them before the prescription can be

dispensed by the Pharmacy. Their prescription cannot be dispensed without proof their INR is being monitored and in the range (NPSA safety alert).

15 Documentation

Patient Register and Patient Records

15.1 The following records will be kept by the patients registered GP:

- Patient Name
- Patient Date of Birth
- NHS number
- Indication for treatment
- Length of treatment
- Target INR
- Named medical practitioner initiating treatment
- Discontinuation date
- INR results, dosage instructions and review dates
- Missed days (i.e. a record of days when the patient has not taken their anticoagulant therapy in accordance with dosing instructions)
- Concurrent medication
- Medical conditions, hospital admissions likely to affect anticoagulation such as an increased risk of haemorrhage
- Bleeding episodes
- Any actions taken, as well as dosing and retest dates e.g. education, advice, whether the INR result is from near patient testing or central lab testing
- Occasions when the patient failed to attend an agreed clinic appointment
- Contact details for patient or for carers responsible for the administration of warfarin

15.2 The patient's yellow warfarin booklet must be updated at each visit. If this booklet is not available, a temporary record booklet must be completed and given to the patient. A printout from CDSS is also acceptable, which must be kept with previous printouts to form the patient's hand-held records.

15.3 The front of the yellow warfarin booklet must be completed i.e. indication, INR target range and duration of treatment, person with clinical responsibility, and emergency contact number.

15.4 For new patients who need to be initiated on warfarin, a risk assessment needs to be completed and a counselling checklist needs to be completed (see Appendix 2). An example of a risk assessment tool can be found at http://www.awmsg.org/awmsgonline/medman_library.html under Advice on the role of oral anticoagulants.

Clinic Attendance

15.5 It is essential all warfarin patients keep their clinic appointments.

15.6 Non-attendees should be identified immediately. The patient should be given and informed of new appointment within one week (see section 13).

16 Warfarin Supply

16.1 Different people require different doses of warfarin. Some pre-existing conditions or genetic dispositions may make patients more or less sensitive to warfarin. Drugs, herbal remedies and diet also have the potential to interact dangerously with anticoagulants, and an indicative list of possible interactions is given at Appendix 5.The BNF is another useful guide.

16.2 Patients will be encouraged to take their warfarin daily and at a regular time, usually 6pm.

16.3 Warfarin will be supplied from the patient's registered GP via a prescription. Wherever possible the patient should not be provided with more than two strengths of warfarin. Tablets should be routinely supplied in 1mg and 3mg strengths to ensure a consistent approach across primary and secondary care and minimize the risk of confusion. In exceptional circumstances e.g. high warfarin sensitivity or high dosage requirements, warfarin may be prescribed in 0.5mg or 5mg strengths. In these instances the prescription must indicate the strength prescribed in both numbers and words ("half mg" or "five mg") to ensure that the correct tablet is given. The patient should be supplied with the least number of different strengths of tablets possible.

16.4 The table below shows the strength and colour of the different warfarin tablets available.

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

16.5 Specific dosing instructions will not normally appear on the dispensing label (must be include advice to follow written dose instructions). All dosing instructions will be given verbally as well as written in the patient's yellow warfarin booklet or on a computerised dosing sheet.

17 INR Testing

17.1 Each time that a patient attends to have their INR tested, the practitioner should obtain the following information:

- Has the patient experienced any signs of bleeding or bruising?
- Is the patient planning any dental or other surgery?
- 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?

17.2 If the practitioner undertaking the blood test is not giving the dosing instructions, then any relevant information obtained from the patient should be passed on to the relevant clinician to inform their dosing decision.

17.3 Those practices undertaking a level 4 anticoagulation service will be using their own testing equipment to obtain an INR result.

17.4 It is recommended to test patient's INR in the morning so if subsequent samples are needed, there is sufficient time to obtain results before the end of the day.

Near Patient Testing and High INR Results

17.5 If the INR result is greater than 4.5, then repeat the patients INR using a new finger stick test using near patient testing device (NPT e.g. CoaguChek XS plus®)

17.6 If the second result is within 0.5 of the original result then accept the result and proceed. If the second test is more than 0.5 different from the first then disregard the results. Send a venous sample to the central laboratory and perform Internal Quality Control on NPT device (see section 23).

17.7 The device will NOT record a specific measurement when an INR > 8.0. For any INR results above 8 repeat the test. If the second result confirms the first then send a venous sample to the central laboratory for testing. This is to obtain a specific INR measurement.

17.8 If a "test error" message is obtained, the NPT device will not provide a reading. Repeat the test and if a second "test error" message is obtained, a venous sample should be sent to the central laboratory for testing.

17.9 If a laboratory sample is required because of a high INR and there is no blood collection from the provider's base within 4 hours, arrangements for a venous sample need to be made depending on locality. Full patient contact details, including alternative telephone numbers, must be on the form in case of urgent need for out of hours providers to contact the patient.

17.10 If an unexpected result occurs (higher or lower than expected from the patient's past history e.g. difference of > 50% of previous result where there is no good reason found), repeat the INR test.

17.11 If the patient has significant anaemia or polycythaemia, this may lead to unreliable results and the device should not be used.

17.12 If INR > 4.5 **ACTION MUST BEEN TAKEN IMMEDIATELY**.
Follow Guidelines of Treatment of Over-Anticoagulation as in Appendix 7 and 8.

18 Dose adjustment of oral anticoagulants

18.1 The anticoagulant dose should be adjusted by the practitioner, with reference to the patient's INR and any other changes that may be identified during the appointment (see 17.1 above).

18.2 Dosage of oral anticoagulants should be **guided** by using Computerised Decision Support Software (CDSS) or by approved clinical guidelines (example is Appendix 1).

18.3 Dosing should not be increased by more than 20% weekly dose.

18.4 There is no maximum dose of warfarin but most patients require 2mg to 10mg per day. A small proportion of patients (5%) are warfarin resistant and so will need higher than expected doses (e.g., over 15mg per day). It is important to determine if this could be due to noncompliance or diet rather than the genetic cause.

Computerised Decision Support Software (CDSS):

18.5 The INR result should be inputted into the CDSS that uses a validated equation for calculation of the recommended dose and date for review.

18.6 The recommended dose and review date should be accepted or overridden depending on whether they are acceptable taking into account all patient factors.

18.7 The clinician can alter dosage and / or reset review dates if clinically appropriate.

Frequency of INR Monitoring

18.8 The length of time between INR test dates varies, the maximum recommended length of time allowed between INR tests is 12 weeks (BCSH Guidelines 1998).For those with mechanical heart valves, the maximum recommended length of time is 8 weeks. The length of time between INR tests will depend on the patient's INR measurement stability and untoward occurrences likely to cause instability. http://cks.nice.org.uk/anticoagulation-oral#!scenariorecommendation:34

18.9 There are shorter periods recommended between INR tests elsewhere in the world. In USA it is 4 weeks and in New Zealand it is 8 weeks.

Communicating Dose Changes

18.10 The provider will need to update the yellow warfarin booklet giving dosage instructions to include:

- details of dose,
- frequency,
- colour and number of tablets,

e.g., 7mg once a day (2 x 3mg – *blue tablets* and 1 x 1mg – *brown tablets*).
A printout of new doses from CDSS will be acceptable to give to the patient, but these need to be kept to form the patient's hand held records, in accordance with the NPSA alert.

18.11 Date of the next INR test and contact numbers for advice should be recorded.

18.12 If dosing decisions are not given to a patient in an appointment, then appropriate arrangements should be made to ensure that results, dosage instructions and the next review date are given to the patient.

18.13 If results are given over the phone, then practices should ensure that a named person is responsible for this. Verbal instructions should be followed up by a posted written instruction. Where practices identify patients for whom it is not appropriate to give results over the phone, then alternative arrangements should be made to ensure that information is received in a timely manner by the patient. Practices are strongly recommended to develop a protocol for this.

18.14 Particular care should be taken when communicating dose changes to patients in social care settings (e.g. nursing or residential care homes). The nurse in charge should be informed of the warfarin dose and next review date over the phone. This information should be confirmed in writing by fax or by post as appropriate. Practices are strongly recommended to develop a protocol for this.

18.15 Particular care should be taken when communicating dose changes to patients using Monitored Dosage Systems (e.g., NOMADs). Both the patient and the Pharmacist filling the monitored dosage system should be informed of the warfarin dose and next review date. The information will be confirmed in writing to the patient and the pharmacist.

It is recommended that a risk assessment is done on patients on MDSS and warfarin. It may not be the most appropriate method of helping with medicine compliance.

19 Initiating therapy

19.1 A GP may choose, or be asked, to initiate warfarin for suitable patients who require non-urgent anticoagulation e.g. in atrial fibrillation. Warfarin should be initiated according to the warfarin slow start guidelines (Appendix 6).

19.2 At the first appointment to initiate warfarin, it is essential that the provider must ensure that the patient is given all the relevant information and education verbally and in writing or via reliable website (e.g., http://www.patient.co.uk/medicine/warfarin-an-anticoagulant-marevan) – (see section 14.3 onwards). The provider should also complete the relevant sections of the yellow hand-held warfarin book and issue this to the patient.

20 Discontinuation

20.1 The maximum duration of overall treatment will be documented on the patient record and in the patient's yellow warfarin booklet.

20.2 Oral anticoagulants will be discontinued completely on a defined date as specified by the registered GP.

20.3 The patient or carer will be informed in clinic or domiciliary visit and followed up by letter to confirm this.

20.4 Consideration may need to be given to the early discontinuation of therapy in situations where the risks outweigh the benefits of continued treatment, e.g. patients not attending regular monitoring, those unable to follow the dosing regime. NOACs are an alternative although they still need to be taken regularly.

21 Training

21.1 Each GP surgery must ensure that **all** staff involved in providing **any** aspect of care under the scheme has the necessary training and skills to do so.

21.2 GPs who have previously provided an anticoagulation service similar to this enhanced service shall be deemed professionally qualified to do so. However, it is strongly recommended that GPs attend one or more days on an approved course to update their skills and knowledge as required.

21.3 Staff are required to complete the MHRA e-learning on anticoagulation.
http://www.mhra.gov.uk/ConferencesLearningCentre/LearningCentre/Medicineslearningmodules/Oralanticoagulants/index.htm
Evidence of undertaking the module and passing the assessment must be submitted to Cumbria CCG before dose adjustments can be made for warfarin (Appendix 11)

21.4 The key competencies that must be demonstrated are as follows:

- Obtaining adequate blood samples
- Determination of INR results
- Compliance with established clinical management protocol for action of INR results by use of computerised decision support software and/or approved clinical guidelines
- Understanding of range of problems likely to be encountered in interpreting INR results
- Giving dosage instructions
- Recognition of instances where it is necessary to seek further advice
- The giving of information and advice to patients

In addition, those using near patient testing equipment must be able to operate the analyser and determine / interpret INR and quality control results.

21.5 All external and in-house training undertaken by the GP surgery staff must be recorded and sent with the annual audit.

22 Reporting near misses, incidents and serious untoward incidents

22.1 It is a condition of participation in the service that providers will report all significant and serious untoward incidents to SIRMS (https://sirms.necsu.nhs.uk) which relate to anticoagulation.

22.2 Reports should be completed within the following timescales:

- Near misses and incidents – 72 hours
- Serious untoward incidents – 24 hours

23 Quality Assurance

General

23.1 Quality must be assured across all aspects of the service including INR testing, dosage advice, record keeping, documentation (patient and quality control records), patient education and patient satisfaction.

23.2 The GP surgery must complete all relevant documentation pertinent to providing the service and record any action taken which is outside the service protocol.

Internal Quality Control (IQC) of Near Patient Testing (NPT)

23.3 Those GP surgeries using near patient testing must perform internal quality control procedures as per the manufacturer's instructions. These are used to establish whether the particular technique is performing consistently over a period of time, to ensure day-to-day consistency. Many manufacturers of Near Patient Testing (NPT) monitors and test strips for INR determination have control materials or electronic devices available for the purpose of IQC.

Frequency of IQC tests

23.4 Performing IQC will vary from GP practice to GP practice depending on the level usage of the meter. As a minimum requirement for every GP practice, an IQC needs to be performed at the beginning of every month. However this may need to be more frequent if there are a large number of INR tests. If a new test strip box is started that has a different lot number from the previous batch, an IQC needs to be performed.

23.5 IQC tests are usually supplied in a box of four vials; each batch number has a different INR range.

23.6 IQC results should be within a range of 1.0 INR units (not the wider range quoted by the manufacturer) for one particular batch of test strips; i.e. within ±0.5 INR of the mean of the first 5 IQC results.

23.7 IQC results should be recorded with the batch number of IQC, and test strips and the identity of the operator.

23.8 If IQC is out of limits patient testing should be **suspended** with that device/test strip batch. The manufacturer should be contacted if there are concerns about the accuracy of the device.

23.9 All IQC results, together with the batch/lot number of test strips employed at each clinic/surgery should be recorded to create an audit trail.

External Quality Control (EQC) of Near Patient Test (NPT)

23.10 Those GP surgeries using near patient testing equipment will be required to join an External Quality Assurance Scheme (e.g., UK NEQAS). Further information is given at Appendix 9.

23.11 External Quality Control (EQC) is used to identify the degree of agreement between one centre's results and those obtained by other centres. External QA is available through the UK National External Quality Assessment Scheme (UK NEQAS) for blood coagulation and is essential in ensure the INR recordings from the meter are accurate and reliable.

Cleaning Procedure

23.12 The Near Patient Testing device should be cleaned and maintained as per the manufacturer's guidance.

Managing Clinical Performance of Computer Decision Software System (CDSS)

23.13 For INR star CDSS, please register for their point prevalence feedback service.
Point prevalence is a way of performing Internal Quality Control on the warfarin dosing. There is a feedback service which compares different practices results every quarter. This is the External Quality Control on the warfarin dosing recommendations given by the CDSS.
http://www.inrstar.co.uk/managing_clinical_performance/point_prevalence_feedback

24 Review of Care Pathway

24.1 It is strongly recommend that in each GP practice there is a nominated Anticoagulation Lead who understands the whole care pathway and reviews this periodically to identify potential problems. In particular, they should ensure:

- There is a system for identifying all INR tests, which includes patients seen on home visits (this must not rely only on the phlebotomist)
- There is a failsafe system which ensures all results are received and appropriately action taken
- The respective responsibilities of those in the pathway are clearly defined
- Patients are aware of how they will be informed of their INR result, dosing instructions and recall date
- Patients with specific needs are identified and appropriately managed, i.e. where the patient has no phone; there are communication problems; patients in social care settings; patients using Monitored Dosage Systems (e.g., NOMADs) etc.

24.2 Key areas of risk are:

- Communications with the hospital over results, because of delays in collecting samples and breakdown of the pathology messaging system
- Induction of new administrative staff to anticoagulation arrangements
- Communication with patients

25 Audit

25.1 All providers will participate in an annual audit that will be based on the safety indicators identified by the National Patient Safety Agency (NPSA) and the criteria listed in the Cumbria CCG Local Enhanced Service document. The audit results will inform what local actions are needed to improve the safe use of anticoagulants, and will also be used as part of the performance management process of Cumbria CCG.

25.2 An audit template will be issued at the financial year end to cover the financial year of the period of the service agreement.

Appendix 1 - Warfarin prescribing guidelines

1 General Guidance

1.1 These guidelines are to guide the prescribing of warfarin where no computer software is available or where advice is sought in conjunction with CDSS. The patient should also have received advice and written information on anticoagulant therapy, normally in the form of a yellow anticoagulant booklet**.** A risk assessment and counselling checklist should have been completed for each patient initiated on warfarin.

2 Background

2.1 The present indications for warfarin, together with the presently agreed degree of anticoagulation for that indication are shown in Table 1:

Table 1: Indication and target INR's

	Target (±0.5)
Treatment of venous thrombosis [DVT]	**2.5**
Treatment of pulmonary embolism [PE]	**2.5**
Atrial fibrillation	**2.5**
Valvular heart disease	**2.5**
Tissue heart valves	**2.5**
Transient ischaemic attacks	**2.5**
Myocardial infarction: prevention of venous thromboembolism	**2.5**
Recurrent deep vein thrombosis and pulmonary embolism	**3.5**
Intravascular stent	**2.5**
Mechanical prosthetic valves – all patients will be discharged from the cardio-thoracic unit with a recommended target INR range(see BSCH guidelines)	

3 Dosage Regimens

3.1 Individuals have different dosage requirements of warfarin. The response in individuals cannot be predicted. This is partly due to the patient's different metabolism of warfarin and partly due to other factors such as disease states and interacting drugs.

3.2 The average dose of warfarin required daily is around 5 mg [range 1 to 9mg] but may vary markedly because of several factors. Warfarin should be given once daily [5-6 pm is an ideal time] and is given as a tablet for oral administration.

4 Duration of therapy

4.1 After a single episode of venous thromboembolism, 3 or 6 months of warfarin therapy is necessary depending on the thrombus position. The duration of therapy needed after a second episode of DVT or PE is uncertain but long-term anticoagulation is normally advocated.

4.2 For patients with atrial fibrillation and heart valves, the duration is as long as the condition is present. In most cases this is long-term. Often it is a change in a patient's condition (e.g. becomes confuses) that requires the cessation of therapy.

5 Frequency of INR Monitoring

For patients in whom no new factor has arisen, the frequency of monitoring can be guided by the criteria shown in Table 2 or by the use of CDSS**.**

Table 2: Warfarin therapy: maximum recommended recall periods during maintenance therapy (not initiation)

One INR high	Recall in 7 to 14 days (stop treatment for 1 to 3 days) (maximum 1 week in prosthetic valve patients)
One INR low:	Recall in 7 to 14 days
One INR therapeutic:	Recall in 1 to 2 weeks
Two INRs therapeutic	Recall in 2 to 3 weeks
Three INRs therapeutic	Recall in 3 to 4 weeks
Four INRs therapeutic	Recall in 4 to 5 weeks
Five INRs therapeutic	Recall in 6 to 8 weeks (maximum of 8 weeks for prosthetic valve patients)
More than 5 INRs therapeutic	Recall period can be increased in a step-wise fashion to a maximum of 12 weeks between appointments if stable.

NB Patients seen after discharge from hospital with prosthetic valves may need more frequent INRs in the first few weeks.
(Based on data from Ryan et al [1989] British Medical Journal 299, 1207-1209)

6 Factors affecting Warfarin Dosing

6.1 When a condition known to cause alteration in the dose requirement of warfarin occurs (e.g. a potentially interacting drug), or the patient has an acute concurrent illness, frequency of monitoring should be increased and dose of warfarin may need to be changed.

6.2 The following conditions cause warfarin sensitivity [i.e., need for reduced dose]:

i. Liver dysfunction
ii. Heart failure
iii. Hyperthyroidism
iv. Some drugs (indicative list is provided in Appendix 5)
v. Acute pyrexial episode

6.3 Some conditions cause warfarin requirements to be increased [i.e. need for greater than normal dose]:

i. Hypothyroidism
ii. Vitamin K containing remedies, e.g. some herbal remedies and enteral feeds
iii. Some drugs (indicative list is provided in Appendix 5)

7 Warfarin Dose Adjustments

7.1 It is recommended that computer dosing decision software be used for dosing. If dosing is performed manually, and a dose adjustment is required, this should not normally be changed by more than 10% a week.

7.2 If INR is low, boosting ("one off") doses should be approximately 50% greater than the patient's regular maintenance dose e.g., if daily dose is 6mg, boosting dose should be 9mg. **Again, consideration should be given to patient's previous pattern of response.**

8 Suggested Dose Adjustments Regimens

8.1 Sub-therapeutic INR

Table 3: For lower therapeutic range (target INR 2.5):

	INR	Dose adjustment	Next Appointment
Slight	1.8 - 1.9	Increase dose if consistently low	2-4 weeks
Moderate	1.6 - 1.8	Increase dose	1-2 weeks
Significant	< 1.6	Consider boosting dose(s), and increase dose.	Within 1 week

If VTE patient and two or more INR results < 1.6 consider starting low molecular weight heparin (LMWH) until INR is within therapeutic range.

Table 4: For upper therapeutic range (target INR 3.5):

	INR	Dose adjustment	Next Appointment
Slight	2.8 - 2.9	Continue as before	2-3 weeks
Moderate	2.0 - 2.7	Consider boosting dose + increase dose	2-4 weeks
Severe	< 2.0	Consider boosting doses + increase dose†	1 week

If INR low due to reversible reason (e.g., missed warfarin), it may be reasonable to administer a stat dose, but not alter the maintenance dose.

†Patients' with prosthetic valves in the mitral position, or a history of previous systemic emboli may require heparin therapy until warfarin becomes effective.
†Those with recurrent VTE or Protein C/S deficiency and two or more INR results < 1.6 consider starting low molecular weight heparin (LMWH) until INR is within therapeutic range.

8.2 Over-anticoagulated

Table 5: For lower therapeutic range (target INR 2.5):

		Dose adjustment	Next Appointment
Slight	3.0 - 3.2	Decrease dose if consistently high	4-6 weeks
Moderate	3.4 - 3.9	Decrease dose	1-2 weeks
Significant	4.0 - 4.9	Omit dose for 1 day, decrease dose	max. 1 week
Severe	5.0 - 5.9	Omit doses for 2 days, decrease dose	max. 1 week
Very Severe	6.0 - 8.0	*Stop warfarin. Restart when INR <5.0 at reduced dose. Consider Vitamin K (see appendix 7&8)	Next day

Table 6: For upper therapeutic range (target INR 3.5):

	INR	Dose adjustment	Next Appointment
Slight	4.0 - 4.9	Decrease dose if consistently high	2-3 weeks
Moderate	5.0 - 5.9	Omit dose for 1day + reduce dose	1 week
Significant	6.0 - 6.9	Omit for 1-2 days and reduce dose	1 week
Severe	7.0 - 8.0	*Stop warfarin Restart when INR <5.0. Consider Vitamin K (see appendix 8&9)	Next day

Evidence of bleeding may require a change in this schedule, or referral to the responsible physician, at any INR. Consideration should be given to correction of the INR in 'high risk' patients whose risk of bleeding is higher (see below).

* Alert **physician** responsible for anticoagulant control.
If high INR occurs on a Friday or weekend it is the responsibility of the prescribing GP to ensure the next INR is done and that the results are acted on.

High risk patients: Age>70 years; hypertension; diabetes; renal failure; previous myocardial infarction, stroke or gastrointestinal bleed.

***Appendix 2* - Counselling Checklist**

Patient name:
Patient No.
Date of Birth:

Please initial and date to confirm counselling has taken place. Ensure that patient has been given the Oral Anticoagulant Therapy Information booklet, alert card and record book.

	Counselling point		Date	Initials
1.	What is an oral anticoagulant and mode of action	Refer to Anticoagulant Therapy Information booklet		
2.	How to take oral anticoagulants and strengths of tablets	Refer to Anticoagulant Therapy Information booklet.		
3.	Monitoring the INR	Refer to Anticoagulant Therapy Information booklet		
4.	Clinic arrangements	Give details of the clinic arrangements & contact details. Refer to front page of Anticoagulant Information booklet		
5.	Ordering repeat prescriptions	Give details of practice policy and that patient may be asked to provide details about current INR or present record book		
6.	Side effects and actions to take	Refer to Anticoagulant Therapy Information booklet		
7.	Signs of poor anticoagulant control and action to take	Give details of signs of over anticoagulation, e.g., bruising, bleeding and of under anticoagulation, e.g., thromboembolism		
8.	Information to others, e.g., pharmacist, dentist, podiatrist	Advice to inform all healthcare staff that they are taking warfarin		
9.	Surgery and dental treatment	Refer to Anticoagulant Therapy Information booklet.		
10	Other medicines	Refer to Anticoagulant Therapy Information booklet.		
11.	Diet	Refer to Anticoagulant Therapy Information booklet.		
12	Alcohol	Refer to Anticoagulant Therapy Information booklet.		
13	Pregnancy/periods	Refer to Anticoagulant Therapy Information booklet.		
14	Other illnesses	Advise on the effects of vomiting, diarrhoea, infections, etc. on absorption of warfarin or effect on INR		
15	Injections	Avoid intramuscular injections if possible		
16	Sports and leisure	Avoid activities or sports which may result in a serious fall or head injury		

***Appendix 3* - Policy for the Appropriate Transfer of Patients from Secondary Care Clinics to Primary Care Clinics**

1. Existing patients

1.1 The Anticoagulation Clinic in secondary care identifies suitable patients for transfer of care into primary care. The clinic faxes the transfer request form (Appendix 4) with the patient's details to the patients registered GP.

1.2 On receipt of the transfer request form, the GP surgery will arrange a first appointment for INR monitoring.

1.3 When the primary care monitoring appointment has been arranged, the patients GP signs the bottom of the transfer request form and faxes this back to the secondary care anticoagulation clinic. The GP takes responsibility for the monitoring arrangements of that patient **from the date that the transfer form is signed**. At this point the patient will be deemed to have been discharged from secondary care.

1.4 If there is a time delay between the secondary care clinic first sending the referral form and the patient being accepted by the GP practice and the patient has attended secondary care for further monitoring, updated documentation on latest dosing and INR results must be sent to the primary care provider.

2. New patients

2.1 The secondary care anticoagulation clinic will transfer all patients as section 1.1 -1.5 above.

2.2 The secondary care anticoagulation clinic may decide to request transfer in situations where the patient's INR is not stable, but where it would be beneficial for the patient to be monitored in primary care.

3 Existing Primary Care Anticoagulation patients - post discharge

3. Patients who were being managed by a primary care anticoagulation service prior to a hospital admission will be referred back to the primary care service post discharge.

3.2 The responsible professional in secondary care will fill in the Anticoagulation Transfer form (Appendix 4). This must be sent to the GP surgery.

3.3 An appointment must be made for the patient for their next INR check.

3.4 Prior to discharge, the patient must have details of their next INR check. However if the patient has left hospital before being given this, the ward staff will be responsible for contacting them about their next appointment.

3.5 Should discharge occur on a weekend, referral to the GP surgery will be made in line with 3.2 above. On Monday morning the GP surgery will arrange an appointment for the patient. If there is sufficient time before the appointment date, the ward will post out a copy of the referral form to the patient, otherwise the ward will contact the patient by phone to give them the appointment details.

Appendix 4* - *Transfer of Care Anticoagulation Referral Form

ANTICOAGULATION REFERRAL FORM

Referrals will not be accepted unless this form is fully completed and accompanied by the current warfarin prescription chart.

Patients Tel N^{o}: GP: GP Fax N^{o}: Referring: Consultant	Name: DoB : (Affix Patient Label Here) Hosp N^{o}: NHS N^{o}:

Name of current anticoagulant: warfarin ☐ other ☐ please specify……

Date anticoagulation started:

√	Tick as appropriate	Target	Duration	√	Tick as appropriate	Target	Duration
	Calf DVT	2.5	12 weeks		AF	2.5	Long term
	Proximal DVT	2.5	26 weeks		TIA	2.5	Long term
	Recurrent DVT	2.5	long term		CVA	2.5	Long term
	Recurrent DVT whilst On warfarin	3.5	long term		Cardiomyopathy/ Mural thrombus	2.5	Long term
	PE	2.5	26 weeks		Mitral/aortic valve Disease	2.5	Long term
	Recurrent PE	2.5	long term		Tissue prosthetic heart valve	2.5	12 weeks
	Recurrent PE whilst On warfarin	3.5	long term		Mechanical Prosthetic heart valve		Long term
	Prophylactic	2.5	long term		Other- please specify		
Please specify if post – op				**Yes/ No**			

Current dose of anticoagulant:

Date and result of last INR:

Significant medical or surgical problems

Is the patient on any anti-platelet drugs? ☐ Yes Specify…….. ☐No
If yes, are these to continue? ☐ Yes ☐ Stop when INR is in target range ☐ No

Other Medication:

Date Risk assessment completed
Date Counselling checklist completed
Next INR appt Made
Yellow book issued
Referring Persons Name and Signature

Signed :
Name: Date

Please sign and return to ……..to confirm receipt and ongoing management of patient

I accept transfer of care for this patient. Signature

Name: Date

Appendix 5 *- Warfarin Drug Interactions*

This guide is intended as a quick reference to highlight significant interactions between warfarin and commonly prescribed medicines or complimentary medicines. It is not intended to be exhaustive or give detailed information. Prescribers should refer to the SPC or the BNF for further information or contact NHS Cumbria Medicines Optimisation Team for advice.

Interacting Drug	Potential problem	Comment
Alcohol	Increases anticoagulant effect of warfarin	Fluctuations in prothrombin time in heavy drinkers or patients with liver disease.
Allopurinol	Increases anticoagulant effect of warfarin	Uncommon but unpredictable interaction – monitor INR more closely when allopurinol started.
Aminoglutethimide	Reduces anticoagulant effect of warfarin	Effect appears to be related to dose of aminoglutethimide. May need up to four times the dose of warfarin.
Amiodarone	Increases anticoagulant effect of warfarin	The onset of this interaction may be slow and may persist after amiodarone has been withdrawn.
Amitriptyline	Unpredictable increase or reduction in anticoagulant effect	Monitor INR closely. INR may be difficult to control in patients taking tricyclic antidepressants.
Anabolic Steroids (e.g. danazol, stanozolol)	Increases anticoagulant effect of warfarin	Interaction develops rapidly, possibly within 2 or 3 days.
Aspirin	Increases anticoagulant effect of warfarin	Avoid aspirin as an analgesic – use paracetamol as a safer alternative. Low dose aspirin 75mg daily appears not to interact to any clinically relevant extent but may increase the risk of bleeding due to antiplatelet effect.
Azathioprine	Reduces anticoagulant effect of warfarin	Warfarin dose may need to be increased when azathioprine started and reduced if azathioprine is stopped.
Barbiturates (e.g., phenobarbital)	Reduces anticoagulant effect of warfarin	May require 30-60% increase in warfarin dose. The reduction in anticoagulant effects begins within a week, reaching a maximum after about 3 weeks and may still be evident up to 6 weeks after stopping the barbiturate.
Bezafibrate	Increases anticoagulant effect of warfarin	Bleeding is likely if the anticoagulant dose is not reduced appropriately (between one-third to one-half and then adjusted as per INR).
Boldo	May increase anticoagulant effect of warfarin	Modest rise in INR seen in a patient taking Boldo and Fenugreek.
Carbamazepine	Reduces anticoagulant effect of warfarin	Dose of warfarin may need to be increased (up to double dose).

Interacting Drug	Potential problem	Comment
		Oxcarbazepine does not appear to interact.
Cefaclor	Increases anticoagulant effect of warfarin	Cefuroxime, cefalexin or cefradine are safer alternatives.
Celecoxib	Increases anticoagulant effect of warfarin	Rare cases of increased INR and bleeding reported.
Cimetidine	Increases anticoagulant effect of warfarin	Unpredictable but common interaction. Use ranitidine instead.
Ciprofloxacin	May increase the anticoagulant effect of warfarin	Rare and unpredictable interaction. Monitor INR. Use alternative antibiotic if possible.
Ciprofibrate	Increases anticoagulant effect of warfarin	Bleeding is likely if the anticoagulant dose is not reduced appropriately (between one-third to one-half and then adjusted as per INR).
Clarithromycin	Increases anticoagulant effect of warfarin	Marked increase in INR has been reported. If a macrolide is required, Azithromycin is a safer alternative.
Clopidogrel	Mild bleeding can occur even though INRs remain stable and within range	Increased risk of bleeding due to antiplatelet effect. Manufacturer advises avoid concomitant use.
Colestyramine	Reduces anticoagulant effect of warfarin by preventing the absorption of warfarin.	Separating the dosages as much as possible may minimise the effects of this interaction.
Coenzymne Q10	Reduces anticoagulant effect	Monitor INR. Avoid use of products containing coenzyme Q10.
Oral contraceptives	Reduces anticoagulant effect of warfarin	Generally avoided in thromboembolic disorders.
Co-proxamol	Increases anticoagulant effect of warfarin	Uncommon and unpredictable. Use Paracetamol as a safer alternative.
Corticosteroids	Variable response	Low to moderate doses can increase or decrease the anticoagulant effect of warfarin. High doses have been reported to increase the anticoagulant effects. Monitor INR.
Cranberry Juice	Increases anticoagulant effect of warfarin	Avoid use in patients taking warfarin.
Cytotoxics	Increases anticoagulant effect of warfarin reported with some cytotoxics	Refer patients on concurrent cytotoxic agents to secondary care for management of anticoagulation.
Danshen	Increases anticoagulant effect of warfarin	Advise patients not to use Danshen whilst taking warfarin.
Devil's Claw	Increases anticoagulant effect of warfarin	Bleeding disorders visible on the skin (purpura) have been reported.
Diclofenac	Cases of bleeding reported with	Unpredictable – monitor INR & adverse effects. Avoid if possible. Ibuprofen or

Interacting Drug	Potential problem	Comment
	concomitant use.	naproxen are less likely to interact with warfarin.
Diflunisal	Increases anticoagulant effect of warfarin	Unpredictable – monitor.
Dipyridamole	Mild bleeding sometimes occur even though INRs remain stable and within range.	Increased risk of bleeding due to antiplatelet effect.
Disulfiram	Increases anticoagulant effect of warfarin	Review concurrent use of warfarin in patients requiring disulfiram.
Dong quai (*Angelica sinensis)*	Reports of marked increases anticoagulant effect of warfarin	Advise patients not to use Dong quai whilst taking warfarin. Increased bleeding time & bruising.
Erythromycin	Increases anticoagulant effect of warfarin	Serious but unpredictable. The elderly are at greater risk. Monitor closely.
Esomeprazole		Monitor INR if adding or stopping esomeprazole.
Fenofibrate	Increases anticoagulant effect of warfarin	Bleeding is likely if the anticoagulant dose is not reduced appropriately (between one-third to one-half and then adjusted as per INR).
Feverfew	Altered bleeding time reported	Advise patients not to use Feverfew whilst taking warfarin. Monitor INR.
Fluconazole	Increases anticoagulant effect of warfarin	Monitor and reduce warfarin dose accordingly.
Flurbiprofen	Cases of bleeding reported with concomitant use.	Unpredictable – monitor INR & adverse effects. Avoid if possible.
Flutamide	Increases anticoagulant effect of warfarin	Monitor and reduce warfarin dose as necessary.
Garlic	Case reports of increased anticoagulant effect of warfarin	Advise patients NOT to take garlic supplements. Regular ingestion of foods containing garlic should not pose a problem.
Gemfibrozil	Increases anticoagulant effect of warfarin	Bleeding is likely if the anticoagulant dose is not reduced appropriately (between one-third to one-half and then adjusted as per INR).
Gingko Biloba	Isolated reports of increased risk of bleeding	Advise patients not to use Gingko Biloba whilst taking warfarin.
Ginseng	Reports of spontaneous bleeding in patients using ginseng without anticoagulants	Ginseng contains antiplatelet components, so avoid use in patients taking warfarin.
Grapefruit juice	Increases anticoagulant effect of warfarin	May cause a modest rise in INR.
Glucagon	Large doses (≥50mg over 2 days) increase	Reduce dose of warfarin & monitor INR closely. Smaller doses (total of 30mg)

Interacting Drug	Potential problem	Comment
	anticoagulant effect of warfarin	are reported not to interact.
Glucosamine	Reports of increases in INRs	Patients on warfarin are recommended not to take glucosamine.
Glucosamine / Chondroitin	Increased risk of bleeding	Chondroitin has anticoagulant activity and should be avoided in warfarin patients.
Griseofulvin	Reduces anticoagulant effect of warfarin	Unpredictable (effects some but not all patients) – monitor INR.
Indometacin	Indometacin inhibits platelet aggregation and so prolongs bleeding	Avoid NSAIDs in patients taking warfarin if possible. If concurrent use essential, monitor INR closely.
Influenza vaccine	Usually safe & uneventful, but small numbers of bleeding episodes reported	Evidence shows that influenza vaccination in those taking warfarin is normally safe & uneventful. Advise patient to report any unexplained bleeding.
Itraconazole	Case report of increased anticoagulant effect of warfarin	Monitor and reduce dose if necessary. Advise patients to report any unexplained bruising or bleeding.
Ketoconazole	Case reports of increased anticoagulant effect of warfarin	Monitor and reduce dose if necessary. Elderly at greater risk. Advise patients to report any unexplained bruising or bleeding.
Ketorolac (oral)	Serious risk of gastro-intestinal bleeding	Oral ketorolac is contra-indicated in patients taking warfarin.
Metronidazole	Increases anticoagulant effect of warfarin	If concurrent use cannot be avoided, reduce the warfarin dose by between one-third and one-half and monitor closely.
Miconazole	Increases anticoagulant effect of warfarin	Avoid - potentially serious interaction. Use nystatin instead.
Non-Steroidal Anti-inflammatory Drugs (NSAIDs)	NSAIDs irritate stomach lining and reduce platelet aggregation	Avoid where possible. If concomitant use cannot be avoided, monitor INR and adverse events. Ibuprofen or naproxen are less likely to interact with warfarin.
Omeprazole	Increases anticoagulant effect of warfarin	A small change in INR may be seen. Occasionally clinically significant interactions occur. Use lansoprazole as an alternative.
Papaya	Increases anticoagulant effect of warfarin	Avoid use in patients taking warfarin. Monitor INR.
Paracetamol	Increases anticoagulant effect of warfarin when large doses are used over a prolonged time	Intermittent use (<2.5g/week) unlikely to affect INR. A reduction in warfarin dose may be needed for regular paracetamol users.
Penicillins	Increases and decreases in the anticoagulant effect of	Uncommon and unpredictable effect. Close monitoring of INR recommended.

Interacting Drug	Potential problem	Comment
	warfarin have been seen	
Phenytoin	Can increase or reduce anticoagulant effect of warfarin	Monitor INR and adjust dose of warfarin accordingly.
Piroxicam	Increases anticoagulant effect of warfarin	Avoid NSAIDs in patients taking warfarin if possible. If concurrent use essential, monitor INR closely and reduce dose of warfarin if necessary. Ibuprofen or naproxen are less likely to interact with warfarin.
Rifampicin / Rifabutin	Markedly reduces anticoagulant effect of warfarin	Monitor closely. Reduces anticoagulant effect within 5-7 days. Warfarin dose may need to be double or trebled and reduced on stopping rifampicin or rifabutin.
Simvastatin	Generally small, clinically irrelevant increase in anticoagulant effects	Monitor initially or after dose increases of simvastatin.
St John's Wort	Moderate reduction in the anticoagulant effects of warfarin	CSM advises stopping St John's Wort and adjusting the dose of warfarin as necessary.
Sulindac	Increases anticoagulant effect of warfarin	Uncommon and unpredictable – monitor INR. Avoid NSAIDs where possible. Ibuprofen or naproxen less likely to interact.
Tamoxifen	Markedly increases anticoagulant effect of warfarin	Monitor and reduce warfarin dose as necessary – may need to reduce dose by half.
Thyroid hormones	Increases anticoagulant effect of warfarin	Monitor and adjust warfarin dose as necessary. Warfarin dose may need to be changed as thyroxine doses are altered.
Vitamin K	Anticoagulant effects of warfarin are reduced or abolished	Vitamin K may be present in enteral feeds, health foods, food supplements, some green vegetables, green tea. If patients are "warfarin resistant" consider this interaction.

References:

Stockley's Drug Interactions 10th Edn. (2013). Ed. Karen Baxter. Pharmaceutical Press, London.

British National Formulary 68, September 2014. British Medical Association and Royal Pharmaceutical Society of Great Britain. Pharmaceutical Press, London.

Ernst, E, Ewings P et al., Co-ingestion of herbal medicines and warfarin. British Journal of General Practice 2004; 50: 439-441

Drugs to watch with WARFARIN. NHSSB Prescribing Team, May 2004.

Interactions between complimentary medicines and conventional medicines. National Collaborative Medicines Management Services Team of East Birmingham PCT, October 2002.

Appendix 6 - Warfarin Slow Start Regimen

This warfarin induction regimen[1] should be used for both primary and secondary care initiation of warfarin for suitable patients (see indications and exclusions below).

Background

Patients not requiring rapid anticoagulation can be safely managed using a slow loading regimen which results in therapeutic anticoagulation within 3 to 4 weeks in the majority of patients[1] [2]. This appears to avoid over-anticoagulation and bleeding associated with rapid loading. There is no need to cover with heparin as no procoagulant state occurs when slow loading the patient.

This regimen allows for induction of anticoagulation therapy requiring only weekly monitoring.

Indications: For use in patients for whom immediate anticoagulation is **not** required.
These include:

- chronic or paroxysmal atrial fibrillation;
- selected patients with left ventricular thrombus;
- selected patients with mitral stenosis;
- stroke outpatients in sustained AF who have waited 14 days following the acute event with a CT head scan that has excluded haemorrhage;
- selected patients with pulmonary hypertension.

Exclusion Criteria: Patients requiring immediate anticoagulation.
These include:

- deep vein thrombosis and / or pulmonary embolus;
- mechanical prosthetic cardiac valve insertion;
- arterial embolus;
- selected patients with atrial fibrillation, left ventricular thrombus, mitral stenosis;
- pulmonary hypertension associated with venous thromboembolic disease.

Regimen:

1. Ensure the patient has no contraindications to warfarin and confirm with a senior member of the medical team that the slow start regimen is appropriate. Generally if a patient is taking aspirin, this should be continued until the INR is therapeutic then STOPPED.
2. Ensure baseline bloods (FBC, U&E, LFT, coagulation screen) are satisfactory.
3. Explain to the patient the indication for warfarin treatment and the risks and benefits of it. Complete risk assessment and counselling checklist.
4. **Prescribe 2mg of warfarin daily at 6pm for 1 week.**
5. Reduce dose to 1mg if patient has concurrent illness or medication which will increase warfarin's effectiveness.
6. Repeat INR after a further 7 days of warfarin therapy.
7. Adjust dose as per nomogram or using CDSS.

References

1. Oates A. Jackson P.R. Austin C.A. Channer K.S. A new regimen for starting warfarin anticoagulation in out-patients. *British Journal of Clinical Pharmacology* 1998 46 157-61
2. Guidelines on oral anticoagulation (warfarin): fourth edition- 2011 *British Committee for Standards in Haematology* http://www.bcshguidelines.com/documents/warfarin_4th_ed.pdf

NOMOGRAM FOR WARFARIN SLOW START REGIMEN

Day 1

Baseline INR < 2 .0
Start 2mg warfarin/day at 6pm
Repeat INR in 7 days

Day 8

INR <2

Continue present dose warfarin.
Repeat INR in 7 days.

INR >2

Warfarin sensitive.
Action depends on level of INR

Day 15

Check INR
Adjust dose according to table below.
Predicted maintenance dosage of warfarin based on the sex of the patient and the INR after 2 weeks of warfarin 2mg/day

Male		Female	
INR at week 2	**Maintenance dose**	**INR at week 2**	**Maintenance dose**
1.0	6mg/day	1.0-1.1	5mg/day
1.1-1.2	5mg/day	1.2-1.3	4mg/day
1.3-1.5	4mg/day	1.4-1.9	3mg/day
1.6-2.1	3mg/day	2.0-3.0	2mg/day
2.2-3.0	2mg/day	>3.0	1mg/day
>3.0	1mg/day		

If INR >4.0 omit warfarin for 2 days and reduce daily dose by 1mg

Day 21

Recheck INR after a further week and adjust dose as below

INR <2

Increase daily Warfarin dose by 1mg.
Repeat INR in 7 days.
Continue in this fashion until INR >2.0

INR 2-3

Continue present dose warfarin.
Repeat INR in 7 days.
Fine tune warfarin dose if INR fluctuates.

INR >3

Fine tune warfarin dose/ omit doses if necessary.

Appendix 7 *- Guidelines for the Management of Over-anticoagulation*

Major Bleeding	
All patients	Treat as a medical emergency and admit to hospital

INR > 8.0 with no bleeding manifestation	
All patients	If using near patient testing, send a venous sample to the central laboratory for testing to obtain INR estimation. Omit warfarin Give oral Vitamin K 1 to 5mg (Konakion MM Paediatric™ 2mg in 0.2ml) Repeat INR test following day. *If this falls on a weekend or bank holiday it is the responsibility of the prescribing GP to ensure the test is done and the results acted upon.* Restart Warfarin when INR <5.0 Reduce maintenance dose and investigate cause of high INR

INR 4.5 – 7.9 (with no bleeding or minor bleeding, e.g. epistaxis)	
High risk patients	Omit warfarin Consider oral Vitamin K 1mg (Konakion MM Paediatric™ 2mg in 0.2ml) Repeat INR test following day. Restart Warfarin when INR <5.0 Reduce maintenance dose and investigate cause of high INR
Low risk patients	Omit warfarin Restart warfarin when INR <5.0 Reduce maintenance dose and investigate cause of high INR
1 High risk: age > 75 years; diabetes; renal failure; stroke; previous gastro-intestinal haemorrhage. The GP will use his or her own judgement in managing the risk for an older person living alone.	

References

1. Guidelines on oral anticoagulation (warfarin): fourth edition- 2011 *British Committee for Standards in Haematology* http://www.bcshguidelines.com/documents/warfarin_4th_ed.pdf
2. http://www.sign.ac.uk/guidelines/fulltext/36/section13.html

Vitamin K Administration

Konakion MM Paediatric™ (phytomenadione 2mg in 0.2ml) 0.2ml ampoules should be used to manage high INRs in the community. Although this product is licensed for several routes of administration this protocol refers to oral use, which is off licence.

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

(1mg = 0.1ml or 2mg = 0.2ml);

- 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

How to obtain Konakion MM Paediatric®

All practices providing an anticoagulation enhanced service must purchase this product on initiation of the service.

Your local community pharmacist can supply this on receipt of a signed order.

When two ampoules remain or the product is out of date stock should be re-ordered.

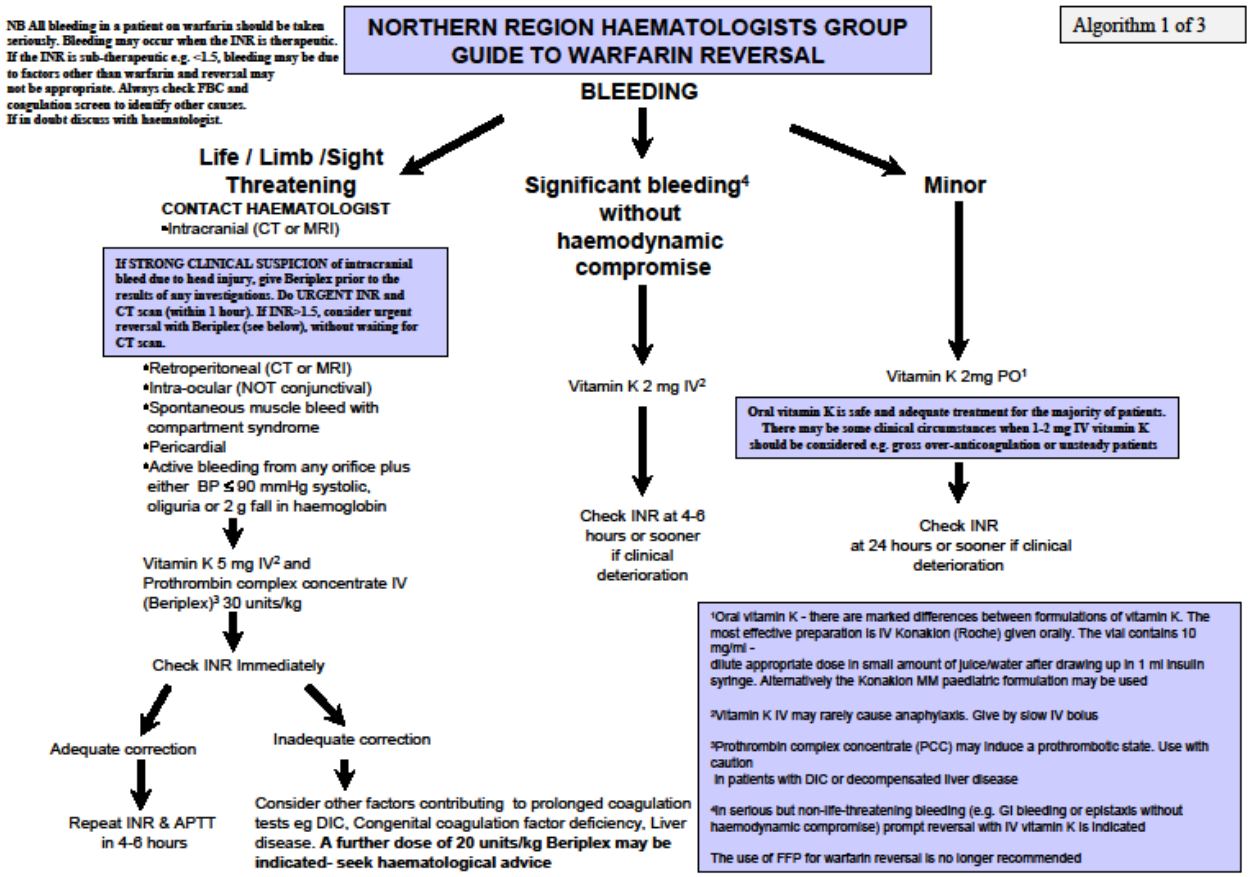
Clinical governance

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

Any near misses or adverse incidents should be recorded.

Using this guidance to administer Vitamin K to manage a high INR should trigger the practitioner to consider whether a Significant Event Analysis needs to be undertaken.

Appendix 8 - Northern Region of Haematologist Group Guide to Warfarin Reversal



Appendix 9 - National External Quality Assessment Scheme (NEQAS)

Cumbria CCG requires all providers to join an external quality assurance scheme, to identify the degree of agreement between one centre's results and those obtained by others.

Registration

To participate in the NEQAS scheme a registration form should be completed and returned to NHS Cumbria's anticoagulation contact. The practice should complete the practice details on the left hand side of the form, and the analyser information further down the page. Please leave the payment details blank to be completed by NHS Cumbria for the first year.

Surveys

Participating centres will be sent four surveys per year each comprising two samples for INR determination. In the case of UK NEQAS, this will be lyophilised human plasma that has been screened for hepatitis B surface antigen; for antibodies to hepatitis C virus and human immunodeficiency virus types 1 and 2.

Participants will be provided with instructions on reconstitution and testing of the samples. Results will be analysed and individual reports sent to participants approximately one week after the closing date for each survey.

Results

Results and associated data from participants will be treated with strict confidentiality. Each registered participant will be given a unique participation number, which should be quoted in all correspondence.

Performance analysis

Approval has been given for performance 'out with consensus' to be defined as a result greater than a 15% deviation.

Contact Details

UK National External Quality Assessment Scheme for Blood Coagulation
3rd Floor, Pegasus House
463A Glossop Road
Sheffield
S10 2QD

Tel: 0114 267 3300
Email: neqas@coageqa.org
URL: http://www.ukneqasbc.org

***Appendix 10* - Example of Training Log Required for Annual Audit**

Name and designation of person in charge of anticoagulation management clinic:

……

Location of anticoagulation management clinic:
……

Name of others involved in anticoagulation management clinic:

GPs:	Practice Nurses:	Other (state designation):

TRAINING

Please give names and dates of training and education relevant to the anticoagulation management service received by practitioners and staff:

	GPs:	Practice Nurses:	Other:
Clinical			
MHRA E learning Module			
Others			
Non-Clinical			
CDSS Training			

	GPs:	Practice Nurses:	Other:
Clinical			
NPT Device Training			

Please give details of any prior knowledge and experience:

……

……

……

Appendix 11* - *Training courses

Mandatory Training

The BMJ e-learning modules which were mandatory in previous versions of this guidance are no longer freely available to NHS staff.
The MHRA have produced an e-learning module for anticoagulation, which includes warfarin and the NOACs (New Oral Anticoagulants).
https://www.gov.uk/government/publications/e-learning-modules-medicines-and-medical-devices/e-learning-modules-medicines-and-medical-devices
Please sign up for MHRA Learning Management System:

Clientele – from drop down menu choose MHRA
Click Learner Log In and then Register Here.
Once registration is completed, search for the Oral Anticoagulants module.
Complete e-learning module and pass the associated assessment.

Evidence of undertaking the module and passing the assessment must be submitted to Cumbria CCG before dose adjustments can be made for warfarin patients

In house Training
Currently under development aimed for Nurses and other health care workers who will be dealing with patients receiving anticoagulation.

eLearning Modules -
http://www.mhra.gov.uk/ConferencesLearningCentre/LearningCentre/Medicineslearningmodules/Oralanticoagulants/index.htm
MHRA eLearning module on anticoagulation.

Birmingham University
http://www.birmingham.ac.uk/research/activity/mds/projects/HaPS/PCCS/anticoagulation/index.aspx
National Centre for Anticoagulation Training provide courses.

CPPE workbook - https://www.cppe.ac.uk
This is a challenging e-learning package designed for pharmacists but has lots of good information on anticoagulants. “Anticoagulation: managing patients, prescribing and problems” for pharmacists

Sunderland University -
http://www.sunderland.ac.uk/courses/appliedsciences/cpd/cid953anticoagulation/
A two day course covering the basics of setting up an anticoagulation course. Aimed at pharmacists interesting in setting up anticoagulant clinics.