Cheshire and Wirral Partnership NHS
NHS Foundation Trust

Document level: Trustwide (TW)
Code: MP21
Issue number: 2

Clinical guidance in anticoagulant therapy in adults

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Type of document	Guidance
Target audience	All inpatient staff
Document purpose	To give information needed for the safe and effective prescribing, administration and monitoring of anticoagulant therapy

Approving meeting	Medicines Management Group	Date 15/09/2017
Implementation date	December 2017	

CWP documents to be read in conjunction with	
HR6	Trust-wide learning and development requirements including the training needs analysis (TNA)
MP1	Medicine Policy

Document change history	
What is different?	1. Quick reference flowchart added to comply with current trust procedures 2. Section 1 reference to Novel Oral Anticoagulants (NOACs) 3. Section 1.3 NOACs added to reflect current NICE recommendations 4. Section 3.1 reference to NOACs added 5. Section 3.2 reference to NOACs added 6. Section 3.3 reference to NOACs added 7. Section 3.10 reference to NOACs added 8. Section 3.10 Table 3 spelling mistakes corrected 9. Section 3.12 reference to NOACs added 10. Appendix 3 Inpatient warfarin chart added
Appendices / electronic forms	Appendix 3 (inpatient warfarin chart) added to provide a warfarin administration chart that can be used throughout the trust
What is the impact of change?	The updated guidance gives clinicians the opportunity to choose between warfarin and NOACs in certain circumstances. NOAC treatment is currently more expensive therefore a change of practice can have financial implications.

Training requirements	Yes - Training requirements for this policy are in accordance with the CWP Training Needs Analysis (TNA) with Learning and Development (L&D)

Financial resource implications	No

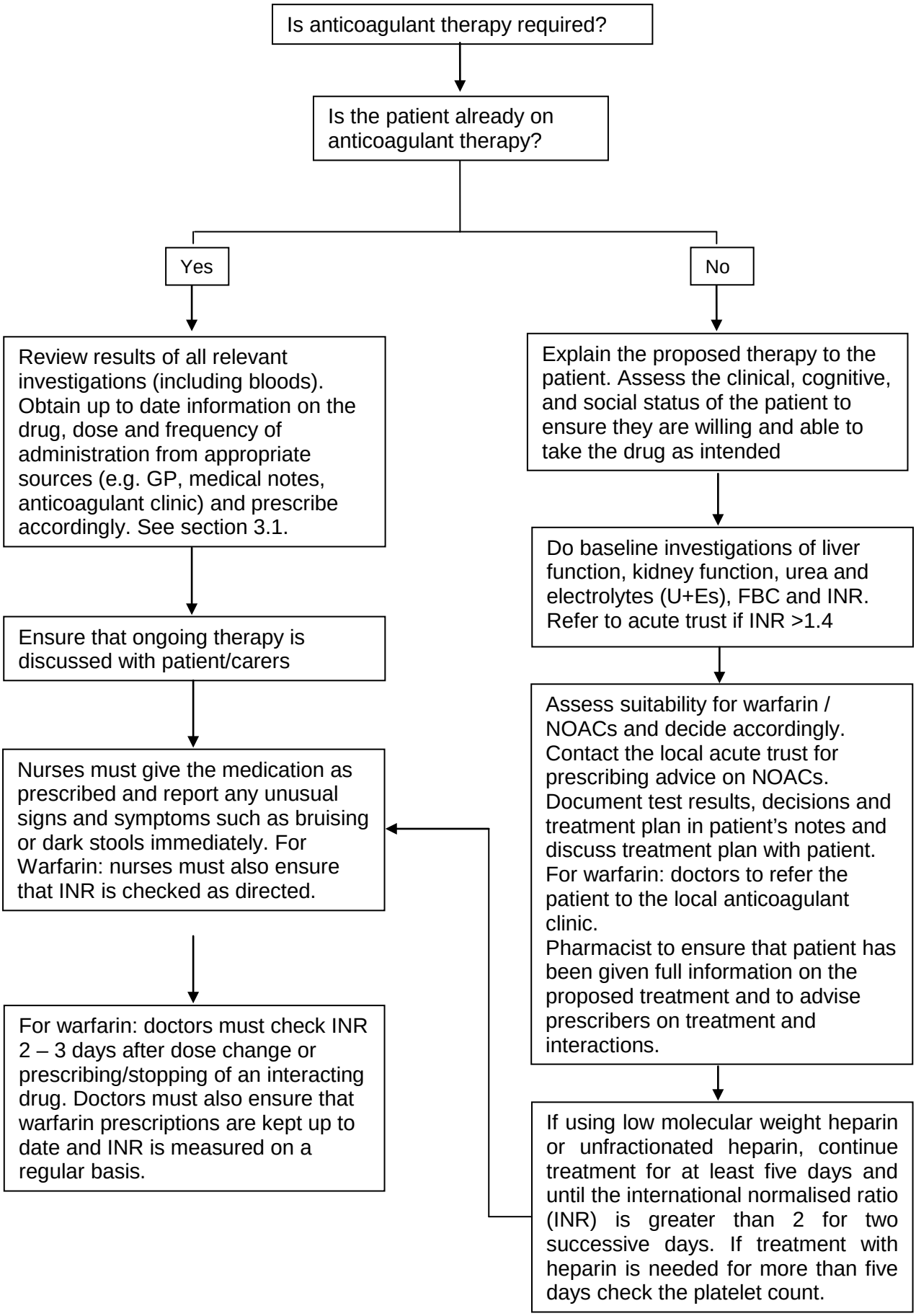
External references
1. NPSA : www.npsa.nhs.uk/
2. electronic British National Formulary May 2016 http://www.evidence.nhs.uk/formulary/bnf/current
3. Scottish Intercollegiate Guidelines network (SIGN). 129 Antithrombotics: indications and management. (URL: http://www.sign.ac.uk/pdf/SIGN129.pdf)
4. Guidelines on Oral Anticoagulation with Warfarin—fourth edition. *British Journal of Haematology* 2011; **154**: 311–324

5. Ryan et al. British Medical Journal. 1989; 299: 1207 - 1209
6. British Medical Association. National Enhanced Service Specification-anticoagulation monitoring
7. Wirral CCG Oral Anticoagulants Guideline for prescribing, monitoring and management April 2016
8. North West CSU: Novel or Non-vitamin K antagonist oral anti-coagulants (NOACs) November 2015
9. Central and Eastern Cheshire MMT: Prescribing Oral Anticoagulants in Non-Valvular AF - July 2012
10. East Cheshire NHS Trust: Outpatient Deep vein Thrombosis Proforma 2015
11. East Cheshire NHS Trust: Medicine Prescription And Administration Record May 2015 WPH013NEW
12. NICE Technical Appraisals on rivaroxaban: 170, 256, 261, 287
13. NICE Technical Appraisals on apixaban: 245, 275, 341
14. NICE Technical Appraisals on edoxaban: 354, 355
15. NICE Technical Appraisals on dabigatran: 157, 249, 327
16. Electronic Medicines Compendium www.medicines.org.uk [accessed 04/2016]

Equality Impact Assessment (EIA) - Initial assessment	**Yes/No**	**Comments**
Does this document affect one group less or more favourably than another on the basis of:		
- Race	No	
- Ethnic origins (including gypsies and travellers)	No	
- Nationality	No	
- Gender	No	
- Culture	No	
- Religion or belief	No	
- Sexual orientation including lesbian, gay and bisexual people	No	
- Age	No	
- Disability - learning disabilities, physical disability, sensory impairment and mental health problems	No	
Is there any evidence that some groups are affected differently?	No	
If you have identified potential discrimination, are there any exceptions valid, legal and/or justifiable?		
Is the impact of the document likely to be negative? - If so can the impact be avoided? - What alternatives are there to achieving the document without the impact? - Can we reduce the impact by taking different action?	No N/A N/A N/A	
Where an adverse or negative impact on equality group(s) has been identified during the initial screening process a full EIA assessment should be conducted. If you have identified a potential discriminatory impact of this procedural document, please refer it to the human resource department together with any suggestions as to the action required to avoid / reduce this impact. For advice in respect of answering the above questions, please contact the human resource department.		
Was a full impact assessment required?	No	
What is the level of impact?	Low	

Content

Quick reference flowchart – Clinical guidance in anticoagulant therapy in adults



1. Introduction

Anticoagulants are used for surgical and medical thromboprophylaxis and also to treat venous thromboembolism (VTE). The role of oral anticoagulant therapy is to keep the International Normalised Ratio (INR) within the agreed ranges to prevent thrombus formation or the extension of a thrombus, depending on the reason the patient has been prescribed an anticoagulant.

The INR is a standard test that measures how long blood takes to clot. Blood that is not anticoagulated has an INR of approximately 1.0.
The dose of oral anticoagulant that a patient needs to take will depend on the INR test result. If the result is out of the range appropriate for the condition, the dose of anticoagulant needs to be increased or decreased accordingly. The anticoagulant dose required to achieve the target range INR varies for each person. The doses of NOACs do not vary depending on INR but rather on other factors such as body weight, renal function and drug interactions. INR does not need to be monitored.

Anticoagulants are one of the classes of medicines most commonly associated with fatal medication errors. In secondary care, warfarin is one of the ten drugs most frequently associated with medication errors.

Warfarin is one of the most frequently prescribed anticoagulants and most parts of this guideline will refer to treatment with warfarin. When treatment with NOACs is considered the local acute trust's guidelines should be taken into account.

It is recommended that staff caring for a patient prescribed anticoagulants should familiarise themselves with the arrangements of the local anticoagulant service. This service can provide help and advice about the care of a patient registered with them.

1.1 Warfarin

Warfarin is the most frequently prescribed oral anticoagulant medicine. Other, less commonly prescribed oral anticoagulants include phenindione and acenocoumarol (formerly nicoumalone). To use these medicines safely their dose needs to be adjusted to maintain the desired therapeutic action and minimise adverse side effects. Under-anticoagulation can result in thrombosis which can be life threatening. Conversely, over-anticoagulation can result in haemorrhage, which can be fatal and outweigh the benefits of preventing the thrombosis. Duration of treatment varies, from three to six months for venous thrombosis, to life for cardiac or recurrent thrombosis indications.

The average daily dose of warfarin to achieve an INR within the desired range of the target (usually 2.0 to 3.0) is 5 mg, but with wide variation (range 1 to 15 mg). Warfarin sensitivity varies widely between individuals, and within the same person, due to variables such as age, diet, diseases and other medicines being taken. Successful anticoagulant treatment relies on the patient being well informed and complying strictly with the prescribed dosage. The stability of the INR also relies on the patient informing clinical staff of any changes in medication, diet and lifestyle. Good patient education and communication with staff responsible for their care is an essential part of the treatment pathway.

The dose of warfarin must be carefully adjusted for each patient. Warfarin tablets are available in strengths of 500 micrograms, 1mg, 3mg and 5mg. Patients are usually given supplies of 1mg tablets (brown) initially to aid dose amendment. Sometimes the dose may be prescribed on alternate days as this prevents patients having to halve tablets or use 500 microgram tablets. The supply of tablets in more than one strength can increase the risk of accidental overdose, especially if patients are confused.

When initially prescribed, it can take between 48 to 72 hours for warfarin to achieve its full effect. This is the time needed for the body to deplete the clotting factors already formed. During this time parenteral heparin may be prescribed and administered by subcutaneous injection to provide immediate protection for the patient.

1.2 Heparin

The administration of heparin provides rapid anticoagulation with a short duration of action. Heparin is often referred to as 'standard' or 'unfractionated' heparin to distinguish it from low molecular weight heparins (LMWH).

Low molecular weight heparins, for example, dalteparin, enoxaparin and tinzaparin, have a longer duration of action, and are usually preferred for routine use. Unfractionated heparin can be used in those with high risk of bleeding because its effect can be terminated rapidly by stopping the infusion.

For deep vein thrombosis (DVT) and pulmonary embolism (PE), subcutaneous low molecular weight heparins are used. Unfractionated heparin can be given as an intravenous loading dose, followed by a continuous intravenous infusion or by intermittent subcutaneous injections (though the latter is not recommended). Oral warfarin therapy is usually started at the same time and the heparin is continued for at least five days until the INR has been in range for two days. Daily blood tests must be taken.

Low molecular weight heparins can be used as prophylaxis of DVT and PE following surgery or in those patients requiring medical thromboprophylaxis e.g. bed bound and oncology patients.

If excessive bleeding occurs heparin should be stopped. If rapid reversal is required the specific antidote for heparin is protamine sulphate although this is only partially effective for low molecular weight heparins.

1.3 Novel oral anticoagulants (NOACs)

Rivaroxaban (Xarelto▼®) is a direct inhibitor of activated factor X (factor Xa). NICE has recently recommended it as an option for treating deep vein thrombosis and preventing recurrent deep vein thrombosis (DVT) and pulmonary embolism (PE) after a diagnosis of acute deep vein thrombosis in adults. For the initial treatment of acute deep vein thrombosis, the recommended dosage of rivaroxaban is 15 mg twice daily for the first 21 days followed by 20 mg once daily for continued treatment and prevention of recurrence. Unlike warfarin rivaroxaban does not routinely require monitoring of therapeutic response.

Apixaban (Eliquis®) is a direct inhibitor of factor X (factor Xa), inhibiting thrombin formation and the development of thrombi. It is administered orally. To treat deep vein thrombosis or pulmonary embolism, 10 mg apixaban should be taken twice a day for the first 7 days, followed by 5 mg twice a day for at least 3 months. For the prevention of recurrent disease, people who have completed 6 months of treatment for DVT or PE should take 2.5 mg twice a day.

Edoxaban (Lixiana▼®) is a direct inhibitor of factor X (factor Xa). NICE has recently recommended it as an option for treatment and prevention of DVT and PE and for prevention of stroke and systemic embolisms. The recommended dose is 60mg once daily with a recommended dose reduction to 30mg once daily for patients with moderate to severe renal impairment (CrCL 15 – 50ml/min), low body weight (<60kg) or concomitant use of a P-glycoprotein inhibitor (e.g. ciclosporin, erythromycin, dronedarone, ketoconazole).

Dabigatran (Pradaxa®) is an oral direct thrombin inhibitor that specifically and reversibly inhibits thrombin, a key enzyme in blood clot formation. It is licensed for the treatment of deep vein thrombosis and pulmonary embolism, and prevention of recurrent DVT and PE in adults. The standard recommended dosage of dabigatran etexilate is 300 mg (150 mg twice daily) following treatment with a parenteral anticoagulant for at least 5 days. Note that the dosage will vary depending on comorbidities, age and drug interactions. For specific dosage advice please always consult the most up to date version of the BNF or SPC. Dabigatran etexilate is contraindicated in people with severely reduced kidney function.
For full dosing guidelines, list of drug interactions and contraindications please refer to the most recent BNF and SPC (www.medicines.org.uk).

Reversal:
In September 2015 the EMA granted a positive opinion to idarucizumab, a specific reversal agent to dabigatran. There are currently no specific reversal agents available for any of the other NOACs. If the patient has bleeding complications (e.g. in case of overdose) advice must be sought from the acute trust.

2. Definitions

AF	Atrial Fibrillation – Irregular heart beat
Anticoagulant	Drug that prevents blood clotting
Antiplatelet	A drug that reduces risk of platelet aggregation
DVT	Deep Vein Thrombosis – blood clot in vein
INR	International Normalised Ratio – measure effectiveness of anticoagulant
NOACs	Novel oral anticoagulants
PE	Pulmonary Embolism – blood clot in lungs
PT	Prothrombin Time – measure effectiveness of anticoagulant

3. Procedure

3.1 Prescribing for patients admitted on oral anticoagulants

- Read the patient's notes, previous prescription and protocol, use the Anticoagulant Treatment Booklet, also known as the "yellow book", where used for consistency and to identify any special instructions. Review the results of all relevant investigations (including blood test results) and identify the indication for the warfarin prescription and any issues on which advice needs to be sought;
- If the patient is prescribed NOACs please note that there is no "yellow book" and no anticoagulant clinic involvement.
- At the earliest opportunity, contact the patient's GP and/or anticoagulant clinic for advice, if the patient is admitted without an up-to-date "yellow book";
- Ensure that the patient understands their anticoagulant treatment and monitoring requirements, if not give clear explanation;
- Discuss with the patient / carer any verbal or written information they have received concerning their on-going anticoagulant therapy;
- Undertake and document measurement of the INR in accordance with the patient's treatment plan (not applicable for NOAC treatment);
- Establish baseline clotting screen (FBC, LFTs, U&Es also required and done routinely on admission);
- Prescribe the warfarin on the appropriate supplementary prescription chart (see appendix 3) ensuring all sections are correctly completed. Prescribe the anticoagulant treatment legibly making sure that the intention for treatment and monitoring is clear, accurate and there are no ambiguities;
- Warfarin should also be prescribed on the prescription chart itself. For dose, as per chart (or APC) should be annotated;
- Prescribe the NOAC on the prescription chart
- Contact the anticoagulant clinic to inform them of patient's admission if the patient is taking warfarin;
- See section below for guidance on continued monitoring and prescribing during admission.

3.2 Indications / contraindications for anticoagulant therapy

Indications for anticoagulant therapy:

- The main indication for an oral anticoagulant is deep-vein thrombosis (DVT). Pulmonary embolism (PE) should also be treated, as are those with atrial fibrillation who are at risk of embolisation and those with mechanical prosthetic heart valves. An anti-platelet drug e.g. aspirin and clopidogrel, may also be useful in these patients but this combination increases the risk of bleeding.

Note that:

- Anticoagulation is not indicated for the following conditions: ischaemic stroke without atrial fibrillation, retinal vessel occlusion, peripheral arterial thrombosis, coronary artery graft or coronary angioplasty and stents;
- Oral anticoagulants should not be used in cerebral artery thrombosis or peripheral artery occlusion as first-line therapy as aspirin is more appropriate here. Heparin or a low molecular weight heparin is usually preferred for the prophylaxis of venous thromboembolism in patients undergoing surgery;
- Warfarin is the oral anticoagulant of choice. Others include acenocoumarol (nicoumalone) and phenindione but these are seldom used. NOACs are sometimes considered an alternative to warfarin and recommended as such by NICE. The local acute trust should be contacted for advice on prescribing and choice of NOACs.

Contraindications to anticoagulant therapy

- Potential bleeding lesions;
- Oesophageal varices, aneurysm, and proliferative retinopathy;
- Recent organ biopsy;
- Recent trauma or surgery to the head, orbit, or spine;
- Recent haemorrhagic stroke;
- Confirmed intracranial or intraspinal bleed;
- Uncontrolled hypertension;
- Infective endocarditis;
- A history of heparin-induced thrombocytopenia or thrombosis is an absolute contraindication for using heparin;
- Homozygous protein C deficiency (risk of skin necrosis) and a history of warfarin related skin necrosis are absolute contraindications to warfarin;
- Pregnancy.

Relative contraindications to anticoagulation are:

- History of gastrointestinal bleeding or active peptic ulcer,
- Liver disease
- Renal failure
- Alcoholism
- Mental impairment
- Thrombocytopenia
- Coagulation disorders
- Interacting drugs, in particular non-steroidal anti-inflammatory drugs
- Poor concordance
- Poor attendance for regular blood tests.

Refer to acute hospital for advice in the above cases.

3.2.1 Indications and Target INR

Indications, target INR values and durations of anticoagulation are shown in Table 1. An INR within 0.5 units of the target value is satisfactory.

Table 1

Indication	Target value INR	Duration of anticoagulation
Pulmonary embolus (PE)	2.5	6 months
Proximal deep vein thrombosis	2.5	6 months *
Calf vein thrombus	2.5	3 months
Recurrence of venous thromboembolism when no longer on warfarin therapy	2.5	Consider long-term
Recurrence of venous thromboembolism	3.5	Consider long-term

whilst on warfarin therapy		
Antiphospholipid syndrome	2.5	Consider long-term
Atrial fibrillation (AF)	2.5	Long-term
Cardioversion	2.5	3 weeks before and 4 weeks after procedure
Mural thrombus	2.5	3 months
Cardiomyopathy	2.5	Long-term
Mechanical prosthetic heart valve	2.5 to 3.5 **	Long term

* Shortening treatment to 3 months will be recommended if circumstances that the risk benefit ratio favours this, for example if a reversible precipitating factor was present and there are risk factors for bleeding (age >65 years).

** Depending on type of valve and/or location.

3.3 Patients who commence anticoagulation while in CWP wards

If a patient is diagnosed with a deep vein thrombosis while they are an inpatient it will be necessary to start anticoagulation with low molecular weight heparin and warfarin. NOACs can be considered as an alternative to warfarin, please contact the acute trust for prescribing and monitoring advice.

Starting low molecular weight heparin:

- See CWP guidance on low molecular weight heparin appendix 1.

3.3.1 Before starting anticoagulation

The doctor must:

- Explain the proposed therapy to the patient. Assess the clinical, cognitive, and social status of the patient to ensure they are willing and able to take the drug as intended;
- Do baseline investigations of liver function, kidney function, urea and electrolytes (U+Es), FBC and INR;
- Refer to acute trust for advice if the baseline INR is greater than 1.4;
- Document the indication for use, target INR, duration of treatment and monitoring plan in the patient's notes;
- Refer the patient to the anticoagulant clinic if warfarin is commenced, using the appropriate documentation for the local acute trust;
- Determine the appropriate loading dose regimen for the patient, which drugs to prescribe, the dosage, the frequency of administration, and the most effective route of administration. Warfarin loading doses are specified on the warfarin chart currently in use at each locality. Advice should be sought from the acute hospital if necessary;
- If using low molecular weight heparin or unfractionated heparin, continue treatment for at least five days and until the international normalised ratio (INR) is greater than 2 for two successive days. If treatment with heparin is needed for more than five days check the platelet count.

The pharmacist must:

- Ensure prescriber is aware of any interacting drugs and advise on management;
- Ensure that patient has been given full information about their treatment using the checklist in appendix 2.

3.4 During admission

Where necessary, the care team must update the patient-held record of anticoagulant treatment – (the "yellow book").

The care team must seek advice and support from the anticoagulant clinic, or appropriate acute services medical team when the needs of the individual and the complexity of the case are beyond their competence and capability.

Warfarin should be prescribed on a separate administration chart (appendix 3) and kept with the drug chart. The drug chart should contain a reference made to the separate administration sheet to alert the care team to the existence of this chart.

Nurses need to monitor the patient and report to the ward doctor if:

- There is excessive or extensive bruising;
- There are cuts to the skin that bleed for longer than usual;
- There is darkening of the patient's stools or urine or any unusual bleeding.

Nurses must also:

- Administer warfarin at the same time each day (usually 6pm), or NOACs at the frequency prescribed;
- Ensure that the INR is checked regularly as requested by the prescriber if warfarin is prescribed;
- Tell anyone who is involved in the patient's care, (including dentists, ECT team etc) that the patient is on an anticoagulant;
- Report any unusual signs or symptoms to the ward doctor without delay.

Doctors need to:

- Be aware of any significant interacting drugs;
- Avoid the use of "as required" aspirin or NSAIDs;
- For warfarin retest INR levels if they initiate or discontinue any interacting drugs. (Test at 2 to 3 day intervals initially);
- Ensure that the prescription is kept updated and INR levels when required are monitored at appropriate intervals.

3.5 Administration of Warfarin

Dose of warfarin should be given in the least number of tablets possible. Doses should be given daily according to the INR and current prescription. There may be a need to dose some patients on alternate days.

Tablets available	**500micrograms**	**White**
	1mg	**Brown**
	3mg	**Blue**
	5mg	**Pink**

The 500micrograms tablets are not widely used and the usual dosing on wards is with 1mg brown tablets.

Although the National Patient Safety Agency (NPSA) has advised that 1mg brown tablets be prescribed as standard other strengths of tablet may be prescribed. It is essential that staff ascertain what strengths of tablets the patient usually takes at the time of admission.

3.6 Action if INR is too high

It may be necessary to withhold doses of anticoagulant therapy when the INR is above the agreed range for that patient. Doses can be withheld until the INR drops sufficiently and the dose can be reviewed and restarted.

Please contact the local anticoagulant clinic and /or pharmacist for further advice.

Refer to earlier section of the current BNF for advice on the treatment of INR greater than 5 and/or there is bleeding. Contact acute hospital for advice if required.

3.7 Monitoring

It is essential that patients taking anticoagulants be monitored during treatment because these drugs have a very narrow therapeutic index. This means that the levels in the blood that are therapeutically effective are close to the levels that cause bleeding.

Patients must have regular tests to check the effect of the warfarin on their blood clotting and this is measured as an International Normalised Ratio (INR). A base-line Prothrombin Time (PT) or clotting time should also be taken before dosing commences and the results of the INR and PT dictate the dose of anticoagulant to be given.

Some people are particularly sensitive to oral anticoagulants and in these individuals small increases in dosage, or introduction/discontinuation of interacting medicines, herbal preparations and certain foods including alcohol, can cause catastrophic increases in anticoagulant effect.

Monitoring of patients on anticoagulation therapy is done by regular blood test. It is essential that the INR be determined daily or on alternate days in early days of treatment, then at longer intervals (depending on response) then up to every 12 weeks. This does not apply to NOAC therapy,

Once a patient has a stable INR, the recall (re-testing) interval can be progressively lengthened and this is built into many computerised dosing support systems run by anticoagulant clinics.

3.8 Adjusting doses according to INR

If the INR is not at the target level the dose of warfarin should be adjusted as recommended in table 2 below. Please note that this is for patients who have been taking warfarin for one week or more and who have no bleeding at INR >5:

Table 2

Dose adjustment of established (maintenance) warfarin i.e. in patients who have been taking warfarin for 7 days or longer. **N.B. Select correct target INR**						
Target INR 2.5				**Target INR 3.5**		
INR	**Dose change**	**Next INR**		**INR**	**Dose change**	**Next INR**
<1.5	30% Increase	3 days		<2	50% Increase	3 days
1.5 - 2	20% Increase			2.1 - 3	20% Increase	
2.1 - 3	No Change			3.1 - 4	No change	
3.1 - 4	20% Reduction			4.1 - 6	Miss 2 days & 20% reduction	4 days
4.1 - 6	Miss 2 days & 30% reduction	4 days				
> 6.1	Miss 3 days	Measure INR daily if there is a high concern for bleeding		> 6.1	Miss 3 days	Measure INR daily if there is a high concern for bleeding

3.9 Side effects/ adverse effects

The main side effect of anticoagulant therapy is haemorrhage. Checking the INR and omitting doses when appropriate is essential. If the anticoagulant is stopped but not reversed the INR should be measured 2 - 3 days later to ensure that it is falling.

Others side effects include:

- Hypersensitivity;
- Rash;
- Alopecia;
- Diarrhoea;
- Unexplained drop in haematocrit (blood volume);

- ‘Purple toes’;
- Skin necrosis;
- Jaundice;
- Hepatic dysfunction;
- Nausea;
- Vomiting;
- Pancreatitis.

Please contact the local anticoagulant clinic and /or pharmacist for further advice.

3.10 Drug Interactions

Oral anticoagulants interact with a wide variety of other medicines (for example, antibiotics and analgesics) and in most cases this leads to an increased anticoagulant effect. Patients taking anticoagulants should be aware of the risks of taking other prescribed or purchased medicines, herbal products and certain foods including alcohol without first seeking advice.

Many drugs interact with warfarin and the BNF contains a useful list in Appendix 1 Interactions.

Warfarin is metabolised in the liver by enzyme CYP2CP. Patients with liver disease of those taking drugs that inhibit the activity of the enzyme (for example, macrolide antibiotics and quinolones) will require less warfarin to reach the target INR.

Patients taking drugs that accelerate the metabolism of warfarin (for example, rifampicin, barbiturates and carbamazepine) will require more warfarin.

Medicines that should be ideally avoided in anticoagulated patients, those that require the dose of anticoagulant to be adjusted and those where close monitoring of the INR is essential are shown in Table 3.

The NOACs share some common interactions and care should be taken when prescribing with P-glycoprotein inhibitors and inducers as well as with cytochrome P450 enzyme inhibitors and inducers. For individual interactions please refer to the eBNF and the SPC.

Table 3 Drug Interactions with warfarin

Avoid	
Aspirin	Except where combination specifically indicated for e.g. mechanical valve prosthesis, recurrent thrombosis
Analgesics	Ketorolac (post-operative)
Antifungals	Miconazole
Diabetes	Glucagon
Non steroidal anti-inflammatory drugs	Azapropazone, diclofenac
Others	Enteral feeds containing vitamin K
Adjust dose	
Ulcer healing	Cimetidine, omeprazole
Antiarrhythmics	Amiodarone, propafenone
Lipid lowering	Fibrates
Antiepileptics	Carbamazepine, phenobarbital, phenytoin, primidone
Dependency	Disulfiram
Antibiotics / Antifungals	Chloramphenicol (oral), ciprofloxacin, co-trimoxazole, erythromycin, clarithromycin, griseofulvin, metronidazole, ofloxacin, rifampicin, sulfonamides
Thyroid	Carbimazole, propylthiouracil, thyroid hormones
Non steroidal anti-inflammatory drugs	Diflunisal (currently not licensed in UK)

Gout	Allopurinol, sulfinpyrazone
Others	Aminoglutethimide, barbiturates, ciclosporin, mercaptopurine, oral contraceptive steroids
Monitor INR	
Antiarrhythmics	Quinidine, amiodarone
Lipid lowering	Colestyramine, statins
Antidepressants	Serotonin re-uptake inhibitors
Antibiotics / Antifungals	Consult BNF if not listed under 'adjust dose'
Diabetes	Tolbutamide
Non steroidal anti-inflammatory drugs	If not listed under 'avoid' or 'adjust dose'
Others	Anabolic steroids, corticosteroids, hormone antagonist, ifosfamide, influenza vaccine, Rowachol ®, sucralfate, sodium valproate

This list is not exhaustive. Please consult the current edition of the BNF, the local anticoagulant clinic and /or pharmacist for further advice.

3.11 Dental treatment

- Patients whose INR is in therapeutic range (<4.0) do not need to stop anticoagulation for dental extraction. Oral tranexamic acid mouthwash can prevent bleeding after dental extraction;
- Some dental procedures require antibacterial prophylaxis and these include extractions or other surgery, surgery involving gingival tissues and scaling. The antibiotics used may interact with warfarin;
- The dental practitioner of any anticoagulated patient requiring dental treatment must be contacted in advance of the appointment for advice and those instructions followed prior to the patient attending for treatment.

3.12 Anticoagulants and Pregnancy

Warfarin is teratogenic (can disturb the development of the embryo or foetus) and should not be given during the first trimester of pregnancy.

The manufacturers of rivaroxaban, apixaban, edoxaban and dabigatran do not recommend their use in pregnancy and lactation.

The Responsible Clinician (RC) who has a pregnant patient needing to take anticoagulants should seek specialist advice.

LMWHs have been used in pregnancy.

3.13 Discharging Patients on Anticoagulant Therapy

Ensure the patient is aware that they must take their anticoagulant dose at the same time each day and that they are fully confident of how to take their tablets.

All patients on warfarin therapy must be given the Oral Anticoagulant Therapy Information Pack and a completed copy of the Oral Anticoagulation Induction/ Advice checklist (Appendix 2). The booklet contains vital information that the patient should be aware of for example, colours of differing strengths of tablet and alcohol consumption. The information on the Oral Anticoagulation Induction/ Advice checklist compliments the yellow book and ensures the patient is fully aware of their treatment

Make sure the current daily dose and INR result is completed in the relevant page of the yellow book before the patient is discharged from the ward and that the patient is referred back to their GP and or local anticoagulant clinic for monitoring. Check that the patient knows when their next INR test is due.

Appendix 1 - CWP guidance to reducing treatment dose errors associated with low molecular weight heparins (LMWH)

RAPID RESPONSE REPORT: NPSA/2010/RRR14

1. Background

Prescribed doses of low molecular weight heparins (LMWHs) for the treatment of a thromboembolic event are dependent on the weight of the patient and renal function. Underdosing has an increased risk of a further thromboembolic event, while overdosing can increase the risk of bleeding. Dosing errors with LMWHs can occur if the prescribed treatment dose is not calculated using the patient's current weight.

LMWH are not used often in CWP but may be prescribed for a suspected or confirmed deep vein thrombosis (DVT) or pulmonary embolism (PE). They may also be used for prophylaxis of DVT/PE after surgery, during pregnancy or if patients are immobile due to physical illness.

Reports to the National Reporting and Learning System (NRLS) indicate that some patients are not weighed prior to dosing, that body weight is estimated or recorded inaccurately, or that doses based on a patient's weight are miscalculated. Additionally, there are numerous reports where the prescribed, dispensed or administered dose and frequency of LMWH were outside accepted guidelines for the required clinical indication and other predisposing conditions such as renal failure. Limited patient information (i.e. weight, dosage, indication and intended duration of treatment) communicated at transfers of care has also led to reports of harm.

2. Guidance

These guidance notes should be read in conjunction with the prescribing advice in the current British National Formulary and the Summary of Product Characteristics (SPC) for individual products.

2.1 Initiation of LMWH

- The LMWH products used in CWP are tinzaparin and enoxaparin;
- The patient should be weighed and the weight in kilograms and the date of weighing recorded on the prescription chart;
- Renal function should be checked. This should be available from urea and electrolyte tests on admission, if not the tests should be done immediately. LMWH may be started and the dose adjusted if necessary when the renal function is known;
- Dosage should be calculated using the dose calculation tools provided in the anticoagulant file taking into account weight, renal function and indication;
- The dosage in units (tinzaparin) or mg (enoxaparin) and the duration of treatment should be clearly documented on the medicine chart and in the patient's notes.

2.2 Administration of LMWH

- The prescription should be clinically checked by a pharmacist;
- The nurse administering should check the dose against the dosage calculation tool and check the duration before giving the dose subcutaneously.

2.3 Continuation of LMWH

- If a patient is admitted on a LMWH, the weight and renal function should be checked to ensure that the dose is appropriate. The indication and duration of course should be ascertained as part of the medicines reconciliation procedure and clearly documented on the prescription chart and in the patient's notes.

2.4 Discharge on LMWH

- If the patient is discharged while still on LMWH the dose and duration of treatment should be clearly specified on the discharge prescription. This prescription must be clinically checked by a pharmacist;

- The discharge letter should contain details of weight, renal function and indication for treatment in addition to the information above.

Appendix 2 - Oral anticoagulation induction / advice checklist

Patient's name		Hospital number	

This list is to be completed by medical staff or a pharmacist and their patient.

The information listed complements the information given in the yellow book. Tick each box as a record of understanding, and both patient and staff sign the completed form.

Give one copy to the patient and attach a second copy to the referral letter in the patient's notes.

As an in-patient		**Tick**
1	Warfarin tablets come in a range of strengths and colours. Strengths of tablet are in milligrams (mg). 1mg = brown, 3mg = blue, 5mg = pink Acenocoumarol (Sinthrome®) 1mg tablets are white Phenindione 10mg and 50mg tablets are white, 25mg are green	
2	Take the tablets that make up your dose all together at the same time each day. If you keep to the same time each day you are more likely to remember.	
3	If you miss a dose of your anticoagulant tablets, you must make a note of the date and tell the staff (or clinic at your next visit). If you miss more than one dose you must ring the clinic.	
4	Do not take an extra dose if you cannot remember taking the last one. If you take too many tablets, there is a danger that you might bleed.	
5	Tell staff or clinic, if you have started any new medicines or if you are taking any food supplements, health food shop products or herbal remedies.	
6	If you want to start taking any health food shop products, food supplements or herbal remedies, you must seek the advice of the staff or clinic, as some products must never be taken with anticoagulants.	
7	Let the staff know if you take aspirin, anything containing aspirin, ibuprofen or diclofenac (or similar medicines). You should not take these unless you have been prescribed them by a doctor who knows you are taking anticoagulants.	
8	Paracetamol is safe to take in normal doses for short periods. Medical advice must be taken for long-term management of chronic pain.	
9	Some antibiotics affect the way anticoagulants work. Tell staff if you are taking any antibiotics.	
10	Tell staff if you experience any of the following while taking anticoagulants: Unexplained bruising Bleeding problems (any bleeding that doesn't stop in good time) Vomiting or diarrhoea	
11	If you vomit blood, see blood in your urine (red or dark brown), pass red or black stools or if you have a major nosebleed (for more than 10 minutes), you must inform staff or if at home, go to the Accident and Emergency department at the hospital.	
12	If you are a woman of child bearing age you should not start a pregnancy without consulting your doctor first. If you think you may be pregnant, you should see your doctor as soon as possible.	
13	Eat a sensible diet. Avoid major changes in your diet and let staff or clinic know if you decide to go on any kind of 'special diet'.	
14	Drinking alcohol is permitted, when you are not in hospital, but in small amounts in a controlled way.	
When you go home		
15	Read your yellow anticoagulant book carefully. Carry it with you at all times.	

16	Tell your GP or any doctor that treats you that you are taking anticoagulants before receiving any treatment or new medicines. Arrange with your GP to have your warfarin or Sinthrome® tablets on repeat prescription. Always have an extra week of tablets and if you are going on holiday always take an extra supply with you. The anticoagulant clinic cannot provide routine supplies.	
17	Tell your dentist that you are taking an anticoagulant. The British Dental Association is happy for dentists to treat most patients taking anticoagulants. If your dentist knows that you are taking anticoagulants then he will be prepared in case there is any bleeding.	
18	Tell your pharmacist / chemist that you are taking an anticoagulant. Pharmacists will be able to advise you about medicines that are safe to take with anticoagulants.	
19	The anticoagulant clinic will check your blood clotting time and adjust your dose if necessary.	
20	It is important that you keep your anticoagulant clinic appointments and tell the clinic if you cannot attend and obtain a new appointment.	

To be completed by the patient at the end of the induction/ advice session

This document has been explained to me and I understand the importance of the points covered

Signature of patient		Date	

To be completed by medical staff or pharmacist

Signature of professional		Date	

Appendix 3 - Inpatient Warfarin chart

Name:	Indication:
Date of birth:	Target INR:
Ward:	Usual maintenance dose:

Suggested starting dose of warfarin:

	INR:	Dose:
Day 1		10mg
Day 2		10mg
Day3	<2.0	10mg
	2.0 - 2.1	5mg
	2.2 - 2.4	4mg
	2.5 - 2.9	3mg
	3.0 - 3.4	2mg
	3.5 - 4.0	1mg
	> 4.0	omit

	INR:	Dose:
Day 4	<1.5	8mg
	1.5 - 1.7	7mg
	1.8 - 1.9	6mg
	2.0 - 2.3	5mg
	2.4 - 3.0	4mg
	3.1 - 4.0	3mg
	4.1 - 4.5	miss 1 day, then 2mg
	> 4.5	miss 2 days, then 1mg
Day 5	onward -	adjust as necessary

Notes:
Use 70% of dose for patients >70yrs or <55kg or on amiodarone or with severe hepatic/renal impairment. Caution with interacting drugs (see BNF). For reversal and target INR see BNF section 2.8.2

(Note: Adapted with permission from East Cheshire NHS Trust: Medicine Prescription And Administration Record May 2015 WPH013NEW)

Day 4 dose usually approximates to maintenance dose.
Warfarin therapy should be given at 6pm
Prescribe on the table below and continue overleaf if necessary.

For advice on adjusting warfarin doses according to INR please refer to table 2 of section 3.8 in MP21

Date	INR	Dose	Dr signature	Given by

Date	INR	Dose	Dr signature	Given by