

## WARFARIN & OTHER ORAL ANTICOAGULANTS GUIDELINES AND PROCEDURES

### Clinical Guideline

#### Introduction

There are three classes of oral anticoagulants available to prescribers in Worcestershire:

- Vitamin K antagonists – warfarin, phenindione and acenocoumarol
- Anti-Xa agents – apixaban, rivaroxaban and edoxaban
- Direct thrombin inhibitors – dabigatran

Traditionally warfarin has been the anticoagulant of choice for several indications. Warfarin has the advantages of:

- It has a wide range of indications
- Its effect can easily be measured
- It can be reversed immediately and simply
- It has very few side-effects, apart from bleeding
- It can be used in renal failure
- It is cheap
- Its long half-life means missing a dose is not important

However its disadvantages are:

- It requires regular monitoring and dose adjustment
- It has multiple drug interactions
- Its effect is changed with diet, age and exercise

There are now four direct oral anticoagulant drugs (DOAC) licensed and NICE approved for use in certain indications. These have the advantages over warfarin of:

- Having a single dose
- Having few drug interactions
- There is no requirement for monitoring or dose adjustment
- There may be an improvement in outcomes and reduction in bleeding when compared to warfarin

They do have disadvantages:

- There is no specific reversal agent for the anti-Xa agents
- They are all in part renally excreted
- Their indications are limited at present
- There is minimal longterm safety data
- Their short half-life means missing a dose leads to the patient being un-anticoagulated
- They are expensive

Therefore the decision on whether a patient should receive warfarin or a DOAC should involve a careful appraisal of the risk/benefit for each drug and a detailed discussion between the patient and the prescriber. Electronic Medicine Compendium (EMC) Summary of Product Characteristics (SPC) and Patient Information Leaflets (PIL) are found in appendix E.

### **Conversion between the drugs**

It is relatively easy to convert between the oral anticoagulants (and low molecular weight heparin). For detailed guidance see appendix A.

### **Monitoring on DOACs**

Patients on a DOAC should have their renal and liver function measured yearly if they are normal and six monthly if abnormal, taking note at what level these drugs can no longer be prescribed.

## Pharmacology

	Warfarin	Dabigatran	Apixaban	Rivaroxaban	Edoxaban
<b>Class</b>	Vitamin K antagonist (reduces factors II, VII, IX and X)	Direct oral anti-thrombin	Oral anti-Xa	Oral anti-Xa	Oral anti-Xa
<b>Bioavailability</b>	>95%	~6%	>50%	>80%	60%
<b>Tmax</b>	Variable but requires alternative additional anticoagulant until INR therapeutic for 2 days if immediate anticoagulation is required	2 hours	1-3 hours	2.5-4 hours	1.5 hours
<b>Half-life</b>	35-45 hours	12-17 hours	8-15 hours	5-9 hours	10-14 hours
<b>Renal clearance</b>	0%	80% ( <b>contra-indicated with GFR&lt;30mls/min</b> , consider dose reduction to 110mg bd in those patient with GFR 30-50mls/min and increased bleeding risk)	25% ( <b>contra-indicated with GFR&lt;15mls/min</b> , use with caution 15-30mls/min, for atrial fibrillation dose reduce to 2.5mg/day in patients with creatinine >133mmol/L)	66% ( <b>contra-indicated with GFR&lt;15mls/min</b> , use with caution 15-30mls/min)	33% ( <b>contra-indicated with GFR&lt;15mls/min</b> , use with caution 15-50mls/min with dose reduction to 30mg od)
<b>Protein binding</b>	99%	35%	87%	>90%	10-59%
<b>Drug interactions</b>	Multiple - any drug that affects the CYP2C9, 3A4, 1A2 enzymes*, alcohol or things that affect vitamin K (antibiotics and foods)	P-gp inhibitors*  PPI	Potent CYP3A4 inhibitors*  P-gp inhibitors*	Potent CYP3A4 inhibitors*  P-gp inhibitors*	Potent CYP3A4 inhibitors*  P-gp inhibitors*
<b>Monitoring of anticoagulant effect</b>	INR	Has some effect on the APTT, if prolonged patient likely to be anticoagulated, if normal cannot exclude residual anticoagulant activity. Laboratory likely to be able to measure effect by late 2016.	Has some effect on the PT, if prolonged patient likely to be anticoagulated, if normal cannot exclude residual anticoagulant activity. Laboratory likely to be able to measure effect by late 2016.	Has some effect on the PT, if prolonged patient likely to be anticoagulated, if normal cannot exclude residual anticoagulant activity. Laboratory likely to be able to measure effect by late 2016.	Has a linear effect on both the PT and APTT but interpretation unclear.
<b>Licensed</b>	Multiple	AF VTE prevention following hip or knee replacement Treatment of VTE	AF VTE prevention following hip or knee replacement Treatment of VTE	AF VTE prevention following hip or knee replacement Treatment of VTE	AF Treatment of VTE
<b>Daily cost (BNF)</b>	£0.03-0.18 per day but does not include cost of monitoring. NHS average of £25 per INR clinic visit.	£2.20 per day	£2.19 per day	£2.10 per day	£2.10 per day

## Indications and choosing the most appropriate drug

### Prophylaxis of venous thromboembolism (VTE) following elective hip or knee replacement surgery.

The National Institute for Health and Care Excellence (NICE) recommends pharmacological VTE prophylaxis for 28-35 days following a hip replacement and 10-14 days following a knee replacement.

Drug	Dose	Duration	VTE events compared to LMWH	Bleeding events compared to LMWH
Enoxaparin	40mg od (20mg with GFR<30mls/min or <50kg) 12 hours before surgery then daily	Hip 28-35 days  Knee 10-14 days	Treatment with LMWH gives rate of 0.8%	Treatment with LMWH gives rate of 4%
Dabigatran	110mg 1-4 hours after surgery then 220mg od starting the following day (75mg 1-4 hours after surgery then 150mg od starting the following day for those with GFR 30-50ml/min, those taking p-gp inhibitors and those over 75 years).	Hip 28-35 days  Knee 10 days	No difference	No difference
Apixaban	2.5mg bd starting 12-24 hours after surgery	Hip 32-38 days  Knee 10-14 days	No difference	3.8% versus 4.7%  NNT 112
Rivaroxaban	10mg od starting 6-10 hours after surgery	Hip 5 weeks  Knee 2 weeks	0.5% versus 1%  NNT 182	4.5% versus 3.5%  NNH 106

NNT – number needed to treat NNH – number needed to harm

From: Dabigatran, rivaroxaban, or apixaban versus enoxaparin for thromboprophylaxis after total hip or knee replacement: systematic review, meta-analysis, and indirect treatment comparisons. *BMJ* 2012;344:e3675

Currently in Worcestershire the preferred method of thromboprophylaxis is with Enoxaparin. There are no plans by the Orthopaedic Surgeons to introduce the DOACs.

## Atrial fibrillation

### Decision to anticoagulate

[NICE Guidance CG180](#) states that all patients with atrial fibrillation are assessed for their stroke risk using the CHA<sub>2</sub>DS<sub>2</sub>-VASC scoring system (appendix C) if they have:

- symptomatic or asymptomatic paroxysmal, persistent or permanent atrial fibrillation
- atrial flutter
- a continuing risk of arrhythmia recurrence after cardioversion back to sinus rhythm

Dependent on the score the following is recommended:

Score	0	1	≥2
Men	No anticoagulation	Consider anticoagulation	Offer anticoagulation
Women	No anticoagulation	No anticoagulation	Offer anticoagulation

For those patients in whom anticoagulation is being considered or offered a HASBLED score (appendix C) should be performed to determine the bleeding risk on anticoagulation. The bleeding risk and the stroke risk should be compared and a discussion with the patient held to determine a preference for anticoagulation. NICE do not recommend withholding anticoagulation because of a risk or history of falls, as the chance of suffering a major bleed because of a fall is low.

NICE approved on-line calculators:

- CHA<sub>2</sub>DS<sub>2</sub>-VASC <http://www.mdcalc.com/cha2ds2-vasc-score-for-atrial-fibrillation-stroke-risk/#how-to-use>
- HASBLED <http://www.mdcalc.com/has-bleed-score-for-major-bleeding-risk/>
- Combined calculator <http://sparctool.com/>

Patients should be regularly re-assessed (yearly and after a major clinical event) to determine if risks have changed and whether they still require/ don't require anticoagulation.

### Choice of anticoagulants in patients newly diagnosed with atrial fibrillation

The five oral anticoagulants that are licensed with four NICE approved (warfarin, dabigatran, apixaban and rivaroxaban) for prevention of stroke and systemic emboli in atrial fibrillation have slightly different licensing indications dependent on risk factors being present:

Risk factor (can be prescribed if present)	Apixaban	Dabigatran	Edoxaban	Rivaroxaban	Warfarin
Valvular AF (mitral stenosis or prosthetic mitral valve)					✓
Previous stroke, TIA or systemic emboli	✓ (but not s.embolism)	✓	✓	✓ (but not s.embolism)	✓
LV ejection fraction below 40%		✓			✓
Symptomatic heart failure NYHA class or above	✓	✓	✓	✓	✓
Age 75 years or older	✓	✓	✓	✓	✓
Age 65 years or older with either diabetes mellitus, CAD or hypertension		✓			✓
Hypertension	✓		✓	✓	✓
Diabetes mellitus	✓		✓	✓	✓

The evidence for the use of the five anticoagulants comes from six clinical trials. None compare the DOACs directly and the patient population and study outcomes are slightly different therefore true comparisons are difficult. It does appear however that there is a trend towards improved outcomes and reduced bleeding with the DOACs.

Trial	Apixaban				Dabigatran			Rivaroxaban		Edoxaban			
	ARISTOTLE		AVERROES		RE-LY			ROCKET		ENGAGE AF-TIMI 48			
Groups	Apixaban	Warfarin	Apixaban	Aspirin	Dabigatran	Dabigatran	Warfarin	Rivaroxaban	Warfarin	Edoxaban		Warfarin	
Dose	5mg bd	As per INR	5mg bd	81-324mg	110mg bd	150mg bd	As per INR	20mg od	As per INR	60mg	30mg	As per INR	
Numbers	9088	9052	2808	2791	6015	6076	6022	7131	7133	7035	7034	7036	
Stroke or embolism	1.27%*	1.60%	1.6%*	3.7%	1.53%	1.11%*	1.69%	1.7%	2.2%	1.18%*	1.61	1.5%	
NNT	307		47		169					132			
Major bleeding	2.13%*	3.09%	1.4%	1.2%	2.71%*	3.11%	3.36%	3.6%	3.4%	2.75%*	1.61%*	3.43%	
NNT	104				148					57		23	
Clinically relevant non-major bleeding	1.94%*	2.92%	3.1%	2.7%				11.8%	11.4%	6.60%*	8.67%*	10.15%	
NNT	102									25		11	
Minor Bleeding			6.3%	5.0%	13.16%	14.84%	16.37%			4.12%*	3.52%*	4.89%	
NNT										52		32	
Death	3.52%*	3.94%	3.5%	4.4%	3.75%	3.64%	4.13%	4.5%	4.9%	3.99%	3.80%	4.35%	
NNT	238												

Percentages are yearly rates. \*denotes statistically significant difference when compared to the warfarin control group. NNT – number needed to treat to prevent an event, calculated when there is a significant difference from warfarin.

RE-LY – Dabigatran versus Warfarin in Patients with Atrial Fibrillation. NEJM 361:1139-1151. <http://www.nejm.org/doi/pdf/10.1056/NEJMoa0905561>  
 AMPLIFY - Oral Apixaban for the Treatment of Acute Venous Thromboembolism. NEJM 369:799-808. <http://www.nejm.org/doi/pdf/10.1056/NEJMoa1302507>  
 ARISTOTLE – Apixaban versus Warfarin in Patients with Atrial Fibrillation. NEJM 365:981-992 <http://www.nejm.org/doi/pdf/10.1056/NEJMoa1107039>  
 AVERROES – Apixaban in Patients with Atrial Fibrillation. NEJM 364:806-817 <http://www.nejm.org/doi/pdf/10.1056/NEJMoa1007432>  
 ROCKET-AF – Rivaroxaban versus Warfarin in Nonvalvular Atrial Fibrillation. NEJM 365:883-891 <http://www.nejm.org/doi/pdf/10.1056/NEJMoa1009638>  
 ENGAGE AF-TIMI 48 – Edoxaban versus Warfarin in Patients with Atrial Fibrillation NEJM 369:2093-2104 <http://www.nejm.org/doi/full/10.1056/NEJMoa1310907#article>

### Doses of DOACs in atrial fibrillation

Please note that the key documents are not designed to be printed, but to be used on-line. This is to ensure that the correct and most up-to-date version is being used. If, in exceptional circumstances, you need to print a copy, please note that the information will only be valid for 24 hours and should be read in conjunction with the key document supporting information page

Drug	Patient factor	Dose
Dabigatran	Standard dose	150mg bd
	<ul style="list-style-type: none"> <li>Age &gt;80 years</li> <li>Taking verapamil</li> </ul>	110mg bd
	<ul style="list-style-type: none"> <li>Age 75-80 years</li> <li>Moderate renal impairment</li> <li>Gastritis, oesophagitis or gastro-oesophageal reflux</li> <li>Increased risk of bleeding</li> </ul>	Consider reduction to 110mg bd
	GFR<30mls/min	Contra-indicated
Apixaban	Standard dose	5mg bd
	Two of the following: <ul style="list-style-type: none"> <li>Age ≥80 years</li> <li>Weight ≤60kg</li> <li>Creatinine ≥133mmol/L</li> </ul>	2.5mg bd
	GFR<15mls/min	Contra-indicated
Edoxaban	Standard dose	60mg od
	Any of the following: <ul style="list-style-type: none"> <li>CrCl 15-50mls/min</li> <li>Weight &lt;60kg</li> <li>Use of ciclosporin, dronedarone, erythromycin or ketoconazole</li> </ul>	30mg od
	GFR<15mls/min	Contra-indicated
Rivaroxaban	Standard dose (no dose adjustment required although 15mg od was used in clinical trial if CrCl	20mg od

	was 30-49mls/min)	
	GFR<15mls/min	Contra-indicated

### Newly diagnosed patients

The decision whether to start warfarin or a DOAC should involve a discussion between the prescriber and the patient. An approved information leaflet is in appendix D. Given the ease of use of DOACs compared to warfarin it is likely that the patient would prefer a DOAC.

Patient likely to benefit most from warfarin:

- Indication not covered by DOAC e.g. valvular AF
- Severe renal failure (GFR<30mls/min) or high chance of significant deterioration
- Hepatic dysfunction
- Prosthetic (metal or tissue) heart valves
- Arterial grafts
- Patient concerns over longterm safety data
- Taking other drugs where DOACs are contra-indicated (seen appendix B)
- Other medical conditions where data on the use of DOACs is limited
- Use of unusual drugs where experience of them alongside DOACs is limited
- Target INR other than 2.5 (2.0-3.0) as DOACs designed to give equivalent anticoagulation to INR 2.5

Patient likely to benefit most from DOAC:

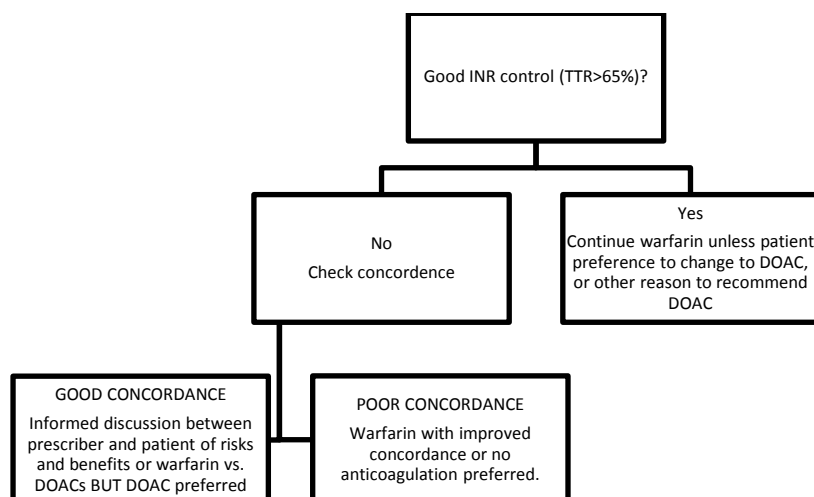
- Regularly prescribed drugs that interferes with warfarin e.g. COPD patient with multiple courses of antibiotics
- GFR 30-50mls/min where NICE recommend the use of apixaban
- Difficulty attending INR clinics (personal or medical reasons)

Likely poor compliance is not a reason for choosing a DOAC, the relative short half-life means missed doses leaves the patients without anticoagulation until the next dose is taken, the relative long half-life of warfarin means an occasional missed dose is unlikely to affect the INR.



### Patients already established on warfarin

Patients on warfarin for atrial fibrillation should be given the option of changing to a DOAC. Patients should be assessed using the following flow-chart.



The reasons for choosing a DOAC or warfarin is discussed above and should also be applied to patients already on warfarin. Changing from warfarin to a DOAC is discussed in appendix A.

### Cardioversion

A common reason for the cancellation of a cardioversion is a sub-therapeutic INR. The use of a DOAC prior and after the procedure should prevent this.

Although there is limited data with the DOAC drugs in the setting of DC cardioversion, all of them have some data and the local decision has been to proceed with cardioversion with any of the drugs. Patients will need to take the DOAC for a minimum of 3 weeks before and 1 month after cardioversion. Because the effect cannot easily be measured, patient compliance is crucial.

### Acute coronary syndrome

There is data regarding the use of rivaroxaban in acute coronary syndromes, but using lower doses than used in AF. There is no data for the other agents. Patients with AF and an acute coronary syndrome, particularly if PCI has been performed, present a particular problem and decisions will be made by the cardiologist on an individual basis. The best data at present is with the combination of warfarin and clopidogrel.

## Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE)

### Choice of anticoagulation for treatment of suspected or confirmed DVT/PE

The options for anticoagulating patients with suspected (while awaiting imaging) or proven DVTs or PEs are:

1. LMWH (standard for care for pregnant patients and patients with cancer)
2. LMWH then conversion to warfarin
3. LMWH then conversion to dabigatran
4. Apixaban
5. Rivaroxaban
6. LMWH then conversion to Edoxaban (not NICE approved).

Four trials compared LMWH/Warfarin with the DOACs for the initial treatment of DVT/PE. Two studies then went on to compare longterm DOAC against placebo. Note dabigatran and edoxaban requires an initial five day treatment with LMWH.

### Initial treatment of DVT/PE

	Apixaban		Rivaroxaban		Edoxaban	Dabigatran		
Trial	AMPLIFY		EINSTEIN		HOKUSAI-VTE	RE-COVER		
Groups	Apixaban	Enoxaparin then warfarin	Rivaroxaban	Enoxaparin then warfarin	Edoxaban	Warfarin	Dabigatran	Warfarin
Dose	10mg bd for 7 days then 5mg bd for 6 months	1mg/kg bd enoxaparin for 5 days then warfarin as per INR for 6 months	15mg bd for 3 weeks then 20mg od for either 3, 6 or 12 months, average 7.7 months	1mg/kg bd enoxaparin for 5 days then warfarin as per INR for either 3, 6 or 12 months average 7.7 months	Initially 'treatment' dose heparin for 5 days then edoxaban 60mg or 30mg for 3-12 months	Initially 'treatment' dose heparin for 5 days then warfarin as per INR for 3-12 months	Initially 'treatment' dose heparin for 5 days then dabigatran 150mg bd for 6 months	Initially 'treatment' dose heparin for 5 days then warfarin as per INR for 6 months
Numbers	2691	2704	4151	4131	4118	4122	1273	1266
Recurrent VTE	2.3%*	2.7%	2.1%	2.3%	3.2%	3.5%	2.4%	2.1%
NNT	237							
Major bleeding	0.6%*	1.8%	1.0%*	1.7%	1.4%	1.6%	1.6%	1.9%
NNT	48		49					
Clinically relevant non-major bleeding	3.8%*	8.0%	8.5%	8.6%	7.2%*	8.9%	4.0%*	6.9%
NNT	24				50		34	
Minor Bleeding								
NNT								
All bleeding	15.5%*	25.8%			21.7%*	25.6%	16.1%*	21.9%
NNT	10				33		17	
Death	1.5%	1.9%	2.3%	2.4%	0.6%	0.6%	1.6%	1.9%

\*denotes statistically significant difference when compared to the warfarin control group. NNT – number needed to treat to prevent an event, calculated when there is a significant difference.

Please note that the key documents are not designed to be printed, but to be used on-line. This is to ensure that the correct and most up-to-date version is being used. If, in exceptional circumstances, you need to print a copy, please note that the information will only be valid for 24 hours and should be read in conjunction with the key document supporting information page

Extended treatment of VTE

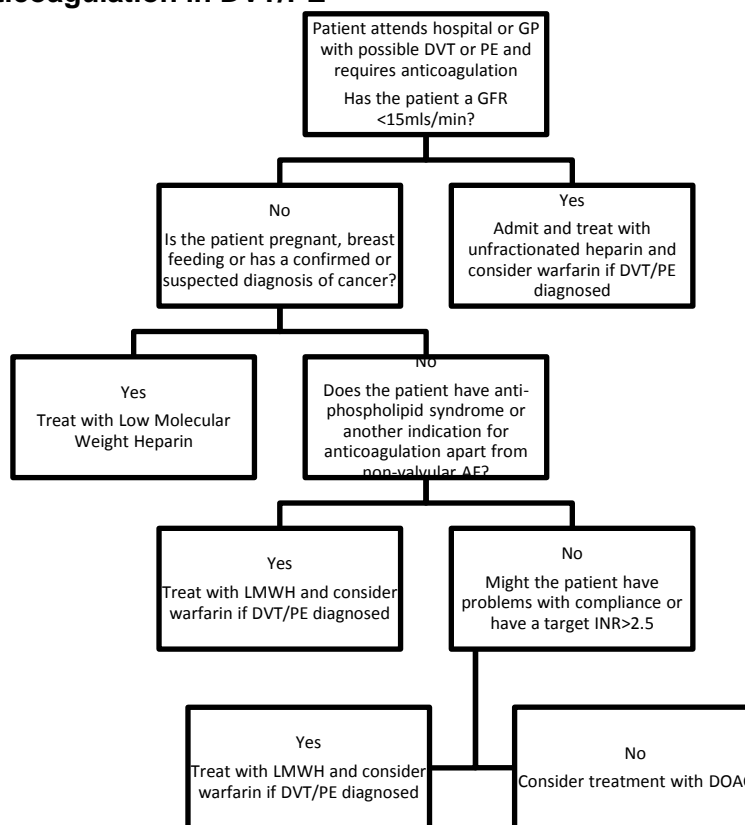
	Apixaban			Rivaroxaban	
Trial	AMPLIFY-EXT			EINSTEIN	
Groups	Apixaban	Apixaban	Placebo	Rivaroxaban	Placebo
Dose	5mg bd for 1 year	2.5mg bd for 1 year	Placebo for 1 year	20mg od for 6-12 months	Placebo for 6-12 months
Numbers	815	842	829	602	595
Recurrent VTE	4.2%*	3.8%*	11.6%	1.3%*	7.1%
NNT	13	13		17	
Major bleeding	0.1%	0.2%	0.5%	0.7%	0%
NNT					
Clinically relevant non-major bleeding	4.2%	3.0%	2.3%	5.4%	1.2%†
NNH				24	
Death				0.2%	0.3%

\* denotes statistically significant difference when compared to the placebo control group where DOAC is superior. NNT – number needed to treat to prevent an event, calculated when there is a significant difference. †denotes statistically significant difference when compared to the placebo control group where placebo is superior. NNH – number needed to harm, calculated when placebo is superior to DOAC.

AMPLIFY - Oral Apixaban for the Treatment of Acute Venous Thromboembolism. NEJM 369:799-808. <http://www.nejm.org/doi/pdf/10.1056/NEJMoa1302507>  
 EINSTEIN-PE - Oral Rivaroxaban for the treatment of symptomatic pulmonary embolism. NEJM 366:1287-1297. <http://www.nejm.org/doi/pdf/10.1056/NEJMoa1113572>  
 EINSTEIN-DVT - Oral Rivaroxaban for the treatment of symptomatic venous thromboembolism. NEJM 363:2499-2510. <http://www.nejm.org/doi/pdf/10.1056/NEJMoa1007903>  
 AMPLIFY-EXT - Apixaban for Extended Treatment of Venous Thromboembolism. NEJM 368:699-708. <http://www.nejm.org/doi/pdf/10.1056/NEJMoa1207541>  
 HOKUSAI-VTE – Edoxaban versus Warfarin for the Treatment of Symptomatic Venous Thromboembolism. NEJM 369:1406-1415. <http://www.nejm.org/doi/full/10.1056/NEJMoa1306638#t=article>

Please note that the key documents are not designed to be printed, but to be used on-line. This is to ensure that the correct and most up-to-date version is being used. If, in exceptional circumstances, you need to print a copy, please note that the information will only be valid for 24 hours and should be read in conjunction with the key document supporting information page

Flowchart for choosing anticoagulation in DVT/PE



For those patients who are to be considered for a DOAC a discussion between the patient and the prescriber is required. A patient information leaflet is available in appendix D.

Patient likely to benefit most from warfarin:

- Indication not covered by DOAC e.g. valvular AF, prosthetic valves
- Severe renal failure (GFR<30mls/min) or high chance of significant deterioration
- Hepatic dysfunction
- Arterial grafts
- Patient concerns over longterm safety data
- Taking other drugs where DOACs are contra-indicated (seen appendix B)
- Other medical conditions where data on the use of DOACs is limited
- Use of unusual drugs where experience of them alongside DOACs is limited

There may be more benefit to treatment of DVT/PE with a DOAC compared to AF as the majority of patients are treated for a short period of time, therefore longterm side-effects are less of a problem. Also the highest risk of bleeding on warfarin is in the first three months and that is when the majority of blood tests are.

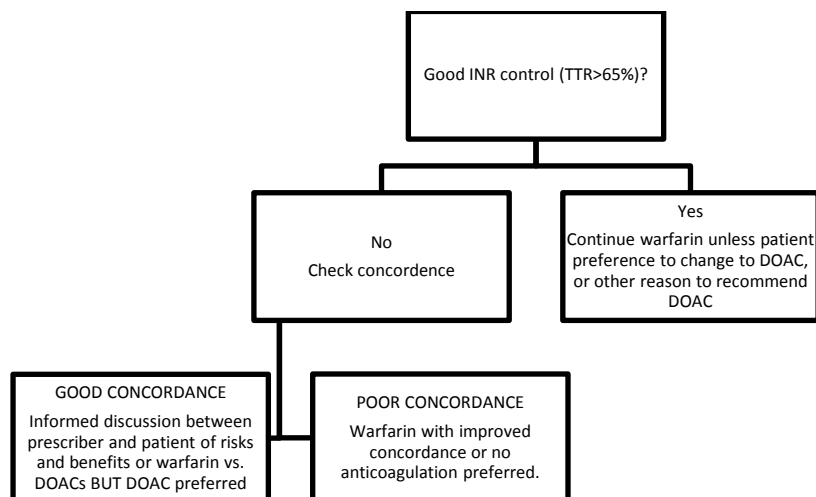
Patient likely to benefit most from DOAC:

- Regularly prescribed drugs that interferes with warfarin e.g. COPD patient with multiple courses of antibiotics
- Difficulty attending INR clinics (personal or medical reasons)

Likely poor compliance is not a reason for choosing a DOAC, the relative short half-life means missed doses leaves the patients without anticoagulation until the next dose is taken, the relative long half-life of warfarin means an occasional missed dose is unlikely to affect the INR.

### Patients with DVT/PE already established on warfarin

Patients on warfarin for atrial fibrillation should be given the option of changing to a DOAC. Patients should be assessed using the following flow-chart.



The reasons for choosing a DOAC or warfarin is discussed above, especially the contra-indications to the DOACs in DVT/PE and should also be applied to patients already on warfarin. Changing from warfarin to a DOAC is discussed in appendix A.

Patients who are longterm LMWH because of problems with blood tests should be considered for a DOAC, except pregnant/breastfeeding mothers or cancer patients.

Doses of DOACs in DVT/PE

Drug	Patient factor	Dose
Dabigatran	Standard dose	Five days of treatment dose LMWH followed by 150mg bd dabigatran
	<ul style="list-style-type: none"> <li>Age &gt;80 years</li> <li>Taking verapamil</li> </ul>	Five days of treatment dose LMWH followed by 110mg bd
	<ul style="list-style-type: none"> <li>Age 75-80 years</li> <li>Moderate renal impairment</li> <li>Gastritis, oesophagitis or gastro-oesophageal reflux</li> <li>Increased risk of bleeding</li> </ul>	Five days of treatment dose LMWH followed by considering dose reduced dabigatran of 110mg bd
	GFR<30mls/min	Contra-indicated
Apixaban	Standard dose (no dose adjustment required)	10mg bd for 7 days then 5mg bd
	GFR<15mls/min	Contra-indicated
Edoxaban	Standard dose	60mg od
	Any of the following: <ul style="list-style-type: none"> <li>CrCl 15-50mls/min</li> <li>Weight &lt;60kg</li> <li>Use of ciclosporin, dronedarone, erythromycin or ketoconazole</li> </ul>	30mg od
	GFR<15mls/min	Contra-indicated
Rivaroxaban	Standard dose (no dose adjustment required)	15mg bd for 21 days then 20mg od
	GFR<15mls/min	Contra-indicated

## Management of patients on oral anticoagulants going for procedures which require interruption of anticoagulation

### Elective procedures

If the indication for the anticoagulation is temporary can the procedure be delayed until after the anticoagulation is stopped?

#### High risk of thrombosis

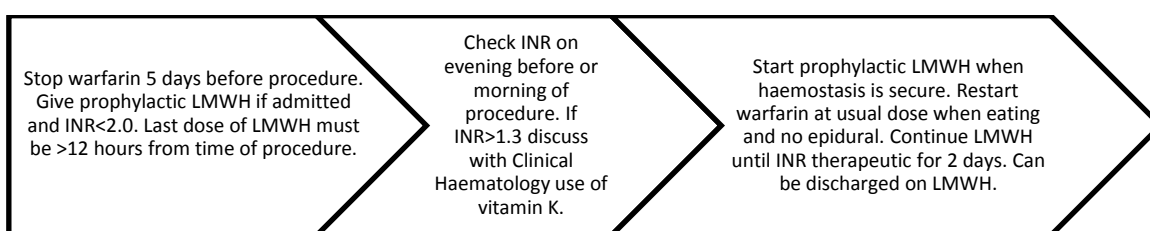
Patients with artificial heart valves should be discussed with Cardiology

Patient who have had a recent thrombosis (within the last 6 weeks) or have a target INR>2.5 should be discussed with Clinical Haematology.

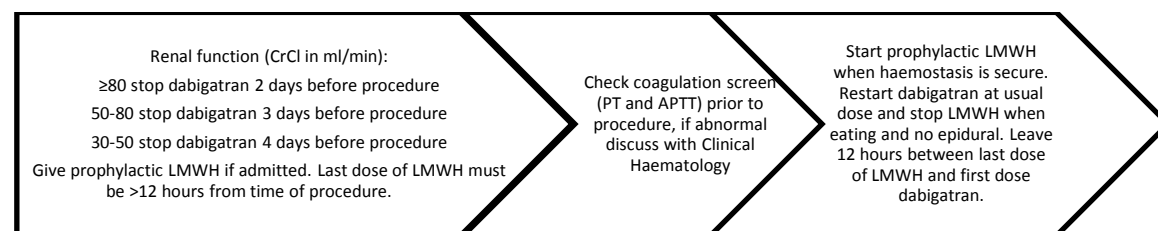
#### Low risk of thrombosis

This is patients with atrial fibrillation or distant thrombosis (more than 6 weeks ago)

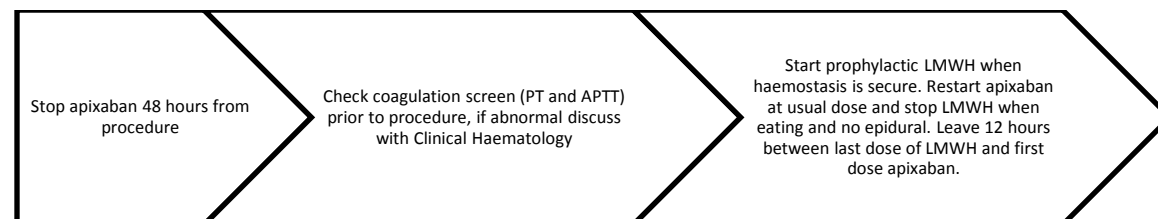
#### Warfarin



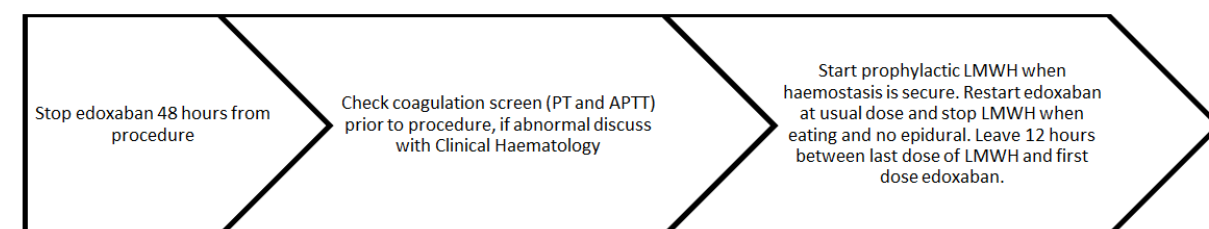
#### Dabigatran



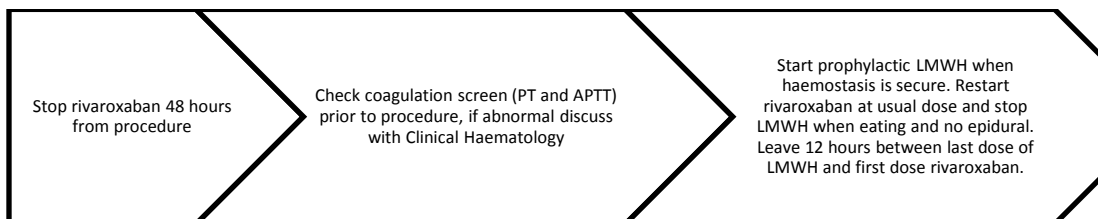
#### Apixaban



#### Edoxaban



#### Rivaroxaban



### **Minor procedures**

Certain minor procedures do not require interruption of warfarin and as long as the INR is within the target range. The DOACs provide a similar level of anticoagulation to warfarin with a target INR of 2.5 but produce more peaks and troughs. Therefore:

- AM procedure: Withhold morning dose of DOAC. For rivaroxaban or edoxaban take missed dose 2 hours after procedure as long as haemostasis is secure, for others take evening dose as planned as long as haemostasis is secure and 2 hours has elapsed from end of procedure
- Procedure after 2pm: Take morning dose of DOAC before 7am and restart when next dose is due as long as haemostasis is secure and 2 hours has elapsed from end of procedure.

### **Protocol for managing anticoagulants when operation cancelled following temporary cessation of oral anticoagulants**

When a patient who is taking oral anticoagulants is listed for planned surgery this information must be clear on the booking form so that cancellation of surgery after cessation of oral anticoagulants is avoided unless on clinical grounds.

When a patient who is taking oral anticoagulants is listed for planned surgery clear advice must be given to the patient at the time of the pre-operative assessment regarding cessation of anticoagulants and who to contact in the event their surgery is cancelled after cessation of their anticoagulants.

On the rare occasion where the patient has ceased taking their oral anticoagulants in preparation for surgery and their operation is cancelled it is the responsibility of the consultant or operating surgeon to give appropriate advice to the patient, this will depend on the indication for the anticoagulation and the date of the rescheduled surgery. Advice can be sought by the consultant or operating surgeon from cardiology or haematology.



## Urgent procedures

### High risk of thrombosis

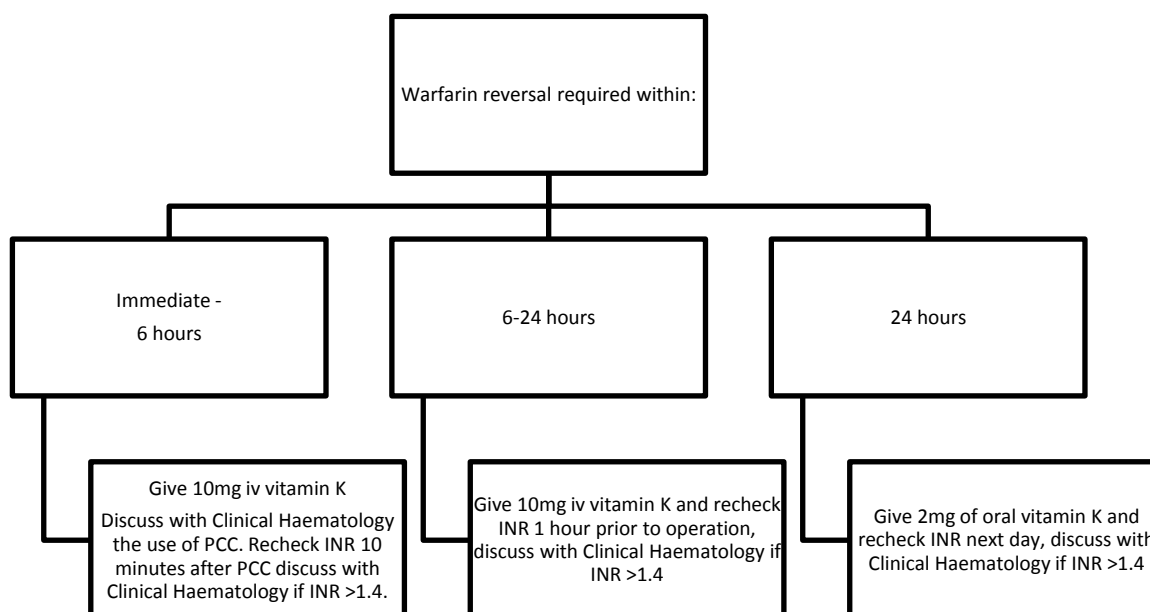
Patients with artificial heart valves should be discussed with Cardiology

Patient who have had a recent thrombosis (within the last 6 weeks) or have a target INR > 2.5 should be discussed with Clinical Haematology.

### Low risk of thrombosis

This is patients with atrial fibrillation or distant thrombosis (more than 6 weeks ago)

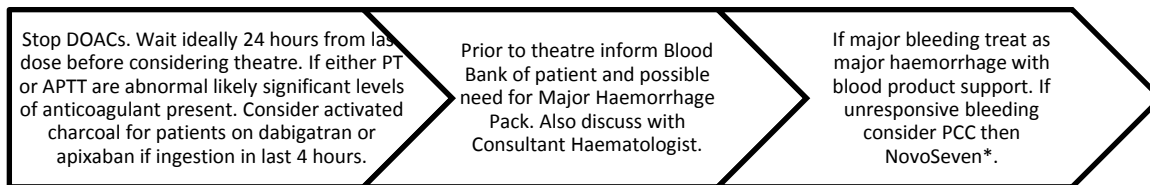
### Warfarin



- Prothrombin Complex Concentrate (PCC), currently Beriplex, is a factor concentrate of II, VII, IX and X. It rapidly reversed warfarin but comes with a significant risk of thrombosis (20%). The patient's weight and INR is required for dosing.
- Patient who attend hospital and may need theatre should be given iv vitamin K as soon as possible as this may prevent the need for PCC if they require an operation later in their hospital stay.
- When haemostasis is secure start prophylactic LMWH. Restart warfarin at usual dose when eating and no epidural. Continue LMWH until INR therapeutic for 2 days. Can be discharged on LMWH.

### DOACs – Dabigatran, Apixaban, Edoxaban or Rivaroxaban

Part from dabigatran there is no specific reversal agent for these drugs, their short half life means they should be cleared from the circulation within 24 hours of the last dose (unless there is significant renal dysfunction).



When haemostasis is secure start prophylactic LMWH and restart DOAC (12-24 hours after last dose of LMWH) when eating and no further risk of bleeding/requirement for surgical procedures.

\*PCC – 50iu/kg max 5000iu; NovoSeven – 90mcg/kg (rounded down to the nearest 1000mcg) repeated one hour later if no response or loss of response.

### Dabigatran

Check patient's eGFR:

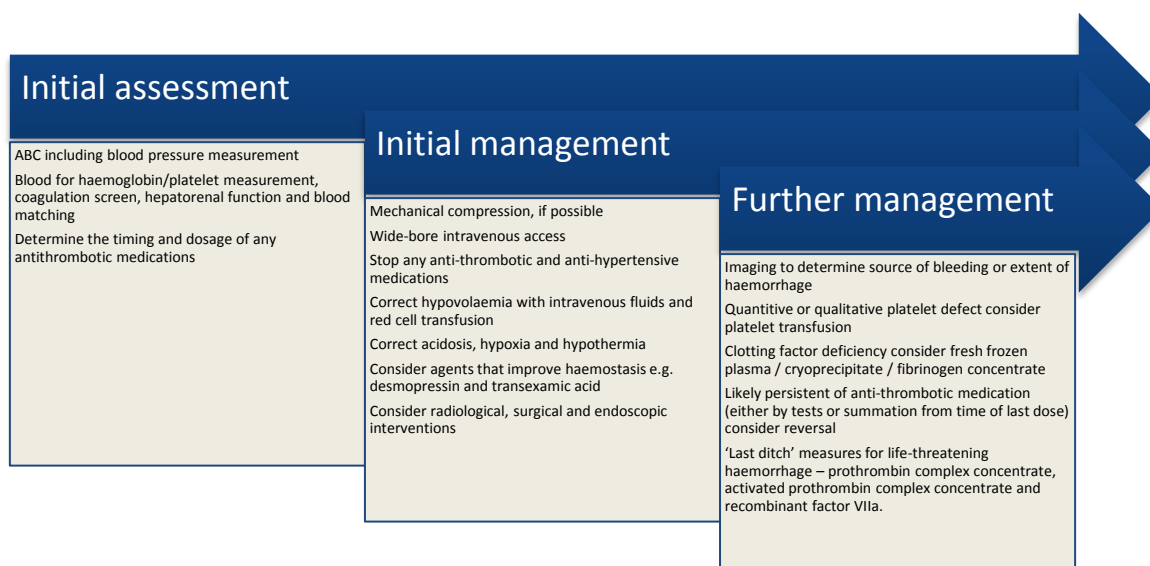
- eGFR >80
  - Last dose >24 hours ago – proceed as normal, consider Idarucizumab\* if major bleeding
  - Last dose <24 hours ago
    - Operation can wait until >24 hours after last dose – after 24 hours proceed as normal, consider Idarucizumab\* if major bleeding
    - Operation cannot wait<sup>‡</sup> until >24 hours after last dose – give 5g Idarucizumab\*
- eGFR 50-80
  - Last dose >48 hours ago – proceed as normal, consider Idarucizumab\* if major bleeding
  - Last dose <48 hours ago
    - Operation can wait until >48 hours after last dose – after 48 hours proceed as normal, consider Idarucizumab\* if major bleeding
    - Operation cannot wait<sup>‡</sup> until >48 hours after last dose – give 5g Idarucizumab\*
- eGFR <30
  - Last dose >72 hours ago – proceed as normal, consider Idarucizumab\* if major bleeding
  - Last dose <72 hours ago
    - Operation can wait until >72 hours after last dose – after 72 hours proceed as normal, consider Idarucizumab\* if major bleeding
    - Operation cannot wait<sup>‡</sup> until >72 hours after last dose – give 5g Idarucizumab\*

\*Idarucizumab is available from both the Alex and WRH Emergency Drug Cupboards after discussion with a Consultant Haematologist. It is given as a 5g infusion over 10 minutes. A second dose should be considered if there is evidence of a significant bleed or need for another procedure.

<sup>‡</sup>The decision on when the patient requires surgery, and therefore whether Idarucizumab is required, should only be made by the Consultant Surgeon.

Please note that the key documents are not designed to be printed, but to be used on-line. This is to ensure that the correct and most up-to-date version is being used. If, in exceptional circumstances, you need to print a copy, please note that the information will only be valid for 24 hours and should be read in conjunction with the key document supporting information page

## Management of patients on oral anticoagulants who are bleeding



### High risk of thrombosis

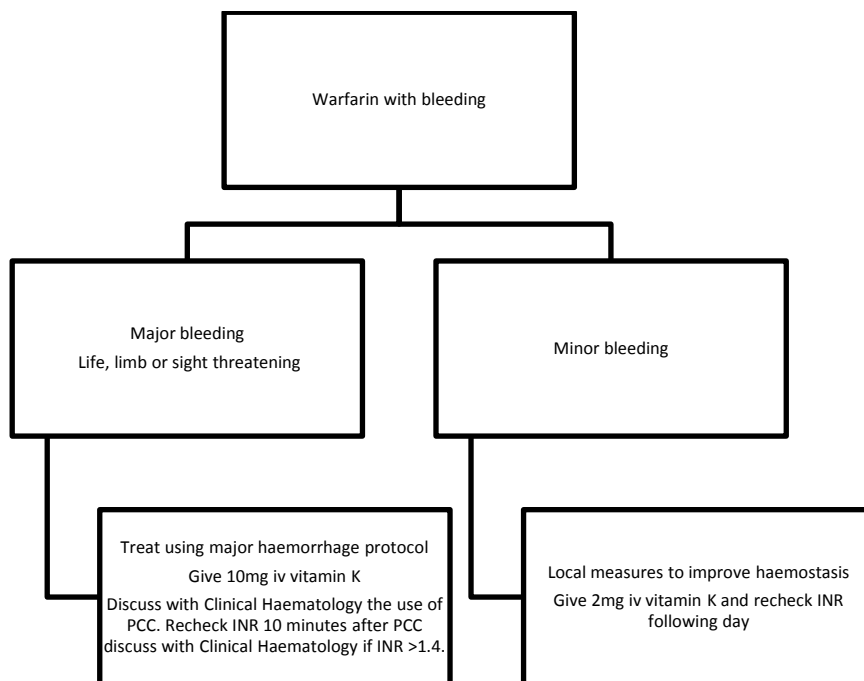
Patients with artificial heart valves should be discussed with Cardiology

Patient who have had a recent thrombosis (within the last 6 weeks) or have a target INR>2.5 should be discussed with Clinical Haematology.

### Low risk of thrombosis

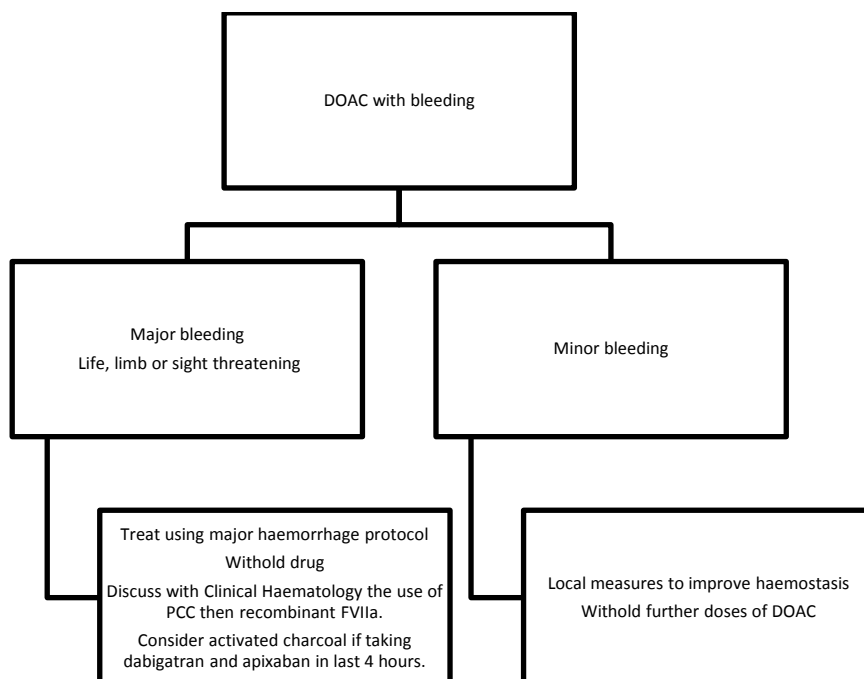
This is patients with atrial fibrillation or distant thrombosis (more than 6 weeks ago)

**Warfarin**



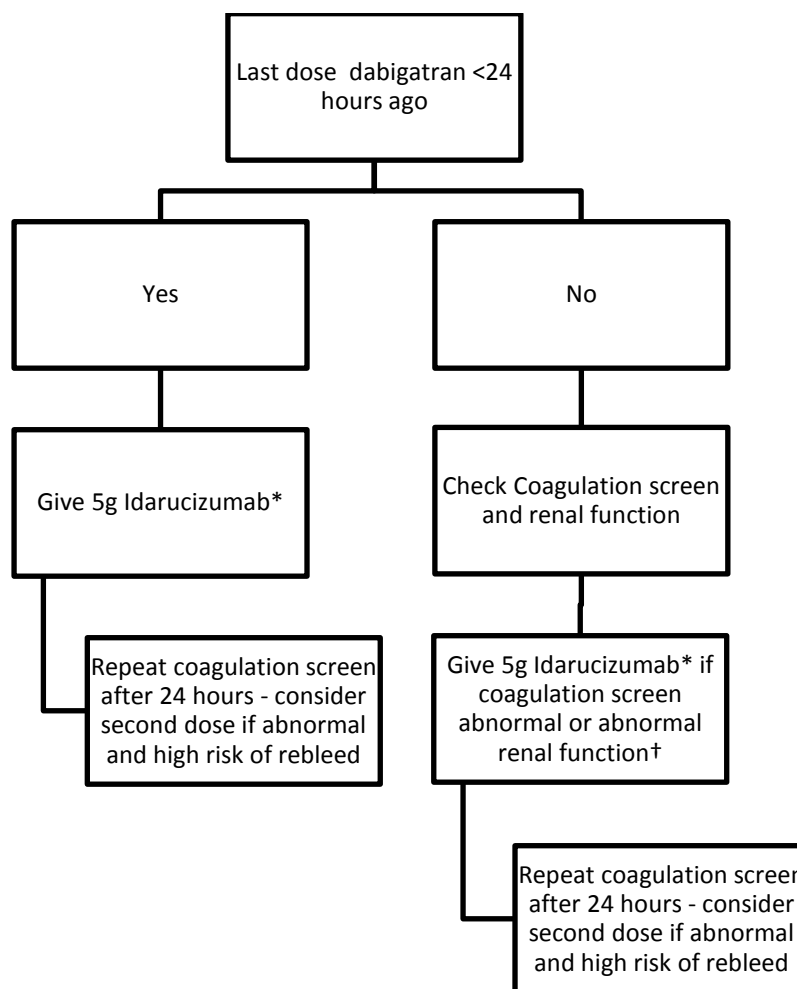
When haemostasis is secure consider prophylactic LMWH. Re-assess patient whether warfarin is beneficial. If re-starting warfarin restart warfarin at usual dose when eating and no epidural. Continue LMWH until INR therapeutic for 2 days. Can be discharged on LMWH.

**DOACs**



When haemostasis is secure consider prophylactic LMWH. Re-assess patient whether DOAC is beneficial. If re-starting DOAC restart at usual dose when eating and no epidural and >12 hours from last dose of LMWH.

**Patient taking dabigatran attends with a major life, limb or sight threatening bleed**



\*Idarucizumab is available from both the Alex and WRH Emergency Drug Cupboard after discussion with a Consultant Haematologist. It is given as a 5g infusion over 10 minutes. A second dose should be considered if there is evidence of a significant rebleed.

†Give Idarucizumab if eGFR:

- 50-80 and last dose within 48 hours
- <30 and last dose within 72 hours

## Overdosage of oral anticoagulants

### Warfarin

INR:

- >8.0 – give 1mg oral vitamin K and repeat following day
- <8.0 – withhold warfarin until INR within normal range (daily INRs)
- Treat bleeding as above

### DOACs

#### Dabigatran

- Withhold further doses
- Consider activated charcoal if ingestion in last 3 hours
- Consider dialysis or Idarucizumab if significant overdosage (>6 tablets in 24 hours or GFR<15mls/min)
- Treat bleeding as above

#### Apixaban

- Withhold further doses
- Consider activated charcoal if ingestion in last 3 hours
- Consider dialysis if significant overdosage (>6 tablets in 24 hours or GFR<15mls/min)
- Treat bleeding as above

#### Rivaroxaban or Edoxaban

- Withhold further doses
- Treat bleeding as above

## Management of low INRs

### Atrial fibrillation

Increase dose as necessary, no requirement for alternative anticoagulation.

### Mechanical heart valves

Refer to the ESC guidelines 2012 for target INR range based on valve type and patient factors – table shown below: (European Heart Journal 2012;33:2451-2496 or <http://www.escardio.org/guidelines-surveys/esc-guidelines/Pages/valvular-heart-disease.aspx>)

**Table 20** Target international normalized ratio (INR) for mechanical prostheses

Prosthesis thrombogenicity <sup>a</sup>	Patient-related risk factors <sup>b</sup>	
	No risk factor	Risk factor $\geq$ 1
Low	2.5	3.0
Medium	3.0	3.5
High	3.5	4.0

<sup>a</sup>Prosthesis thrombogenicity: Low = Carbomedics, Medtronic Hall, St Jude Medical, ON-X; Medium = other bileaflet valves; High = Lillehei-Kaster, Omniscience, Starr-Edwards, Bjork-Shiley and other tilting-disc valves.

<sup>b</sup>Patient-related risk factors: mitral or tricuspid valve replacement; previous thromboembolism; atrial fibrillation; mitral stenosis of any degree; left ventricular ejection fraction <35%.

## Management of a Sub-Therapeutic INR during Routine Monitoring

- If the INR is below the recommended range but 2.0 or more (e.g. target INR 3.0, range 2.5 – 3.5), increase warfarin dose and repeat INR weekly until in range
- If the INR is <2.0 but >1.6 (i.e. 1.7/1.8/1.9), administer low molecular weight heparin (e.g. enoxaparin 1mg/kg bd), increase the warfarin dose and repeat INR every 48-72 hours until >2.0
- If the INR is 1.6 or less, administer low molecular weight heparin immediately (e.g. enoxaparin 1mg/kg bd), but also consider discussing with cardiology urgently, particularly if mechanical valve is mitral, as iv unfractionated heparin may be preferred
- If eGFR is <30 and heparin is required, administer a single dose of enoxaparin 1mg/kg and discuss patient with cardiology as iv unfractionated heparin may be required
- Consider patient factors if INR control is poor (adherence to prescribed therapy, illness, interacting drug therapy, lifestyle factors including diet and alcohol, cognitive function)
- Novel anticoagulants (dabigatran, rivaroxaban, apixaban, edoxaban) **CANNOT** be used in place of warfarin for anticoagulation with mechanical heart valves.

**If patient is unwell with new heart failure or chest pain, please contact cardiology consultant or registrar urgently via Worcestershire Royal Hospital switchboard**



### Treatment of DVT/PE

- Recent thrombosis (previous 6 weeks) with sub-therapeutic INR
  - INR 1.6-2.0 – increase dose of warfarin, recheck INR next day and give treatment dose LMWH if still <2.0 until INR >2.0
  - INR <1.6 – increase dose of warfarin, give treatment dose LMWH until INR >2.0
- Distant thrombosis (more than 6 week previously) with sub-therapeutic INR
  - INR 1.6-2.0 – increase dose of warfarin, recheck INR after 48 hours and give treatment dose LMWH if still <2.0 until INR >2.0
  - INR <1.6 – increase dose of warfarin, recheck INR after 24 hours and give treatment dose LMWH if still <2.0 until INR >2.0

Patients who have previously had a recurrent thrombosis with a sub-therapeutic INR should be started on therapeutic LMWH whenever the INR is lower than the normal range.

## Inpatient warfarin management

### Prescription charts

All VKAs should be prescribed on the designated WHAT 'Adult Oral Anticoagulant Chart & Discharge Referral' WR1779 Version 5, called 'oral anticoagulant chart' in this document. All the required information should be entered for each patient. The chart is designed for warfarin prescribing, if acenocoumarol or phenindione is used then this should be written clearly on the chart. It should also be recorded on the patient's main drug chart that they are on a VKA and that the oral anticoagulant chart is also in use.

### Initiation of Warfarin

Before initiation of warfarin the patient should be fully counselled over the risks and benefits of warfarin, family members/carers may also be involved. This discussion along with the indication, target INR and intended duration should be documented in the notes and on the anticoagulant chart. Warfarin requires a loading dose which is higher than the normal maintenance dose, it is during the initiation of warfarin that there is the highest risk of a high INR and therefore bleeding complications. There are three initiation regimens:

1. Standard dose induction, this aims to achieve a therapeutic INR within 3-4 days and is used to reduce the time that the patient is on alternative anticoagulants, e.g. heparin, following the diagnosis of a thrombosis.
2. Low dose induction, this is for patients that require a therapeutic INR within 3-4 days but are at a higher risk of bleeding.
3. Very low dose induction, this is for patients usually in the community who require warfarin for AF without evidence of thrombosis. The patient receives 1mg for a week then has an INR check and the dose is increased by 1mg/week until the INR is therapeutic. The advantage to this regimen is the lower frequency of INR checks and the low probability of a high INR.

The first two regimens tend to be used in hospital. When commencing a patient on warfarin it is important to determine if the patient requires a standard or low dose induction. Risk factors requiring a low dose regimen are listed at the front of the oral anticoagulant chart. If a patient has one of these factors then the low dose regimen should be used. The person prescribing the warfarin must tick if a risk factor is present and sign that either the low or standard induction regimen is to be used.

Once it is determined which regimen is to be used then that days INR and warfarin dose must be entered in the chart, this is then signed for. The nurse administering the warfarin should only administer the warfarin if the chart is properly completed. For the first four days there must be a daily INR performed and recorded on the chart. Dosing is dependent on the INR and suggested doses are recorded on the chart. Warfarin should not be administered without a daily INR.

It might be prudent to start warfarin at the start of a week, maintaining them on low molecular weight heparin (LMWH) if there is a thrombosis, if the patient is going home to prevent problems with INR checks over the weekend.

Alternative anticoagulation given when there is a thrombosis, usually LMWH, needs to continue for at least five days and until the INR is therapeutic for 2 days, this is due to the initial pro-coagulant activity of warfarin. Consideration should be given to the re-introduction of alternative anticoagulation if the INR falls below the desired therapeutic range in the first 4 weeks of treatment for a thrombosis or if there is a prolonged period (>3 days) when the INR is sub therapeutic.

## Warfarin maintenance

The important factor when managing long-term warfarin is to make only minor changes to the dose to avoid large variations in the INR, suggestions are:

- Not to worry about one off readings slightly outside the normal range (e.g 1.8 or 3.6)
- Trends are more important than one off readings
- Small daily doses of warfarin require small adjustments, adjust total weekly dose rather than daily dose.

When a patient is admitted on warfarin page 2 of the oral anticoagulant chart needs to be completed. Information on pre-admission dose, target INR, indication and intended duration needs recording on the chart and in the medical notes. An INR must be recorded on admission and no warfarin should be prescribed or administered without an INR. For each day the prescriber must write the dose and the INR, where the INR is not required an 'X' must be put in the box and this signed for. The nurse administering the warfarin must sign and note the time of the dose, warfarin shouldn't be administered without either an INR or an 'X' in the box.

Hospital in-patient monitoring requirements are higher than outpatients as illness, drugs and changes in diet may affect the INR, suggested monitoring schedule is:

- Daily INR for very ill patients, those started on antibiotics, those with liver dysfunction and those who have had drugs started or stopped which are known to interact with warfarin (see Appendix 1 'Interactions' of the British National Formulary, further information can also be sought from Medicines Information ext 30235).
- Every third day INR for patients not discussed in 1.
- Outpatient style monitoring is suitable for long-term rehabilitation patients.

Suggested dose changes for a target INR of 2.5:

INR	<1.5	1.5-1.9	2.0-3.0	3.1-3.9	4.0-5.0
Dose adjustment	Increase by 20%	Increase by 10%	No change	Decrease by 10%	Decrease by 20%

## Drugs interacting with warfarin

Prescribers and pharmacists must check the potential interaction of any medicine that is to be prescribed concomitantly with oral anticoagulants - see the latest edition of the BNF Appendix 1: Interactions or call the local Medicines Information Centre (ext 30235). Patients must be told to check any new or existing non-prescription medicines with the pharmacist or with a doctor if they are unsure. It usually takes between five to seven days for the drug to effect the INR.

In patients who are stabilised on warfarin and whose INR is within the target range on oral anticoagulants, control can be disrupted by:

- Initiating a new medicine which potentiates or inhibits the oral anticoagulant effect.
- Stopping an interacting medicine, the effect of which has already been compensated for through dose adjustment with the oral anticoagulant.

**For short courses (up to 5 days) of a new medicine**, oral anticoagulant dose adjustment is not usually necessary but the dose of warfarin should be reduced or omitted over this timescale if a strongly potentiating medicine is prescribed.

**For longer courses of treatment**, some initial alteration to the anticoagulant dose should be considered (especially if the INR is towards or at the upper limit) but in all cases, INR must be checked regularly after starting the new medicine and the oral anticoagulant dose adjusted accordingly. When the new medicine is stopped, a return to the previous maintenance dose may be needed.

**Antibiotics** – antibiotics may alter the gut flora changing the amount of vitamin K absorbed by the gut, therefore altering the INR. Patients starting antibiotics should have their INR more closely monitored.

**Alcohol** - in regular amounts alcohol acts as a hepatic enzyme inducer and can result in an increase in the maintenance oral anticoagulant dose. However, pulsed alcohol excess can potentiate the anticoagulant effect in a dose-dependent way. Patients should be warned to drink only in moderation, to avoid binge drinking and to be reasonably consistent in their alcohol consumption. Variable alcohol intake is one of the commonest reasons for poor anticoagulant control.

**Diet** - Major changes in diet (especially involving salads and vegetables) may affect warfarin control. Cranberry juice should be avoided. Refer to booklet/GP for further information on diet and lifestyle changes.

### **Discharge arrangements**

Inadequate follow-up arrangements are a major cause of VKA incidents. When a patient is discharged on VKAs it is the duty of the discharging doctor to ensure that the patient, GP and anticoagulant clinic are fully informed of the follow-up arrangement for INR testing. The patient must be discharged with their warfarin book completed and the trust patient information leaflet 'Anticoagulation Therapy Monitoring'. It is important if the patient is on drugs that potentially interact with warfarin that this information is passed onto the clinic taking over the warfarin dosing. Page 3 of the oral anticoagulation chart must be completed. There are three scenarios for discharge:

1. Patient newly started on warfarin. Initial follow-up is with the hospital for all patients. A follow-up appointment must be arranged by phoning ext 30863/30722. If the patient is discharged over the weekend this can be done on Monday morning, but it is unlikely there will be space for a clinic appointment that day so alternative arrangements may have to be made. Once follow-up arrangement has been made then page 3 of the anticoagulation chart must be completed in full and pages 1 to 3 faxed to the anticoagulant clinic on ext 30136.
2. Patient established on warfarin normally attending the hospital anticoagulant clinic, same arrangements as above.
3. Patient established on warfarin normally managed by the GP. An appointment must be made for follow-up by the GP anticoagulant clinic. Page 3 of the anticoagulant chart must then be completed and pages 1-3 faxed to the GP practice. If the GP practice is unwilling to take the patient back they must be referred to the hospital INR clinic.

Pharmacy will not dispense warfarin without pages 1 to 3 of the anticoagulant chart being correctly completed. Patients in whom there has been a recent dose change or have had drugs that interact with warfarin started or stopped must have arrangements for a INR check in the first 3 days of discharge, this

may mean them returning to the hospital for the INR check. Patients felt safe to be discharged with an INR greater than 4 should have an INR performed the following day.

### **Information for Patients**

All patients discharged from hospital who are newly started on oral anticoagulants should be given:

The yellow BSH/NPSA 'Oral Anticoagulant Therapy Record Book', completed with their recent INR results and doses.

A copy of the Trust Anticoagulant Service Information leaflet for patients.

A supply of 0.5mg, 1mg, and 3mg warfarin tablets (or appropriate phenindione tablets if this is used), depending on the patient's dose

Verbal instructions about oral anticoagulant therapy.

An appointment to have the next anticoagulant test / dose on an appropriate day.

All patients who are discharged on warfarin (new or old patients) should be given a copy of their inpatient anticoagulant chart to take home.

## Part 2 – In-Patient Anticoagulation With Oral Anticoagulants In WHAT -

### Responsibilities Of Each Profession

The Trust Oral Anticoagulant Guideline and Procedures is available on the Intranet and contains all the clinical information needed to prescribe oral anticoagulants safely and effectively. However there are still many occasions where this does not happen. It has been suggested that defining the responsibilities of each profession in managing oral anticoagulants would help to address the difficulties in the practical implementation of the guideline, and thereby improve the safety of warfarin prescribing within the Trust. This document defines all the tasks required by the MDT to ensure that anticoagulation treatment with warfarin is safe and appropriate to individual patient need. The overall responsibility for ensure each defined task is completed is identified to provide role definition and further enhance patient safety.

Task	Responsibility Of
<b>Newly initiated patients</b>	
<b>Pre-Treatment</b>	
Decision to initiate oral anticoagulant	AUTHORISED PRESCRIBER
Discussion of risks/benefits with patient and obtaining patient consent	AUTHORISED PRESCRIBER
Decision on: Target INR Duration of treatment Frequency of INR testing	AUTHORISED PRESCRIBER
Documentation of all of above in notes and relevant section on oral anticoagulant prescription chart	AUTHORISED PRESCRIBER

<b>ALL PATIENTS (NEW AND ESTABLISHED)</b>	
<b>Prescribing</b>	
Organisation of baseline bloods and INR	AUTHORISED PRESCRIBER*
Documentation of baseline bloods and INR	AUTHORISED PRESCRIBER*
Annotation made on in-patient drug chart to indicate patient on oral anticoagulant as per Trust Medicines Policy	AUTHORISED PRESCRIBER*
Request card completed for INR to be taken the next morning or where INR result not required that day, INR box crossed through on oral anticoagulant prescription chart	AUTHORISED PRESCRIBER*
Nurse looking after patient informed of decision to treat and arrangements for blood test communicated	AUTHORISED PRESCRIBER*
Check that blood for INR taken by 10am daily	NURSE **
Where no phlebotomy service or generic worker available, to ensure blood taken by 10am, refer back to prescriber	NURSE

INR written in the chart and dose prescribed on oral anticoagulant chart by 6pm that day in line with Trust dosing guidance	AUTHORISED PRESCRIBER*
<b>Pre-administration checks</b>	
INR documented on drug chart or INR box crossed through (indicating INR result not due that day) and days dose signed for.	NURSE
Appropriateness of prescribed dose to be administered evaluated against documented INR and guideline dosing advice Where doubt as to: <ul style="list-style-type: none"> <li>appropriateness of dose</li> <li>impact of interacting concurrent medicines by checking relevant section on chart or where not known</li> <li>discussion with pharmacist</li> <li>change to clinical condition exists, <b>referral</b> to prescriber or clinical pharmacist made (on-call pharmacist out of hours).</li> </ul>	NURSE
Checking oral anticoagulant prescription is prescribed according to oral anticoagulant guideline: <ul style="list-style-type: none"> <li>Appropriateness of dose</li> <li>Concurrent medication evaluated for potential interaction with oral anticoagulant, clinical significance evaluated and details documented on oral anticoagulant chart and appropriate paperwork</li> <li>Administration guidance to nursing staff pro-actively and as requested</li> </ul> <b>Where dose change required</b> , prescriber <b>verbally</b> contacted, clinical decision made and agreed adjustments documented on oral anticoagulant prescription chart and associated paperwork according to guideline and communicated to the responsible nurse	PHARMACIST
<b>Administration</b>	
Dose administered and administration details documented on oral anticoagulant prescription chart	NURSE
In the event of a non-administration, <ul style="list-style-type: none"> <li>appropriate coding, documentation and notification of the non-administration made to the prescriber</li> <li>Clinical impact evaluated and alternative plan defined and undertaken</li> </ul>	NURSE  AUTHORISED PRESCRIBER
<b>Discharge</b>	
<b>1. Anticoagulation clinic-managed oral anticoagulant treatment</b> (including ALL newly initiated patients)	

Completing discharge prescription and referral paperwork	AUTHORISED PRESCRIBER*
Documenting indication, target INR, required frequency of testing, dose definition for discharge and any other clinically significant information on appropriate paperwork <b>AND the patient-held record (OAT PACK)<sup>1</sup></b>	AUTHORISED PRESCRIBER*
Supplying an appropriate quantity of oral anticoagulant in appropriate strengths seeking to minimise risk of patient confusion and enhance concordance	PHARMACIST
Ensuring patient has had supplementary counselling on oral anticoagulant therapy and the opportunity to ask questions if needed	PHARMACIST/ NURSE
Arranging appointment with clinic, sending referral form and copy of in-patient chart to clinic	NURSE/WARD CLERK***
<b>2. GP-managed oral anticoagulant treatment</b>	
Contact made with GP and agreement to take over oral anticoagulant management made	AUTHORISED PRESCRIBER*
Arrangements in place with GP surgery on when blood monitoring to be next undertaken (date to be specified) after discharge and communication of this to patient/carer/relative/nursing home as appropriate	AUTHORISED PRESCRIBER*
Discharge prescription and referral paperwork completed in a timely manner appropriate to discharge date and time	AUTHORISED PRESCRIBER*
Indication, target INR, required frequency of testing, initial dose definition and any other clinically significant information documented on appropriate paperwork and patient-held record	AUTHORISED PRESCRIBER*
Appropriate quantity of oral anticoagulant in appropriate strengths supplied (to minimise risk of patient confusion over dose).	PHARMACIST
Ensuring patient has had supplementary counselling on oral anticoagulant therapy and the opportunity to ask questions as needed	PHARMACIST/ NURSE

**Notes:**

\* Where Trust approved local arrangement exists as appropriate Advanced Nurse Practitioner role

\*\*This should be done by phlebotomist or generic worker whenever possible but it remains the overall responsibility of the nurse to ensure happens.

\*\*\*Where local agreement exists this may be done by ward clerk but proper arrangements must be in place to ensure this happens if ward clerk not available/present that day or outside of their hours

<sup>1</sup> Oral Anticoagulation Therapy Pack (contains the OAT Record Book, the OAT Important Information for Patients Booklet, the OAT Important Information for Dental Patients Leaflet, and an Anticoagulant Alert card). OAT Packs are to be supplied from Ward or Clinic stocks

Please note that the key documents are not designed to be printed, but to be used on-line. This is to ensure that the correct and most up-to-date version is being used. If, in exceptional circumstances, you need to print a copy, please note that the information will only be valid for 24 hours and should be read in conjunction with the key document supporting information page



## Procedures/Competences

The following documents are adapted from the work competences published by the NPSA to include local detail as described in the Trust 'Oral Anticoagulant Guideline and Procedures'. The content should be used by the appropriate professional groups when assessing the competences of staff to initiate, monitor, dispense, administer and discharge patients on warfarin, within their own individual professional competency assessment framework.

### Initiating oral anticoagulant therapy – Authorised Prescribers

Some aspects (excluding prescribing) also undertaken by Anticoagulant Nurses and Advanced Nurse Practitioners

- 1. Ensure you are familiar with the Trust Guidelines and Procedures on ORAL ANTICOAGULANTS WAHT-HAE-002.** Read the patient's notes and prescription, and identify any special instructions, investigations (including abnormal blood test results), or issues for which you need to seek advice.
- 2.** Assess the appropriateness and risks of the intended treatment against the patient's diagnosis, current health and social status, medication, allergy status, other treatment and the patient's preferences.
- 3.** Determine the appropriate loading dose regimen for the patient, which medicines to prescribe, the dosage, the frequency of administration, and the most effective route of administration.
- 4. Decide who will monitor and dose the anticoagulants** and what day would be the safest time to start treatment (see loading dose schedule), bearing in mind the need for daily INR monitoring for the first 4-5 days. If there is any doubt it is safest to start warfarin on a Sunday, Monday or Tuesday, giving extra days of therapeutic dose Clexane if necessary until the INR is within therapeutic range
- 5.** Document the indication for use, target INR, duration of treatment and monitoring plan in the patient's notes. If uncertain, set a review date, which should be at least annual.
- 6.** Order and document baseline INR, APTT ratio and platelet count blood tests prior to the administration of the first dose of anticoagulant. Check liver function if in any doubt about this. Abnormal results may influence the decision to anticoagulate. Consider haemophilia screening if appropriate (see Appendix 1)
- 7.** Ensure that the patient receives verbal and written information concerning their anticoagulant therapy prior to the first dose of anticoagulant, using the yellow BSH/NPSA Oral Anticoagulant Therapy Important Information for Patients pack (including Record

Book and Anticoagulation Alert Card) In addition, give the Trust Anticoagulation Service leaflet explaining local arrangements for anticoagulation dosing and monitoring. If patient to be transferred to GP dosing then it needs to be explained that GP service may be different.

8. Prescribe the anticoagulant treatment according to the Medicines Policy and the Trust Oral Anticoagulant Guidelines and Procedures and before 6pm daily to ensure safe and optimal delivery of treatment

9. Prescribe the warfarin on the main prescription chart in the Regular Medicines section, but write across the administration boxes ' see separate chart' and then complete the separate Trust warfarin prescription chart, including:

- indication and target INR
- the approved name of anticoagulant medicine(s);
- dose, route and frequency of administration;
- monitoring plan

10. Prescribe legibly, ensuring your intention for treatment and monitoring is clear, accurate and complete and that there are no ambiguities.

11. Inform/ discuss with the nurse looking after the patient of the decision to treat and the arrangements for the blood tests

12. Review the anticoagulant prescription in accordance with the monitoring plan. When there have been two consecutive INR results within the therapeutic range, the frequency of testing may be reduced to every 3 days providing that the clinical situation remains stable and no interacting medicines have been prescribed. **If the INR is not to be measured put a cross in the INR box for that day, otherwise it will be queried and/or the patient may not receive their dose.**

13. Modify any subsequent prescriptions in accordance with national and local guidelines and in light of the laboratory test results, side effects, complications and response to treatment. If any doses have not been administered as prescribed, take account of this and seek advice where necessary.

14. Recognise when you need help and seek advice and support from an appropriate source when the needs of the individual and the complexity of the case are beyond your

<p>competence and capability.</p> <p><b>15.</b> When transferring the care of the patient to another healthcare team and especially on discharge from hospital, ensure that the new team is sent information concerning the clinical indication for use, target INR, intended duration of therapy, current prescription and recent laboratory test results.</p> <p><b>16.</b> Arrange for the patient to receive an initial supply of warfarin along with clear instructions of how to make up the dose and when to take it.</p>	
----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------	--

### MAINTAINING ORAL ANTICOAGULANT THERAPY

<p><b>You need to:</b></p> <ol style="list-style-type: none"><li><b>1.</b> Read the patient's notes, previous prescription and protocol, and identify any special instructions. Review the results of all relevant investigations (including blood test results) and identify any issues on which you need to seek advice.</li><li><b>2.</b> Greet, accurately identify the patient and introduce yourself and any colleagues present to the patient and/or carer.</li><li><b>3.</b> If a carer is present, ensure that the patient consents to their presence throughout the assessment and is willing for them to receive the same information as that given to the patient.</li><li><b>4.</b> Undertake and document measurement of the INR in accordance with national and local guidelines.</li><li><b>5.</b> Review the patient's history since their last attendance.</li><li><b>6.</b> Following agreed protocols and/or care pathways, explain the treatment alternatives and their risks and benefits to the patient and/or carer together with any potential side effects and their management, and accurately answer any questions at a pace and level that is appropriate to:<ul style="list-style-type: none"><li>• their emotional state;</li><li>• their level of understanding;</li><li>• their culture and background;</li><li>• their preferred ways of communicating;</li></ul></li></ol>	
---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------	--

<ul style="list-style-type: none"> <li>• their needs.</li> </ul> <ol style="list-style-type: none"> <li>7. Explain any lifestyle changes that will be needed in order to ensure good anticoagulant control.</li> <li>8. Check that the patient and/or carer understand the treatment choices being offered, the implications of this choice and any potential side effects together with their management.</li> <li>9. Ensure that the patient receives verbal and written information concerning the way in which their anticoagulant therapy is to be continued.</li> <li>10. Update the patient-held record of anticoagulant treatment in response to the patient's INR using local guidelines and decision support software e.g. DAWN</li> <li>11. Inform the patient and their GP about the outcome of the assessment, in accordance with local policy. If the patient has a high or low INR take appropriate action, following the clinical guideline and local procedures.</li> <li>12. Record and report your findings, recommendations, patient and/or carer's response and issues to be addressed according to local guidelines.</li> <li>13. Recognise when you need help and seek advice and support from an appropriate source when the needs of the individual and the complexity of the case are beyond your competence and capability.</li> <li>14. When transferring the care of the patient to another healthcare team and especially on discharge from hospital, ensure that the new team is sent information concerning the clinical indication for use, target INR, intended duration of therapy, current prescription and recent laboratory test results.</li> </ol>	
--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------	--

**DISPENSING ORAL ANTICOAGULANTS**

<p><b>Please note Pharmacy staff should follow the more detailed departmental SOP and associated competency documents.</b></p> <p><b>You need to:</b></p> <ol style="list-style-type: none"> <li>1. Find out what the patient already understands and remembers.</li> <li>2. Ensure that the patient has been issued with appropriate information (e.g. yellow book), and has had the contents fully explained to them</li> <li>3. Ensure that arrangements are in place for INR monitoring and follow-up, and that the patient and/or carer understand these. In particular, that the patient knows if they</li> </ol>	
-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------	--

Please note that the key documents are not designed to be printed, but to be used on-line. This is to ensure that the correct and most up-to-date version is being used. If, in exceptional circumstances, you need to print a copy, please note that the information will only be valid for 24 hours and should be read in conjunction with the key document supporting information page

have to wait for a phone-call from the GP/clinic before taking their dose.

4. Check that the INR level is safe before issuing or dispensing repeat prescriptions for oral anticoagulants. Check if the patient is prescribed any interacting medicines and if so make arrangements for additional INR blood tests, and to inform the anticoagulant service that an interacting medicine has been prescribed.

5. Accurately answer any questions relating to the patient's therapy at a pace and level that is appropriate to:

- their emotional state;
- their level of understanding;
- their culture and background;
- their preferred ways of communicating;
- their needs.

6. Explain in clear and simple terms what the medicines are for and when the patient needs to take them.

7. Explain any lifestyle changes that will be needed in order to ensure good anticoagulant control.

8. Check that the patient and/or carer understand the prescribed treatment and the lifestyle implications of that treatment.

9. Ensure that the patient and/or carer understands how to take the correct dose in relation to the number of milligrams and the number of tablets to be taken.

10. Ensure the medicines are dispensed with written instructions (e.g. patient information leaflet) on what they are for, how and when to take them, the date dispensed and the expiry date.

11. Explain the importance of remembering to take every dose prescribed.

12. Inform the patient of side effects or symptoms the medicines may produce, how common or rare these are, how to recognise them and what action to take.

13. Ensure the patient is aware of the potential for anticoagulants to interact with other medicines, including those bought over-the-counter, and that they understand the need

<p>to consult with a pharmacist or the prescriber before taking other medicines.</p> <p>14. Offer compliance aids, if appropriate, to help the patient to remember to take every dose prescribed. However, a risk assessment should be undertaken on the use of Monitored Dosage Systems for anticoagulants for individual patients. The general use of Monitored Dosage Systems for anticoagulants should be minimised as dosage changes using these systems are more difficult.</p>	
---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------	--

### **ADMINISTERING (AND DISCHARGING PATIENTS ON) ORAL ANTICOAGULANTS**

<p><b>Administration to in-patients</b> <b>You need to:</b></p> <ol style="list-style-type: none"><li>1. If INR test ordered, check that the blood for INR has been taken by 10am daily, if not take blood or refer back to prescriber</li><li>2. Document the INR result on the warfarin prescription chart by the end of the early shift 4pm each day, or if not possible to obtain result hand over to late shift</li><li>3. Evaluate the appropriateness of the prescribed dose against the documented INR. Consider the Trust Guideline dosing advice/prescription chart, any interacting medicines or change to patient's clinical condition. If in doubt refer to prescriber or clinical pharmacist (on-call out of hours)</li><li>4. Accurately answer any questions relating to the patient's therapy at a pace and level that is appropriate to:<ul style="list-style-type: none"><li>• their emotional state;</li><li>• their level of understanding;</li><li>• their culture and background;</li><li>• their preferred ways of communicating;</li><li>• their needs.</li></ul></li><li>5. Explain in clear and simple terms what the medicines are for and when the patient needs to take them.</li><li>6. Explain any lifestyle changes that will be needed in order to ensure good anticoagulant control.</li><li>7. Check that the patient and/or carer understand the prescribed treatment and the</li></ol>	
----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------	--

lifestyle implications of that treatment.

8. Where the INR box is completed (either with a result or a cross indicating that an INR is not required) ,administer the prescribed dose and document on warfarin prescription chart

9. If the dose is not administered for whatever reason, document and inform the prescriber

### Discharge

#### You need to:

1. Find out what the patient already understands and remembers.

2. Ensure that the patient has been issued with appropriate information (e.g. yellow book), and has had the contents fully explained to them

3. Ensure that arrangements are in place for INR monitoring and follow-up (date, time and location of new test) as per agreement with the commissioner (making appointments and sending referral form/copy of in-patient chart to GP/clinic may be delegated to the ward clerk), and that the patient and/or carer understand these. In particular, that the patient knows if they have to wait for a phone-call from the GP/clinic before taking their dose.

4. Ensure that the patient and/or carer understands how to take the correct dose in relation to the number of milligrams and the number of tablets to be taken.

5. Ensure the medicines are dispensed with written instructions (e.g. patient information leaflet) on what they are for, how and when to take them, the date dispensed and the expiry date.

6. Explain the importance of remembering to take every dose prescribed.

7. Inform the patient of side effects or symptoms the medicines may produce, how common or rare these are, how to recognise them and what action to take.

8. Ensure the patient is aware of the potential for anticoagulants to interact with other medicines, including those bought over-the-counter, and that they understand the need to consult with a pharmacist or the prescriber before taking other medicines.

9. Discuss with the pharmacist whether a compliance aid would be appropriate, to help the patient to remember to take every dose prescribed. However, a risk assessment should be undertaken on the use of Monitored Dosage Systems for

<p>anticoagulants for individual patients. The general use of Monitored Dosage Systems for anticoagulants should be minimised as dosage changes using these systems are more difficult.</p>	
---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------	--



**Appendix A - Conversion between the drugs**

Starting drug	Convert to	Instructions
Warfarin	LMWH†	Stop warfarin, check INRs daily, start LMWH when INR sub-therapeutic
	Apixaban	Stop warfarin, check INRs daily, start apixaban when INR sub-therapeutic
	Dabigatran	Stop warfarin, check INRs daily, start dabigatran when INR sub-therapeutic
	Rivaroxaban	Stop warfarin, check INRs daily, start rivaroxaban when INR sub-therapeutic
	Edoxaban	Stop warfarin, check INRs daily, start edoxaban when INR <2.5
LMWH	Warfarin	Continue LMWH for at least 5 days and until INR has been therapeutic for 2 days then stop LMWH
	Apixaban	Stop LMWH, start apixaban 0-2 hours before next dose of LMWH would have been due
	Dabigatran	Stop LMWH, start dabigatran 0-2 hours before next dose of LMWH would have been due
	Rivaroxaban	Stop LMWH, start rivaroxaban 0-2 hours before next dose of LMWH would have been due
	Edoxaban	Stop LMWH, start edoxaban 0-2 hours before next dose of LMWH would have been due

Apixaban	LMWH	Stop apixaban, start LMWH 0-2 hours before next dose of apixaban would have been due
	Dabigatran	Stop apixaban, start dabigatran 0-2 hours before next dose of apixaban would have been due
	Rivaroxaban	Stop apixaban, start rivaroxaban 0-2 hours before next dose of apixaban would have been due
	Edoxaban	Stop apixaban, start edoxaban 0-2 hours before next dose of apixaban would have been due
	Warfarin*	Stop apixaban, start LMWH 0-2 hours before next dose of apixaban would have been due, start warfarin next day, continue LMWH for at least 5 days and until INR has been therapeutic for 2 days then stop LMWH
Dabigatran	LMWH	Stop dabigatran, start LMWH 0-2 hours before next dose of dabigatran would have been due
	Apixaban	Stop dabigatran, start apixaban 0-2 hours before next dose of dabigatran would have been due
	Rivaroxaban	Stop dabigatran, start rivaroxaban 0-2 hours before next dose of dabigatran would have been due
	Edoxaban	Stop dabigatran, start edoxaban 0-2 hours before next dose of dabigatran would have been due

	Warfarin*	Stop dabigatran, start LMWH 0-2 hours before next dose of dabigatran would have been due, start warfarin next day, continue LMWH for at least 5 days and until INR has been therapeutic for 2 days then stop LMWH
Rivaroxaban	LMWH	Stop rivaroxaban, start LMWH 0-2 hours before next dose of rivaroxaban would have been due
	Apixaban	Stop rivaroxaban, start apixaban 0-2 hours before next dose of rivaroxaban would have been due
	Dabigatran	Stop rivaroxaban, start dabigatran 0-2 hours before next dose of rivaroxaban would have been due
	Edoxaban	Stop rivaroxaban, start edoxaban 0-2 hours before next dose of rivaroxaban would have been due
	Warfarin*	Stop rivaroxaban, start LMWH 0-2 hours before next dose of rivaroxaban would have been due, start warfarin next day, continue LMWH for at least 5 days and until INR has been therapeutic for 2 days then stop LMWH
Edoxaban	LMWH	Stop edoxaban, start LMWH 0-2 hours before next dose of rivaroxaban would have been due
	Apixaban	Stop edoxaban, start apixaban 0-2 hours before next dose of rivaroxaban would have been due
	Dabigatran	Stop edoxaban, start dabigatran 0-2 hours before next dose of

		rivaroxaban would have been due
	Rivaroxaban	Stop edoxaban, start rivaroxaban 0-2 hours before next dose of edoxaban would have been due
	Warfarin*	Stop edoxaban, start LMWH 0-2 hours before next dose of rivaroxaban would have been due, start warfarin next day, continue LMWH for at least 5 days and until INR has been therapeutic for 2 days then stop LMWH

\*as the DOACs affect the INR it is difficult to determine the effect of the warfarin while also taking a DOAC therefore it is safer to convert to LMWH while introducing the warfarin.

†Low molecular weight heparin

## Appendix B – Drug Interactions

### Interactions with warfarin

#### Examples of drugs which potentiate the effect of warfarin

Allopurinol, capecitabine, erlotinib, disulfiram, azole antifungals (ketoconazole, fluconazole etc), omeprazole, paracetamol (prolonged regular use), propafenone, amiodarone, tamoxifen, methylphenidate, zafirlukast, fibrates, statins (not pravastatin, predominantly associated with fluvastatin), erythromycin, sulfamethoxazole, metronidazole,

#### Examples of drugs which antagonise the effect of warfarin

Barbiturates, primidone, carbamazepine, griseofulvin, oral contraceptives, rifampicin, azathioprine, phenytoin

#### Examples of drugs with variable effect

Corticosteroids, nevirapine, ritonavir

### Interactions with dabigatran

#### P-gp inhibitors which results in increased dabigatran concentration

Contra-indicated: systemic ketoconazole, cyclosporine, itraconazole, tacrolimus and dronedarone.

Caution with co-prescribing: amiodarone, posaconazole, quinidine, verapamil and ticagrelor

#### P-gp inducers which results in decreased dabigatran concentration

Contra-indicated: rifampicin, St. John's wort (*Hypericum perforatum*), carbamazepine, phenytoin and ritonavir (and other proteasome inhibitors).

### Interactions with apixaban

#### P-gp or CYP3A4 inhibitors which results in increased apixaban concentration

Contra-indicated: azole-antimycotics and HIV protease inhibitors.

#### P-gp or CYP3A4 inducers which results in decreased apixaban concentration

Caution with co-prescribing: rifampicin, St. John's wort (*Hypericum perforatum*), carbamazepine, phenytoin and phenobarbitone

### Interactions with edoxaban

#### P-gp or CYP3A4 inhibitors which results in increased edoxaban concentration

Decrease dose to 30mg od when also prescribed ciclosporin, dronedarone, erythromycin, or ketoconazole

### Interactions with rivaroxaban

#### P-gp or CYP3A4 inhibitors which results in increased rivaroxaban concentration

Contra-indicated: azole-antimycotics (except fluconazole), dronedarone and HIV protease

inhibitors.

Caution with co-prescribing when renal dysfunction: clarythromicin and erythromicin

**P-gp or CYP3A4 inducers which results in decreased rivaroxaban concentration**

Contra-indicated: rifampicin, St. John's wort (*Hypericum perforatum*), carbamazepine, phenytoin and phenobarbitone

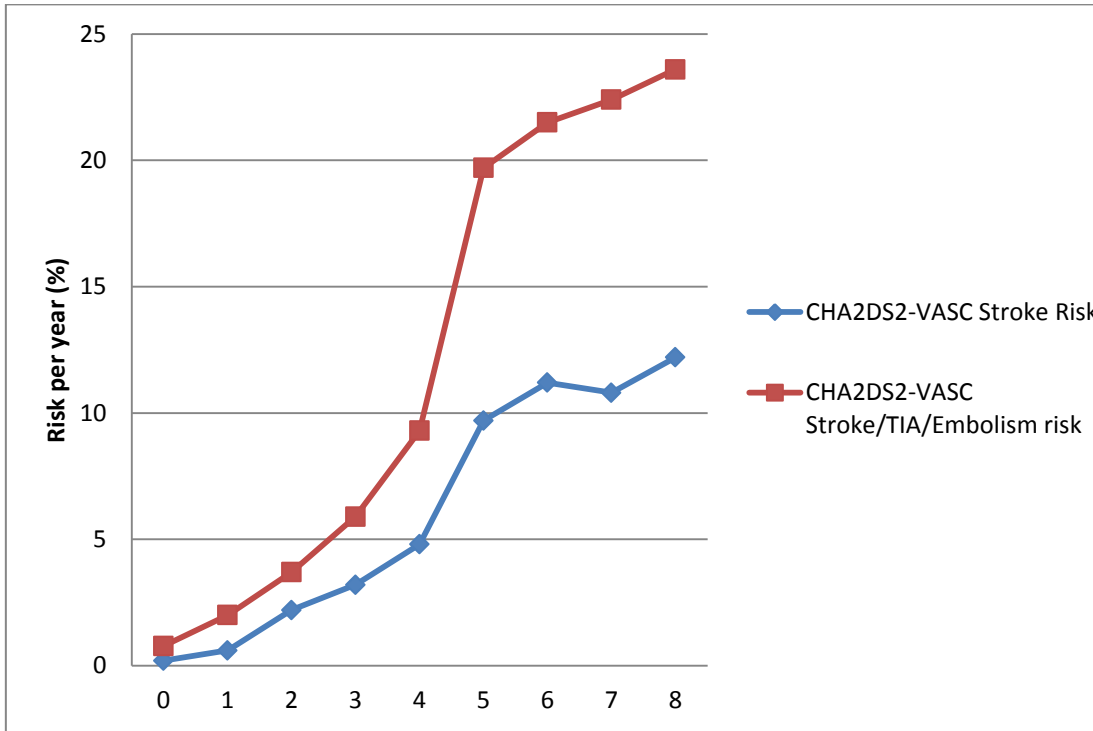
Data from Electronic Medicine Compendium's Summary of Product Characteristics  
(<https://www.medicines.org.uk/emc/>)

## Appendix C – Atrial fibrillation risk calculators

### CHA<sub>2</sub>DS<sub>2</sub>-VASC Score

Risk factor		Score
Age	<65 years	0
	65-74 years	1
	>75 years	2
Female sex		1
Congestive cardiac failure		1
Hypertension		1
Stroke/TIA/Thromboembolism		1
Vascular disease		1
Diabetes		1

TotalScore	Yearly stroke risk (%) without anticoagulation	Yearly stroke, TIA or embolism risk (%) without anticoagulation
0	0.2	0.78
1	0.6	2
2	2.2	3.7
3	3.2	5.9
4	4.8	9.3
5	9.7	19.7
6	11.2	21.5
7	10.8	22.4
8	12.2	23.6



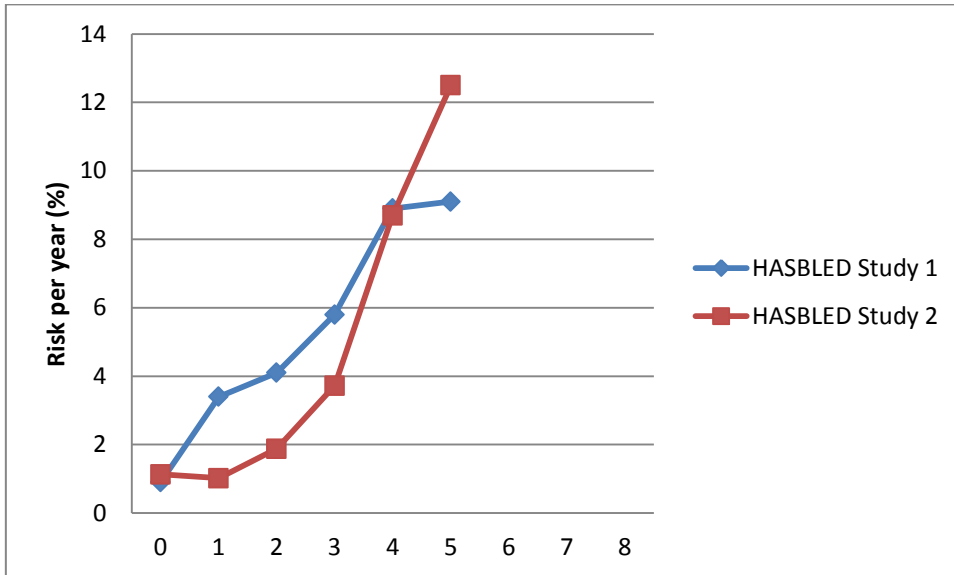
Please note that the key documents are not designed to be printed, but to be used on-line. This is to ensure that the correct and most up-to-date version is being used. If, in exceptional circumstances, you need to print a copy, please note that the information will only be valid for 24 hours and should be read in conjunction with the key document supporting information page



### HASBLED Score

Risk factor	Score
Uncontrolled hypertension (>160 systolic)	1
Renal disease (dialysis, transplant, creatinine >200mmol/L)	1
Liver disease (Bilirubin >2x normal or AST/ALT/ALK PHOS >3x normal)	1
History of stroke	1
Previous major bleeding/predisposition to bleeding	1
Labile INR (TTR<60%)	1
Age >65 years	1
Medication which increases bleeding risk (antiplatelet/NSAIDs)	1
Alcohol/drug use (≥8 drinks/week)	1

Total Score	Yearly major bleeding risk (%)	Yearly major bleeding risk (%)
	Study 1	Study 2
0	0.9	1.13
1	3.4	1.02
2	4.1	1.88
3	5.8	3.72
4	8.9	8.7
≥5	9.1	12.5



Please note that the key documents are not designed to be printed, but to be used on-line. This is to ensure that the correct and most up-to-date version is being used. If, in exceptional circumstances, you need to print a copy, please note that the information will only be valid for 24 hours and should be read in conjunction with the key document supporting information page

## Appendix D – Worcestershire patient information sheets

### Atrial Fibrillation



Patient\_frequently\_a  
sked\_questions\_(Anti

### DVT/PE



Patient information  
on NOACs for the tre

## Appendix E – Electronic Medicines Compendium (EMC) Summary of Product Characteristics (SPC) and Patient Information Leaflets (PIL)

### Apixaban

#### SPC



Apixaban SPC.docx

<https://www.medicines.org.uk/emc/medicine/27220>

#### PIL



Apixaban PIL.pdf

### Edoxaban

#### SPC



Edoxaban SPC.docx

<http://www.medicines.org.uk/emc/medicine/30513>

#### PIL



Edoxaban PIL.pdf

## Rivaroxaban

### SPC



Rivaroxaban  
SPC.docx

<https://www.medicines.org.uk/emc/medicine/25586>

### PIL



Rivaroxaban  
PIL.docx

<https://www.medicines.org.uk/emc/PIL.25591.latest.pdf>

## Dabigatran

### SPC



Dabigatran SPC.docx

<https://www.medicines.org.uk/emc/medicine/24839>

### PIL



Dabigatran PIL.docx

<https://www.medicines.org.uk/emc/PIL.24840.latest.pdf>

## Warfarin

### SPC



Warfarin SPC.docx

<https://www.medicines.org.uk/emc/medicine/25626#PRODUCTINFO>

### PIL

<https://www.medicines.org.uk/emc/PIL.27301.latest.pdf>

Appendix F – ED anticoagulation protocols



Warfarin\_Beriplex\_E  
mergManagement\_04



WRH\_ED\_bleeding\_n  
ewPOanitcoag\_03111