CLINICAL GUIDELINE **Subject: Anticoagulation Policy** **TRUSTWIDE**	NHS Bedford Hospital NHS Trust
Reviewed by: Consultant Haematologist Lead Pharmacist for Anticoagulation	**Key Reference:** NPSA Patient Safety Alert No. 18 Guidelines on oral anticoagulation – British Journal of Haematology 4th Edition
Date of Approval: March 2019	**Review Date: March 2021**

Purpose	This policy aims to amalgamate all current Trust guidance relating to anticoagulation. To reduce the incidence of VTE and provide a consistent and coherent approach towards the use and monitoring of anticoagulant therapy, patient management and co-ordination within Bedfordshire in compliance with the NPSA safety alert, 'Actions that can make anticoagulant therapy safer', March 2007. For the purpose of this guideline 'anticoagulation' refers to warfarin, NOACs, LMWH and heparin. This policy and related policies provide guidance on the management of anticoagulation in adults only.
Objectives	The guidance covers the following key areas: - Prescribing responsibilities for medical and non-medical prescribers: initiation, continuation, monitoring and discontinuation of anticoagulant therapy including switching between anticoagulants - Competency of all staff involved with anticoagulant prescribing, administration, supply and discontinuation. - Safe systems for documenting results and treatment, including effective communication on discharge - Providing the patient with the appropriate information at commencement, throughout the course of treatment and on discharge from inpatient services. - Providing standardised and clinically effective anticoagulation management whilst minimising the risks associated with treatment. - Optimising care to patients receiving anticoagulant therapy in terms of accessibility, continuity and waiting times - Ensuring complete and accurate documentation of the clinic process.
For Use By	All qualified medical and nursing staff prescribing / dispensing / administering parenteral, subcutaneous and oral anticoagulants
Related Policies *Any policies or guidelines that directly impact or are impacted by this Guideline*	Listed within policy.
Definitions *Any Acronyms or Abbreviations used in Guideline*	**ACS** - Acute Coronary Syndrome **AF** - Atrial Fibrillation **APS** - Antiphospholipid syndrome **BSH** - British Committee for Standards in Haematology **CVA** - Cerebral Vascular Accident (Stroke) **DOAC** - Direct Oral Anticoagulant **DTI** - Direct thrombin inhibitor **DVT** - Deep Vein Thrombosis

	FBC - Full blood count **FFP** - Fresh frozen plasma **FXa** - Activated factor X **GORD** - Gastro-oesophageal Reflux Disease **INR** - International Normalised Ratio **IV** - Intra-Venous **LMWH** - Low Molecular Weight Heparin (e.g. tinzaparin) **LFT** - Liver function tests **LSCS** - Lower segment caesarean section **MI** - Myocardial Infarction **NICE** - National Institute for Health and Care Excellence **NMP** - Non-medical Prescriber **NOAC** - Non-Vitamin K antagonist oral anticoagulant **NPSA** - National Patient Safety Agency now National Reporting and Learning System (NRLS) **OAS** Outpatient anticoagulation service **OAT** - Oral Anticoagulation Therapy: including warfarin and NOACs **OOH** - Out of Hours **PCC** - Prothrombin Complex Concentrate **PE** - Pulmonary Embolism **PIL** - Patient information leaflet **PO** - Per os (orally) **POC** - Point of Care **PUD** - Peptic Ulcer Disease **PVD** - Peripheral Vascular Disease **TTO** - 'To Take Out' Discharge prescription **TTR** - Time in Therapeutic Range **VKA** - Vitamin K Antagonist e.g. warfarin **VTE** - Venous Thromboembolism: including DVT, PE and post-thrombotic syndrome **Key words:** *Warfarin, Oral anticoagulants, Anticoagulation, INR, NOAC, DOAC, LWMH, Heparin, Tinzaparin, Beriplex, Apixaban, Edoxaban, Rivaroxaban, Dabigatran, Praxbind, Idarucizumab*
Status / Version Control *Previous versions of the Guideline should be stated here with former name if changed along with dates when they were approved.*	Version 1.0 Supersedes 'Warfarin (Use in adult inpatients)' and 'Oral anticoagulation (Vitamin K antagonists) and the role of the outpatient clinic' clinical guidelines.

Contents

INTRODUCTION

Anticoagulants are high risk medications. This policy provides guidance and signposts to all Trust clinical guidance related to the prescribing, dispensing and administration of warfarin, NOACs/DOACs, tinzaparin and unfractionated heparin to ensure safe and cost-effective use of these medicines.

ASSOCIATED GUIDELINES

- Prevention of Hospital Acquired Venous Thromboembolism
- Prevention and treatment of Venous Thromboembolism in pregnancy and the puerperium
- Atrial Fibrillation in the Acute Setting (investigation and management of)
- Non Vitamin K Antagonist Oral Anticoagulants (NOACs) in Non-Valvular Atrial Fibrillation: Initiation of treatment
- Non Vitamin K Antagonist oral anticoagulants (NOACs): Management of cardiac patients on NOACs
- Unstable angina and non-ST elevation myocardial infarction (management of patients with)
- Prevention of Hospital Acquired Venous Thromboembolism
- Use of Treatment Dose Low Molecular Weight Heparin and Unfractionated Heparin
- Deep vein Thrombosis (DVT) – The management of patients with suspected and confirmed DVT in the Acute Assessment Unit
- Pulmonary Embolism (PE) - The management of patients with suspected and confirmed PE in the Acute Assessment Unit
- The Diagnosis and Management of Heparin induced Thrombocytopenia
- Peri-operative Management of patients on Anti-coagulant and Anti-platelet Agents
- Blood Transfusion Policy

Please refer to the above policies/guidelines for information in relation to these specific medicines/treatments.

1. WARFARIN GUIDANCE

Initiation
Before starting anticoagulation, check: FBC, U+E, LFTs and coagulation screen
Warfarin is prescribed on MedChart under the variable dose tab.

Venous Thromboembolism
Concomitant treatment with LMWH/UFH (bridging) is required for patients with/at high risk of developing venous thromboembolism. Treatment dose LMWH or unfractionated heparin is usually required for 5-7 days until INR is within therapeutic range.

Daily INRs **MUST** be performed for the first four days of treatment.

Warfarin Induction Dosage Chart for Venous Thrombosis
Based on Fennerty et al 1984 and Gedge at al 2000.
*Risk factors: Age >70 years, Liver impairment, Low albumin <36g/L, Weight <60kg, Parenteral feeding, Increased bleeding risk, CCF, COPD, interacting medicines

Day	INR Value in Patients <70 years	Warfarin dose (mg)	INR Value in Patients with risk factors*	Warfarin dose (mg)
1	<1.4	10	<1.4	10
2	<1.8 1.8 >1.8	10 1 0.5	<1.8 1.8-2.0 >2.0	5.0 1.0 0
3	<2.0 2.0-2.1 2.2-2.3 2.4-2.5 2.6-2.7 2.8-2.9 3.0-3.1 3.2-3.3 3.4 3.5 3.6-4.0 >4.0	10 5 4.5 4 3.5 3 2.5 2 1.5 1 0.5 0	<2.0 2.0-2.5 2.6-2.9 3.0-3.2 3.3-3.5 >3.5	5 4 3 2 1 0
4	<1.4 1.4 1.5 1.6-1.7 1.8 1.9 2.0-2.1 2.2-2.3 2.4-2.6 2.7-3.0 3.1-3.5 3.6-4.0 4.1-4.5 >4.5	8 8 7.5 7 6.5 6 5.5 5 4.5 4 3.5 3 Miss next dose then 2mg Miss 2 doses then 1mg	<1.4 1.4-1.5 1.6-1.7 1.8-1.9 2.0-2.3 2.4-3.0 3.1-3.2 3.3-3.5 3.6-4.0 >4	7 7 6 5 4 3 2 1 0 Seek advice

Warfarin Induction Dosage Chart for Atrial Fibrillation

Patients starting warfarin for AF do NOT need bridging with LMWH. Unless they have valve replacements or are at high risk of developing VTE (CHADS >5).

AF – Standard Induction protocol (Oates et al 1998)

Day	INR	Dose	Interval (days) to next test
1	0.0-1.3	2mg	14
15	1.0	6mg	7
15	1.1-1.2	5mg	7
15	1.3-1.5	4mg	7
15	1.6-2.1	3mg	7
15	2.2-3.0	2mg	7
15	3.1-4.0	1mg	7

AF – induction for patients requiring early cardioversion (Ageno 2003)

Day	INR	Dose	Interval (days) to next test
1	0.0-1.3	5	1
2	0.0-1.4	5	1
2	1.5-1.9	2.5	1
2	2.0-2.4	1	1
2	2.5-5.0	0	1
3	0.0-1.4	5	1
3	1.5-1.9	2.5	1
3	2.0-2.4	1	1
3	2.5-5.0	0	1
4	0.0-1.3	7.5	1
4	1.4-1.9	5	1
4	2.0-2.9	2.5	1
4	3.0-3.4	1	1
4	3.5-5.0	0	1
5	0.0-1.3	10	1
5	1.4-1.7	7.5	1
5	1.8-2.4	5	1
5	2.5-3.0	2.5	1
5	3.1-3.5	1	1
5	3.6-5.0	0	1

Recommended Therapeutic INR Targets and Duration

Indication	INR target	Suggested Duration
Pulmonary Embolus	2.5	6 months
Distal DVT due to temporary risk factors	2.5	3 months
Isolated Calf vein DVT	2.5	6 weeks
Proximal DVT or DVT of unknown cause or those associated with on-going risk factors	2.5	3 months then review
Venous Thromboembolism associated with malignancy	2.5	6 months then review
Recurrence of VTE—NOT on Warfarin	2.5	Long term
Recurrence of VTE—WHILST on Warfarin	3.5	Long term
Atrial fibrillation	2.5	Long term
AF for cardioversion	3.0	3 weeks pre-cardioversion at least, 4 weeks post
Cardiomyopathy	2.5	Long term
Mural thrombus	2.5	3 months
Rheumatic mitral valve disease	2.5	Long term
Mechanical prosthetic heart valves (Low thrombogenicity) Aortic carbomedics, Medtronic Hall, St Jude Medical	2.5 (3.0†)	Long term
Mechanical prosthetic heart valves (Medium thrombogenicity) Bjork-Shiley, other bileaflet	3.0 (3.5†)	Long term
Mechanical prosthetic heart valves (High thrombogenicity) Starr-Edwards, Omniscience, Lillehei-Kaster	3.5	Long term
Antiphospholipid syndrome	2.5	Long term
Peripheral Vascular disease (acute arterial embolism proceeding to embolectomy)	2.5	Long term

† Patient related risk factors: Mitral, tricuspid, pulmonary position. Previous arterial thromboembolism, atrial fibrillation, left atrial diameter >50mm; mitral stenosis; left atrial ejection fraction <35%; left atrial dense spontaneous echo contrast

Dosage Management and Monitoring

The warfarin dose required to achieve full anticoagulation will vary for each individual patient. It is important to confirm the maintenance dose for patients taking warfarin prior to admission. This information can be obtained from: the patient/carer, their yellow NPSA book or postal dosage slip or the anticoagulation clinic managing their warfarin.

Patients in Bedfordshire will have their warfarin managed by one of the following:

- Bedford Warfarin Service (01234 893413)
- BHT Anticoagulation Clinic ext. 2207, Bleep 467
- OR Patients' own GP

Patients can receive their dosing schedule in their yellow book or via a Postal Dosage Slip (see below).

INR testing and managing out of range results

INR testing should be tested at least once or twice a week during the initial stages of treatment. Once the maintenance dose is established and the INR remains in the therapeutic range, the interval between testing can be increased. The maximum testing interval is 12 weeks.

INR should be tested more frequently (daily/twice a week), when a medication is started/stopped, when the warfarin dose is changed or (for inpatients) if the clinical condition changes.

There are many factors than can destabilise a patients INR including:

- Over/under dosing
- Drug interactions (Prescribed medicines, OTC and herbal medicines)
- Use of alcohol or drugs.
- Factors affecting absorption (e.g. gut oedema)
- Factors affecting distribution (e.g. albumin)
- Factors affecting metabolism (e.g. hyperthyroidism)
- Food and drink intake (e.g. green vegetables and cranberry juice).

In patients with an INR outside the therapeutic range, a dose adjustment will be required. The size of the adjustment will be determined by the deviation of INR from the target, the presence or otherwise of any destabilising factors or known risk factors for haemorrhage/VTE and the ease of monitoring the patient.

In general, when adjusting the dose, a 15% change in dose is expected to result in a change in the INR of 1, and a 10% dose adjustment is expected to result in a 0.7–0.8 change in the INR. Dose adjustments should be increased or decreased by looking at the **weekly** dose not the daily dose.

Sub-therapeutic INRs

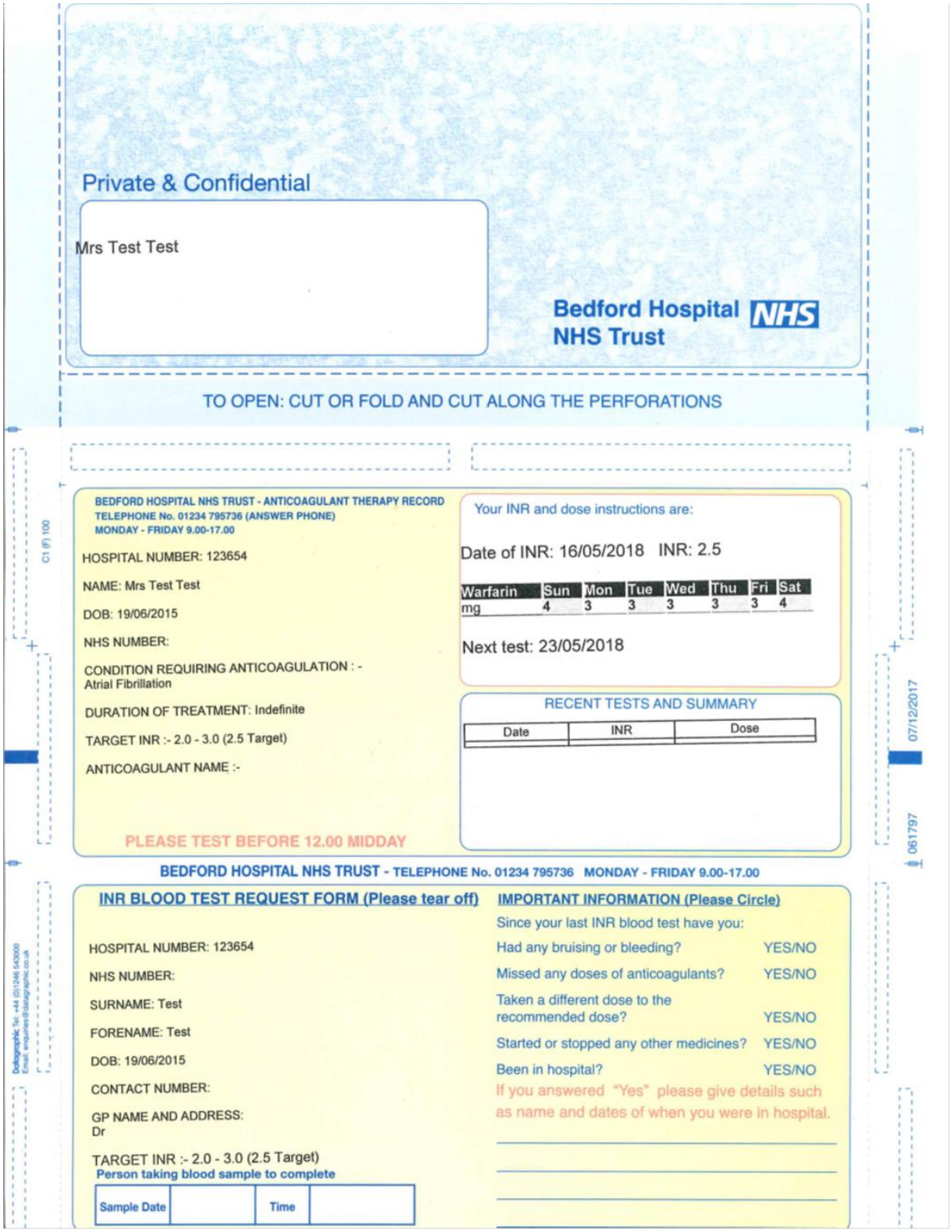
Depending on the INR, the warfarin dose may need to be (temporarily) increased, and sometimes a booster dose may be required (25-50% of the maintenance dose for 1 -2 days) — the INR should then be measured 2 or 3 days later to ensure that it is increasing. If the patient is at high risk of developing a VTE then LMWH cover may be necessary.

High INRs

If the INR is less than 0.5units above the target value (i.e. INR target range is 2-3 and INR is 3.4), withholding doses is **NOT** necessary and a temporary dose reduction may suffice. Destabilising/risk factors must be taken into account and INR retested in 2-3 days. See Appendix 15 – Management of over anticoagulation and reversal of bleeding.

If INR remains poorly controlled (TTR <65%) then consider switching to another anticoagulant.

Postal Dosage Slip



Private & Confidential

Mrs Test Test

Bedford Hospital NHS Trust

TO OPEN: CUT OR FOLD AND CUT ALONG THE PERFORATIONS

BEDFORD HOSPITAL NHS TRUST - ANTICOAGULANT THERAPY RECORD
TELEPHONE No. 01234 795736 (ANSWER PHONE)
MONDAY - FRIDAY 9.00-17.00

HOSPITAL NUMBER: 123654

NAME: Mrs Test Test

DOB: 19/06/2015

NHS NUMBER:

CONDITION REQUIRING ANTICOAGULATION : -
Atrial Fibrillation

DURATION OF TREATMENT: Indefinite

TARGET INR :- 2.0 - 3.0 (2.5 Target)

ANTICOAGULANT NAME :-

PLEASE TEST BEFORE 12.00 MIDDAY

Your INR and dose instructions are:

Date of INR: 16/05/2018 INR: 2.5

Warfarin	Sun	Mon	Tue	Wed	Thu	Fri	Sat
mg	4	3	3	3	3	3	4

Next test: 23/05/2018

RECENT TESTS AND SUMMARY

Date	INR	Dose

BEDFORD HOSPITAL NHS TRUST - TELEPHONE No. 01234 795736 MONDAY - FRIDAY 9.00-17.00

INR BLOOD TEST REQUEST FORM (Please tear off)

HOSPITAL NUMBER: 123654

NHS NUMBER:

SURNAME: Test

FORENAME: Test

DOB: 19/06/2015

CONTACT NUMBER:

GP NAME AND ADDRESS:
Dr

TARGET INR :- 2.0 - 3.0 (2.5 Target)

Person taking blood sample to complete

Sample Date		Time	

IMPORTANT INFORMATION (Please Circle)

Since your last INR blood test have you:

Had any bruising or bleeding? YES/NO

Missed any doses of anticoagulants? YES/NO

Taken a different dose to the recommended dose? YES/NO

Started or stopped any other medicines? YES/NO

Been in hospital? YES/NO

If you answered "Yes" please give details such as name and dates of when you were in hospital.

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2. DISCHARGE OF INPATIENTS TAKING ANTICOAGULANTS

It is the prescriber's responsibility to make sure that the following are documented on the discharge letter:

- Indication for anticoagulation
- Date of initiation (if newly started during current admission)
- Dosage (until follow up appointment with anticoagulation clinic)
- Required duration
- Target INR (Warfarin only)

Warfarin

INR should be therapeutic on discharge. It is the clinical teams' responsibility to dose the patient until their next scheduled anticoagulation appointment this will be done in their Yellow Book (issue a new one for patients who have not brought theirs in or usually have postal dosage slips).

The nurse looking after the patient MUST arrange the follow up appointment before discharge with the relevant GP surgery or clinic.

Particular care should be taken when discharging patients close to the weekend or public holidays to ensure blood tests can be arranged at an appropriate interval after discharge. For VTE patients, it may be safer to discharge on therapeutic tinzaparin and refer to anticoagulation clinic for warfarin loading than to load during the inpatient stay and discharge prior to day 4.

All patients taking warfarin pre-admission should be re-referred back to the clinic they were originally managed by:

- Bedford Warfarin Service via telephone 01234 893413
- BHT Anticoagulation Clinic – send referral form (Appendix 9) to POD18, ext. 2207, Bleep 467
- OR Patients' own GP

Patients **newly started** on warfarin should be referred to the BHT Anticoagulation Clinic. The prescribing doctor MUST complete the Oral Anticoagulation Referral form (Appendix 9)

A 'Warfarin Discharge Checklist' must be completed by the nurse looking after the patient and filed in the medical notes.

Patients requiring administration of tinzaparin should be referred to the Ambulatory Emergency Care Unit (ext 6331/6337) for daily administration and INRs.

Where patients have undergone day case procedures a full referral is not required. However, to ensure continuity of care the anticoagulant services should receive notification of the procedure that has been carried out and any changes that were made to the patients' anticoagulation.

Out of area patients

Patients under the care of GPs outside of Bedfordshire should have a referral made to their local secondary care anticoagulation clinic.

NOACs
Inpatients **newly started** on NOACs should be counselled appropriately. The nurse/pharmacy staff looking after the patient must complete the NOAC checklist (see below) and file in the medical notes. Patients can also be referred to the Anticoagulation Clinic for a follow up counselling appointment post discharge. Complete the referral form in Appendix 9 and send to Anticoagulation Clinic POD 18.

Tinzaparin
Patients must be supplied with a sufficient amount of syringes, appropriately counselled on administration on injection technique and given a sharps bin for disposal. Refer to AECU as above if necessary.

Patient Education, Counselling and documentation
Patients discharged on anticoagulants must be appropriately counselled so they understand the high risk nature of the medication and the importance of compliance (See warfarin and NOAC checklists below).

Patients should receive:
NPSA Yellow Warfarin information Pack (new *warfarin patients only)*
Yellow warfarin dosing book - containing dosing instructions up until anticoagulant clinic follow up appointment.
In-house patient information leaflets
Oral Anticoagulant Alert card

Dosette boxes
Warfarin, Apixaban, Edoxaban and Rivaroxaban can be used in compliance aids.
Dabigatran is not suitable for compliance aids.

Letter to Primary Care
On initiation of a NOAC, clinicians should write an informative letter to Primary Care regarding future prescribing and monitoring.

Example letters to primary care can be found in the Appendices of the following guidelines:
Non Vitamin K Antagonist Oral Anticoagulants (NOACs) in Non-Valvular Atrial Fibrillation: Initiation of treatment
Deep vein Thrombosis (DVT) – The management of patients with suspected and confirmed DVT in the Acute Assessment Unit
Pulmonary Embolism (PE) - The management of patients with suspected and confirmed PE in the Acute Assessment Unit

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WARFARIN DISCHARGE CHECKLIST *(For Nurses Use)*

Patient Name:
Hospital Number:
(or addressograph)

Ward: Consultant: Date of discharge:

Please **fill** and **sign** ALL sections on completion of each task, and **file** in medical notes with TTO.

Oral Anticoagulant Therapy/ Yellow Book completed (In particular: patient's ID, dose, next test date & venue and tinzaparin details if needed) *(tick)* ☐ **Are there any safety concerns?** *YES/NO* *- state:*_____ *(tick)* ☐ **If YES, contact the appropriate person**	**Nursing staff** *(sign)*
On discharge patient's warfarin will be dosed/managed by: *(tick)* □ **Bedford Hospital Anticoagulation Clinic** ☐ o complete "Anticoagulation Referral Form" and procedure □ **Bedford Warfarin Clinic** ☐ o call 01234 317182 to arrange F/U appointment □ **General Practitioner** ☐ o call patient's GP surgery to arrange F/U appointment □ **Bedford Hospital AECU – *for patients requiring Tinzaparin on discharge*** ☐ o call Ext. 6331/6337 to arrange F/U appointment □ **Others (e.g. other hospitals)** - *state:*_____ ☐ o call the relevant clinic to arrange F/U appointment **Patients must be reminded to present their discharge letters to the staff at their F/U appointment.**	**Nursing staff** *(sign)*
Is daily tinzaparin for warfarin bridging required? *YES/NO* – **if YES find out if:** ☐ • **Patient / Carer administering** o Correct and sufficient pre-filled syringes (dispensed from pharmacy) and sharps bin are provided; patient/carer understands treatment duration and injection technique. • **Bedford Hospital AECU administering** ☐ o Referral is completed and transport is booked if needed. • **GP Surgery administering** o Referral is completed and correct and sufficient pre-filled syringes or vials dispensed by pharmacy are provided. ☐ • **District Nurse administering** o Referral is completed and correct and sufficient pre-filled syringes or vials dispensed by pharmacy are provided. ☐	**Nursing staff** *(sign)*
Patients / Carers are counselled on: ■ **Strength of tablets they have been prescribed and dispensed** ☐ ■ **How many tablets and milligrams they need to take each day** ☐ ■ **Time and place where their next INR test is scheduled** ☐	**Nursing staff** *(sign)*
Queries about warfarin follow-up? Contact Anticoagulation Administrator Ext 2207	

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Patient Name:
Hospital/NHS Number:
(or attach addressograph)

Ward:

NOAC (Non vitamin K antagonist oral anticoagulant) INITIATION CHECKLIST
This checklist is for patients taking apixaban (Eliquis®) edoxaban (Lixiana®) or rivaroxaban (Xarelto®)

	Tick	Nursing / Pharmacy staff (sign)	Doctors (sign)
NOAC treatment commenced prior to discharge			
NOAC treatment to be commenced by GP/Other after discharge			
Clinical Indication			
Establish the indication patient is taking the NOAC for (AF/DVT/PE) if taking If taking for other indication, note in space……			
Is the patient on an Antiplatelet therapy *(Aspirin/Clopidogrel)*			
Is this clinically indicated? *(check medical notes/check with prescriber)*			
If previously on warfarin ensure this has been discontinued.			
Counselling information			
Patient/Carer administering *(ensure NOAC patient information leaflet is provided to carer/patient)*			
Dose and Frequency check			
Administration information: • Apixaban and Edoxaban can be taken with or without food • Rivaroxaban MUST be taken with food to maximize absorption			
If taking for newly diagnosed PE/DVT patient is aware of when to commence on the maintenance dose.*(refer to medical notes/TTO letter for dosing schedule)*			
Importance of adherence and persistence with treatment • Fairly rapid fall in drug levels (and therefore loss of effectiveness) if poorly compliant • Discuss ways of remembering to take. • Ensure patient is aware how to order a resupply from GP			
What to do if a dose is missed - If unsure, talk to healthcare provider • If a dose is missed take it as soon as possible. Do not take a double dose* (but see below for rivaroxaban and acute VTE) • **Once daily dosing**: take within 12 hours of missed dose, if more than 12 hours, omit the dose and then continue at the usual time. • **Twice daily dosing**: take within 6 hours of missed dose, if more than 6 hours, omit the dose and then continue at the usual time. **NOTE**: *rivaroxaban 15mg twice daily (acute VTE): take one tablet as soon as remembered. Do not take more than two 15mg tabs in a single day (but can take 2x15mg at the same time to make a total of 30mg on one day). Continue with 15mg twice daily the following day			
Duration of treatment check *(refer to medical notes/TTO letter)*			
Potential for drug interactions: avoid OTC medicines containing aspirin (e.g. flu remedies), NSAIDs or herbals. Paracetamol is the preferred analgesic. Pt to inform healthcare professional of any new meds.			
What to do if bleeding or bruising occurs *(minor bleeding consult GP/111, major bleeding go to A&E)*			
• Patient issued/already has a NOAC alert card and advised to carry at all time. *(Fill in as much detail you can)* • Patient should be advised to inform other HCPs they are visiting for treatment e.g. Drs, Dentists & Pharmacists.			
Monitoring and Review			
Reassure patient that there is no requirement for regular anticoagulant monitoring with NOAC. *(GP should check kidney function & FBC at least annually or more frequently if clinically indicated.)*			
Date of completion……			

3. ANTICOAGULATION REFERRAL FORM

NHS Bedford Hospital NHS Trust

Anticoagulation Referral Form

Please ensure the patient is given a prescription for relevant anticoagulant and an appointment at the time of referral. **NOTE: ANTICOAGULATION CONTROL WILL BE THE RESPONSIBILITY OF THE REFERRING CLINICIAN UNTIL REVIEW IN THE ANTICOAGULATION CLINIC**

Mon – Fri 9 am – 4 pm. TEL: 01234795736 EXT: 2207 / FAX: 01234792148 / BLEEP 467

Patient details:
(Affix addressograph here)

New Referral ☐
Re-Referral ☐

Reason for Referral:
Warfarin Initiation / Monitoring ☐
NOAC Counselling ☐
Switch from NOAC to Warfarin ☐
Switch from Warfarin to NOAC ☐

Current Anticoagulant *Please (√) tick as appropriate*	**Warfarin ☐**	**Edoxaban ☐**	**Apixaban ☐**	**Rivaroxaban ☐**	**Dabigatran ☐**
Date Anticoagulation started: ___/___/____		**Current Dose:**		*(Optional)* **Switching to:**	

INDICATION for Anticoagulation	(√) Tick	TARGET	DURATION	INDICATION for Anticoagulation	(√) Tick	TARGET	DURATION
Pulmonary Embolism		2.5	3 months	Atrial Fibrillation (non-valvular)		2.5	Long Term
Recurrent Pulmonary Embolism		2.5	Long Term				
Pulmonary Embolism (whilst on anticoagulation)		3.5	Long Term	AF for cardioversion		3.0	3 weeks prior, 4 weeks post.
Calf DVT		2.5	6 weeks	Proximal DVT		2.5	3 months
Recurrent DVT		2.5	Long Term	Cardiomyopathy		2.5	Long term
Recurrent DVT (whilst on anticoagulation)		3.5	Long Term	Mural Thrombus		2.5	Long Term
VTE associated with malignancy		2.5	6 months then review	Rheumatic Mitral Valve disease		2.5	Long Term
Mechanical prosthetic heart valves (depending on thrombogenicity: see guidelines-Appendix 7)		2.5 3.0 3.5	Long Term	Peripheral Vascular disease (acute arterial embolism proceeding to embolectomy)		2.5	Long Term
Tissue Prosthetic Heart Valve		2.5	3 months and review	Other (Please Specify)			

Clinical Information

See overleaf for scoring system
CHA_2DS_2VASc Score(AF pts only): _____ HASBLED Score: _____
Coagulation Screen / LFTs / U&Es checked: Yes / No CrCl (ml/min):_____
Is patient on Aspirin ☐ Clopidogrel ☐ Other _____
Stop Aspirin when INR >2.0 Yes ☐ No ☐ *(See guidelines)*

Is patient on LMWH: Yes ☐ No ☐
Which LMWH: _____
Dose: _____
Date started: ___/___/____

Oral Anticoagulation History (Warfarin/Phenindione/ Other_____)

Recent dosing history:

DATE	INR	DOSE

Past Medical History & Other Medications:

Name of Referring Clinician: _____ Ward: _____ Bleep: _____ Date: ___/___/____

Consultant responsible for patient_____

Clinic Appointment on ___/___/____ Time: _____:_____

Is transport required? (ward to arrange for 1st visit for inpatient)	Yes ☐	No ☐	District nurse required? (ward to arrange for 1st visit for inpatient)	Yes ☐	No ☐

Anticoagulation Referral Form/Anticoagulation)/July 2018 Version 1.0

Reverse of Anticoagulation Referral Form

	CHA_2DS_2VASc Score – clinical characteristics:	Points
C	Congestive heart failure (or left ventricular systolic dysfunction)	1
H	Hypertension: blood pressure consistently above 140/90mmHg (or treated hypertension on medication)	1
A_2	Age ≥75 years	2
D	Diabetes Mellitus	1
S_2	Prior Stroke or TIA or thromboembolism	2
V	Vascular disease (e.g. peripheral artery disease, myocardial infarction, aortic plaque)	1
A	Age 65-74 years	1
Sc	Sex - Female	1

	HAS-BLED Score – clinical characteristics:	**Points**
H	Hypertension	1
A	Abnormal renal and liver function (1 point each)	1 or 2
S	Stroke	1
B	Bleeding	1
L	Labile or unstable INRs	1
E	Elderly (> 65 years)	1
D	Drug or alcohol (1 point each)	1 or 2

Reverse of Anticoagulation Referral Form

4. SWITCHING BETWEEN ANTICOAGULANTS

SWITCHING BETWEEN ANTICOAGULANTS						
To➔ / From⬇	**Warfarin**	**LMWH**	**Apixaban**	**Edoxaban**	**Rivaroxaban**	**Dabigatran**
Warfarin		Stop warfarin and start LMWH when INR < 2.0 In patients with high risk of thrombosis consider starting when INR <3.0	Stop warfarin. If INR<2 start. If INR 2-2.5 start the next day	Stop warfarin. If INR < 2 start. If INR 2-2.5 start the next day	Stop warfarin. If INR <2 start. If INR 2-2.5, start the next day	Stop warfarin. If INR <2 start. If INR 2-2.5, start the next day
LMWH	Start warfarin in combination with LMWH and monitor INR. Discontinue LMWH when INR in therapeutic range for 2 consecutive days		Start when next dose is due	Start when next dose is due	Start when next dose is due	Start when next dose is due
Apixaban	Start warfarin. Do not stop apixaban. Consider measuring INR daily until in range then stop Apixaban (~2 days)	Start when next dose is due		Start when next dose is due	Start when next dose is due	Start when next dose is due
Edoxaban	If patient is taking: - 60 mg, prescribe 30 mg OD with warfarin. - 30 mg, prescribe 15 mg OD with warfarin. Consider measuring INR daily until in range then stop edoxaban	Start when next dose is due	Start when next dose is due		Start when next dose is due	Start when next dose is due
Rivaroxaban	Start warfarin. Do not stop rivaroxaban. Consider measuring INR daily‡ until in range then stop rivaroxaban	Start when next dose is due	Start when next dose is due	Start when next dose is due		Start when next dose is due
Dabigatran	Start warfarin*. Do not stop dabigatran. Consider measuring INR daily until in range then stop dabigatran	Start when next dose is due	Start when next dose is due	Start when next dose is due	Start when next dose is due	

Please note: Dabigatran and apixaban slightly increase INR, therefore if dabigatran and warfarin OR apixaban and warfarin are taken together a normal INR does not mean that the patient is fully anticoagulated.

‡INR should be tested just before next dose of Rivaroxaban as rivaroxaban can increase the INR.

*If CrCl >50ml/min start warfarin 3 days before stopping dabigatran, if CrCl 30-50ml/min start warfarin 2 days before stopping dabigatran

5. DRUG INTERACTIONS AND ADMINISTRATION IN PATIENTS WITH SWALLOWING DIFFICULTIES AND/OR ENTERAL FEEDING TUBES

Significant Drug Interactions with Warfarin –Mechanism and Management

Warfarin is metabolised by the liver via cytochrome P450. Certain drugs may increase or decrease the effect of **Warfarin** and the risk of bleeding/ thrombosis. Drugs that induce hepatic P450 enzymes reduce clearance of warfarin and vice versa. This guide is intended as a quick reference to highlight significant interactions between Warfarin and commonly prescribed and OTC medicines. It is not intended to be an exhaustive list. For further information, please refer to the medicines SPC (*www.medicines.org.uk*), BNF or contact the pharmacy department.

Drug	Effect on INR	Clinical Importance	Management
Allopurinol	↑ INR	Anticoagulant effects possibly enhanced	Monitor INR when initiated
Amiodarone	↑ INR	Occurs in most individuals after 2weeks and may persist for many weeks after stopping amiodarone	Monitor INR during and after. May need to reduce warfarin
Barbiturates (e.g. Phenobarbitol)	↓INR	Serious interaction- the effect of the barbiturates may persist for 6weeks after they have discontinued	Monitor INR warfarin dose may need to increased
Carbamazepine	↓ INR	Serious interaction –unpredictable	Monitor INR during and after, warfarin may need to be increased
Cholestyramine	↓/↑INR	Minimize effect by giving warfarin and cholestyramine doses 4-6 hours apart	Monitor INR
Cimetidine	↑INR	Famotidine, nizatidine and ranitidine appear not to interact	Select an alternative H2 antagonist
Clarithromycin	↑INR	Potential serious interaction –however unpredictable and uncommon (also with Azithromycin)	Monitor INR on initiation and within 3 days of starting
Clopidogrel		↑ risk of bleed due to antiplatelet effect	Avoid concomitant use if possible
Dipyridamole	Unchanged or ↑INR	Increase risk of bleeding can occur with concurrent use due to antiplatelet effect	Monitor INR
Disulfiram	↑INR	Occurs in most individuals	Monitor on initiating & withdrawing
Erythromycin	↑INR	Potential serious interaction –unpredictable, but most patients are unlikely to develop a clinically significant interaction	Elderly at greatest risk. Monitor closely within 3 days of starting.

Fibrates (Clofibrate, Bezafibrate, Fenofibrate, Gemfibrozil)	↑INR	Serious interaction. Incidence between 20 and 100%, but prudent to assume that most individuals will demonstrate this interaction	Reduce Warfarin dose by a third to a half initially and adjust according to INR – monitor closely
Fluconazole	↑INR	Serious interaction. Occurs in most individuals	Monitor on initiating and stopping
Fluoxetine	↑INR	Isolated reports of raised INR and/or haemorrhage - unpredictable	Monitor INR and signs of altered anticoagulation
Glucagon	↑INR	Potential serious interaction but not for doses ≤ 30mg over 1 or 2 days.	Monitor INR and reduce warfarin dose
Itraconazole	↑INR	Isolated reports but clinically significant	Monitor closely
Ketoconazole	↑INR	Small number of reports in elderly patients	Monitor closely – esp. elderly
Metronidazole	↑INR	Potential serious interaction, although documentation is small.	Warfarin dose may need to be adjusted. Monitor closely
Miconazole(e.g. buccal gel)	↑INR	Avoid – potentially serious interaction.	Use Nystatin as an alternative
NSAIDS	↑INR	Unpredictable serious interaction, effect on platelet activity plus GI irritation can result in GI bleed	Anticoagulant effects possibly enhanced – monitor closely
Oral contraceptive		Generally avoid in thromboembolic disorders	Monitor closely
Paroxetine		Can increase the likelihood of bleed without affecting INR	Use with caution
Proton pump inhibitor (PPI) (lansoprazole, omeprazole)	↑INR	Anticoagulant effects possibly enhanced although interactions do not appear to be clinically significant.	Monitor INR
Quinolones (ciprofloxacin)	↑INR	Unpredictable	Monitor INR
Rifampicin/ Rifabutin	↓INR	Reduces anticoagulant effects within 5 to 7days and persists for a 2 to 5 week after discontinuation. Monitor closely.	Warfarin dose may need to be doubled or trebled then reduced on stopping use.
Sertraline	↑INR	Low risk – Isolated reports of thrombocytopenia, abnormal bleeding or purpura.	Monitor INR
Simvastatin	↑INR	Possible enhanced anticoagulant effect (also with rosuvastatin)	Monitor initially & after dose change
Sulphinpyrazone	↑INR	Serious interaction-well established	Monitor INR and reduce warfarin
Sulphonamide(Co-trimoxazole)	↑INR	Serious interaction-well established	Monitor INR and reduce warfarin
Tamoxifen	↑INR	Occurs in some, but not all individuals	Monitor INR, reduce Warfarin dose as necessary (may require dose reduction of up to half)
Tricyclic Antidepressants	↑/↓INR	Can cause fluctuation in INR- insufficient evidence	Monitor INR
Vitamin K	↓INR	Consider this interaction if patients are Warfarin resistant. Vitamin K may be present in enteral feeds, health foods, food supplements, green tea.	

NOAC Drug Interactions	
All NOACS	Nonsteroidal anti-inflammatory drugs (NSAIDs) — increased risk of bleeding with concomitant use of NSAIDs and NOACs. The risk is thought to be greatest with NSAIDs that have a half-life greater than 12 hours (e.g. piroxicam). ◦Avoid concomitant use if possible. If concurrent use is unavoidable, an NSAID with a short half-life such as ibuprofen (2 hours) is preferred. ◦Advise the person that they should seek medical advice if they experience any unexplained bruising, bleeding gums, nosebleeds, prolonged bleeding from cuts, and blood in the urine or stools.
	Other anticoagulants (e.g. heparin, warfarin, NOACS) — there is an increased risk of bleeding if other anticoagulants are given with NOACs. Avoid concomitant use except when switching to or from warfarin treatment.
	Antiplatelets - there is an increased risk of bleeding with concomitant therapy; avoid concomitant use with NOACs, except on specialist advice.
	Carbamazepine, phenytoin, rifampicin, and St John's Wort — plasma concentration of NOACs are reduced by all of these drugs. All manufacturers of NOACs have advised that concomitant use should be avoided.
Apixaban	Itraconazole, ketoconazole, voriconazole, posaconazole, and HIV protease inhibitors (e.g. ritonavir) — the plasma concentration of apixaban is increased by all of these drugs as they are strong inhibitors of both CYP3A4 and P-glycoprotein (P-gp). The manufacturer of apixaban has advised that concomitant use should be avoided.
	Diltiazem, naproxen, amiodarone, verapamil, and quinidine are weak inhibitors of CYP3A4 and P-gp. However, no dose adjustment is needed when these drugs are co-administered with apixaban.
Edoxaban	Amiodarone, quinidine and verapamil— no dose reduction is required.
	Ciclosporin, dronedarone, erythromycin, itraconazole, and ketoconazole — the plasma concentration of edoxaban is increased by all of these drugs. The manufacturer has advised that the dose of edoxaban should be reduced to 30 mg daily.
Rivaroxaban	Ketoconazole, itraconazole, voriconazole, posaconazole, dronedarone, or HIV protease inhibitors — the plasma concentration of rivaroxaban is increased by all of these drugs as they are strong inhibitors of both CYP3A4 and P-glycoprotein (P-gp). The manufacturer of rivaroxaban has advised that concomitant use should be avoided.
Dabigatran	Amiodarone and verapamil — plasma concentration of dabigatran is increased by amiodarone and verapamil. If concurrent use of dabigatran and amiodarone or verapamil is indicated, reduce the dose of dabigatran to 110 mg twice daily.
	Ciclosporin, dronedarone, itraconazole, ketoconazole, and tacrolimus — the plasma concentration of dabigatran is increased by all of these drugs. The manufacturer of dabigatran has advised that concomitant use should be avoided.
	Selective serotonin reuptake inhibitors (SSRIs) or serotonin norepinephrine re-uptake inhibitors (SNRIs) — there is a possible increased risk of bleeding when dabigatran is given with an SSRI or SNRI. The manufacturer of dabigatran advises close clinical monitoring, especially if other risk factors which increase plasma levels are also present.

Administration to patients with enteral feeding tubes or swallowing difficulties

	Swallowing difficulties	Enteral Feeding tubes
Edoxaban	The tablets can be crushed and dispersed in water. Can be mixed with apple puree in patients who are unable to swallow	Can be administered via NG tube. No specific instructions.
Apixaban	The tablets can be crushed and dispersed in water, glucose 5%, apple juice, or apple puree for administration to patients with swallowing difficulties. Take care to ensure the whole dose is administered.	The tablets can be crushed and dispersed in water or in glucose 5% for administration (the manufacturers recommend 60mL). They are licensed for administration through nasogastric tubes - administration through other types of enteral feeding tube would be outside the product license. Take care to ensure the whole dose is administered, and flush well after each dose.
Rivaroxaban	The tablets can be crushed and mixed with water or apple puree immediately prior to administration for patients with swallowing difficulties. Xarelto® tablets are licensed to be administered in this way.	NG/PEG: The tablets can be crushed and mixed with water for administration. Click here for further information. Re-start the feed immediately after the dose has been given and the feeding tube flushed (15mg and 20mg doses). Xarelto® tablets are licensed to be administered in this way. NJ/PEJ/: Rivaroxaban is not suitable for administration via enteral feeding tubes terminating beyond the stomach (i.e. in the duodenum or jejunum) due to decreased absorption of the drug when given in this manner. Bioavailability is significantly reduced when rivaroxaban is administered beyond the stomach.
Dabigatran	Dabigatran capsules should not be opened. The capsule shell is specially formulated to release slowly at the correct point in the gastrointestinal tract. The pellets inside the shell are designed to create an acidic micro-environment to improve drug dissolution and absorption. Opening the capsules may greatly affect the oral bioavailability of the drug, with a risk of increased side effects (i.e. bleeding), therefore this should never be done.	
Warfarin	5mg/5ml oral suspension available. The tablets can be crushed and mixed with water for administration. Without crushing they disperse in two to five minutes.	NG/PEG: Liquid and crushed/dispersed tablets can be administered NJ/PEJ: Warfarin appears to be absorbed high in the GI tract and so there is a risk of reduced absorption if the drug is given through enteral feeding tubes terminating beyond the stomach. When such administration is necessary, monitor the patient closely for effect, and take particular care if the site of delivery is altered (i.e. if the jejunal tube is changed for a gastric one).

6. MANAGEMENT OF OVER ANTICOAGULATION AND REVERSAL OF BLEEDING

Contact Haematology on 585 or via switchboard out-of-hours if patient is haemorrhaging on anticoagulants.

See Clinical guideline – Perioperative management of patients on anticoagulant and antiplatelet agents and the Blood Transfusion Policy for further guidance.

Important considerations:

- Recombinant factor VIIa is not recommended for emergency warfarin reversal.
- Fresh Frozen plasma produces suboptimal anticoagulation reversal and should only be used if prothrombin complex concentrate is not available.
- For surgery that requires reversal of warfarin and that can be delayed for 6 -12 hours, the INR can be corrected using Vitamin K. PCC should not be used for elective or non-urgent surgery.
- For surgery that requires reversal of warfarin which cannot be delayed, INR can be corrected using PCC and Vitamin K.
- For some conditions such as prosthetic heart valves, the degree of reversal must be decided on an individual basis.
- **All patients** with bleeding should be investigated for underlying cause (particularly in unexpected bleeding at therapeutic levels). A **DATIX** should be completed for patients taking anticoagulation.

Warfarin

Vitamin K exists in both water soluble form (Menadiol) and water insoluble form (Phytomenadione). Phytomenadione is licensed for reversal of anticoagulation. Menadiol is licensed for prevention of Vitamin K deficiency in malabsorption syndromes. Phytomenadione 2mg/0.2ml and 10mg/1ml can be given by both IV injection and orally. Use of Vitamin K may be followed by a period of warfarin resistance; high thrombosis risk patients may require LMWH (once cessation of bleeding is confirmed).

Management of high INRs (NICE CG144)	
Major bleeding + high INR	Stop warfarin. Seek Haematology Advice. See Blood Transfusion Policy for Beriplex guidance
INR >8 no bleeding or minor bleeding	Stop Warfarin Give Phytomenadione 0.5-1mg slow IV OR 1-5mg by mouth (IV Phytomenadione can be administered orally). *2mg PO is given to non-bleeding outpatients
INR between 6.0 – 8.0 no bleeding or minor bleeding	Stop Warfarin Restart when INR <5
INR Less than 6, but more than 0.5units above the target value	Reduce dose OR stop warfarin Restart when INR <5
INR Less than 5.0	Reduce dose and/or omit 1-2 doses Retest INR in 2-3 days

NOACs

See table below and contact haematology for advice.

Reversal of NOAC associated bleeding

Consider giving activated charcoal orally, if last dose ingested <2 hours ago

Mild Bleeding
- Local Haemostatic measures
- Consider Tranexamic acid* (15mg/kg oral)
- Delay next dose of NOAC

Moderate to severe bleeding
- Local measures
- Fluid replacement
- Platelets > 75 x 10^9/L
- Tranexamic acid 15mg/kg IV*
- Call Haematologist for advice

Life threatening bleeding &/or emergency surgery**
Measures as for moderate to severe bleeding
Consider PCC
Consider rVIIa
For dabigatran see below

* There is no published data on using tranexamic acid in individuals receiving NOACs

** Hb drop >2.0g/L or bleeding at critical site

Dabigatran Reversal
Give Idaracuzimab (Praxbind) 5g IV
See Praxbind info sheet

Haemodialysis can also be considered. 4 hours of haemodialysis will remove approx. 50- 60% of dabigatran from circulation

NOAC	Half life	Relevant clotting marker
Dabigatran	13 – 18 hour (depending on age/renal impairment)	TT – low levels suggest low plasma concentration
Rivaroxaban	5 – 13 hours (depending on age/renal impairment)	PT – low levels suggest low plasma concentration
Edoxaban	10 – 14 hours	As above
Apixaban	12 hours	None

Praxbind (Idarucizumab) Information

Call Haematology Consultant on-call before use

What is Praxbind?

Praxbind (Idarucizumab) 2.5g/50mL is a specific reversal agent for dabigatran. Idarucizumab (a humanized monoclonal antibody fragment) binds to dabigatran and its metabolites with high affinity and neutralises their anticoagulant effect.

What is Praxbind used for?

Praxbind is indicated in adult patients treated with Pradaxa (dabigatran) when rapid reversal of its anticoagulant effects is required:

- For emergency surgery or urgent procedures
- In life-threatening or uncontrolled bleeding

Dabigatran plasma levels peak within 2–3 hours. In individuals with normal renal function, the half-life is 13 h (plasma half-life 22–35 hours with creatinine clearance < 30 ml/min). For **elective** surgeries/procedures, dabigatran should be stopped 24-48 hours prior to admission.

Location: Praxbind can be obtained from Pharmacy during opening hours or from the Treatment room fridge on AAU out of hours.

What is the recommended dose?

The recommended dose is 5g (2 x 2.5g/50ml vials).

Administration of a second 5g dose may be considered if:

- Recurrence of clinically significant bleeding together with prolonged clotting times **OR**
- If potential re-bleeding would be life-threatening and prolonged clotting times are observed **OR**
- Patients require a second emergency surgery/urgent procedure and have prolonged clotting times No dose adjustment is required in renal impairment, hepatic impairment or the elderly.

Coagulation Screening Tests

PT, APTT, TT, Fibrinogen and D-dimer should be done **as soon as possible** prior to administration of praxbind (unless a delay in waiting for results has life-threatening consequences).

Effect of Dabigatran on specialist tests of haemostasis	
APTT	Curvilinear response to dabigatran, however some patient with therapeutic concentrations of dabigatran can still show a normal APTT
TT	Linear concentration response. A normal TT suggests the dabigatran level is minimal
PT	Dabigatran has a less marked effect on PT than APTT. Mean PT/INR ratio <1.5
Fibrinogen	No effect on several assays
D-Dimer	Unaffected

How is Praxbind administrated?

Praxbind is for intravenous use only. It does not require reconstitution. It is administered as two consecutive infusions over 5 to 10 minutes each via a syringe driver or as a bolus injection.

Side effects

No adverse effects have been identified. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme.
www.mhra.gov.uk/yellowcard

How and when do you restart antithrombotic therapy?

Reversing antithrombotic therapy exposes the patient to the thrombotic risk of their underlying condition.

Dabigatran can be restarted 24 hours after administration of Praxbind, if the patient is clinically stable and adequate haemostasis has been achieved.

Other antithrombotic therapy such as low molecular weight heparins can be started any time after the administration of Praxbind, if the patient is clinically stable and adequate haemostasis has been achieved.

Storage

Praxbind is to be stored in a refrigerator (2-8^{O}C).

Prior to use, the unopened vial may be kept at room temperature for up to 48 hours, if stored in the original package in order to protect from light, or up to 6 hours when exposed to light. After opening, chemical and physical in-use stability has been demonstrated for 1 hour at room temperature.

References

Makris, M., Van Veen, J., Tait, C., Mumford, A. and Laffan, M. (2012) 'Guideline on the management of bleeding in patients on antithrombotic agents', British Journal of Haematology, (160), pp. 35 - 46.
Kitchen, S., Gray, E., Mackie, I., Baglin, T., and Makris, M. (2014) 'Measurement of non-coumarin anticoagulants and their effects on tests of Haemostasis', *British Journal of Haematology,* (166), pp. 830 - 841.
SPC Praxbind. Accessed December 2017.www.emc.medicines.org.uk

Use of Prothrombin Complex Concentrate (Beriplex) at Bedford Hospital

Beriplex® P/N is a Prothrombin Complex Concentrate (PCC) containing all four vitamin K-dependent coagulation factors II, VII, IX and X. It also contains small amounts of Anti-thrombin III, protein C and S.

Beriplex® P/N is issued from the **Transfusion lab**.

Beriplex® P/N will not be issued unless an accurately completed checklist accompanies the request.

Further guidance relating to the management of bleeding, the use of Beriplex and Fresh Frozen Plasma can be found in the Blood Transfusion Policy.

The Beriplex website (www.beriplex.co.uk/hcp-beriplex) also has prescribing information to assist with dosing and administration.

7. MANAGEMENT OF ENDOSCOPY PATIENTS ON ANTICOAGULATION

Separate guidance is available on the management of endoscopy patients.

The British Society of Gastroenterologists has guidance on the management of patients undergoing elective endoscopic gastro-intestinal procedures. Recommendations are outlined in algorithms in the policy.

The European Society of Gastrointestinal Endoscopy has a policy that discusses the management of anticoagulation in acute non-variceal upper gastro-intestinal haemorrhage.

8. ANTICOAGULATION AND EPIDURAL INFUSIONS

An epidural should not be inserted or removed within 12 hours of a dose of heparin (fractionated or unfractionated). Once the catheter is removed 6 hours must elapse before any further dose of heparin is given.

See Clinical Guideline – Management of epidural infusions (adults) for further guidance.

9. OTHER VITAMIN K ANTAGONISTS

This section is for information only these drugs are not to be routinely prescribed. Seek advice from haematology if patients are not suitable for warfarin, NOACs or LMWH.

Approximate dosage conversions		
Phenindione dose	**Acenocoumarol dose**	**Warfarin dose**
20mg	0.5mg	1mg
35mg	1.0mg	2mg
50mg	1.5mg	3mg
70mg	2.0mg	4mg
80mg	2.5mg	5mg
100mg	3.0mg	6mg
120mg	3.5mg	7mg
135mg	4.0mg	8mg
150mg	4.5mg	9mg
170mg	5.0mg	10mg

10. THROMBOPHILIA AND TESTING

Thrombophilia is an abnormality of blood coagulation associated with hypercoagulability (or prothrombotic state) which increases the risk of thrombosis. Thrombophilia can generally be regarded as either heritable or acquired (see examples below).

Heritable thrombophilia:

1. Factor V Leiden
2. Prothrombin G20210A
3. Protein C deficiency
4. Protein S deficiency
5. Antithrombin III deficiency
6. Dysfibrinogenaemia

Acquired thrombophilias:

1. Antiphospholipid Syndrome
2. Hyperhomocysteinaemia
3. Myeloproliferative disorders
4. Paroxysmal nocturnal haemoglobinuria

Patients with protein C deficiency are at risk of developing skin necrosis when starting warfarin treatment. In patients with protein C deficiency, therapy should be introduced without a loading dose of warfarin even if heparin is given. Patients with protein S deficiency may also be at risk and it is advisable to introduce warfarin therapy slowly in these circumstances.

Thrombophilia testing:

- Do not offer thrombophilia testing to patients who are continuing anticoagulation treatment
- Consider testing for antiphospholipid antibodies in patients who have had unprovoked DVT or PE if it is planned to stop anticoagulation treatment, and should be done at least 4 weeks after stopping anticoagulation.
- Consider testing for hereditary thrombophilia in patients who have had unprovoked DVT or PE and who have a first-degree relative who has had DVT or PE if it is planned to stop anticoagulation treatment, and should be done at least 4 weeks after stopping anticoagulation.
- Do not offer thrombophilia testing to patients who have had provoked DVT or PE.
- Do not routinely offer thrombophilia testing to first-degree relatives of people with a history of DVT or PE and thrombophilia.
- Thrombophilia testing rarely alter the patient's management.
- There is no clear evidence base for testing.
- It does not predict the risk of recurrence in unselected VTE patients.
- It is not recommended in arterial clots except for antiphospholipid syndrome.
- It is not indicated in Retinal Vein Occlusion.
- Unknown significance/indication for upper limb thrombosis, cerebral sinus thrombosis, and intraabdominal vein thrombosis.

11. TRAVEL-RELATED VENOUS THROMBOEMBOLISM

Global use of compression stockings and anticoagulation for long distance travel is not indicated. Assessment of risk should be made on an individual basis (see tables below).

Traveller's at the highest risk of travel-related thrombosis undertaking journeys of >3hrs should wear well fitted below-knee compression hosiery. Where pharmacological prevention is considered appropriate, anticoagulants as opposed to anti-platelets are recommended (unless contraindicated).

Duration of travel	**<3 hours**	**3 – 8 hours**	**>8 hours**
Low Risk	Nil	Nil	Nil
Medium Risk	Nil	Nil or Stockings	Stockings
High Risk	Nil	Stockings	Stockings +/- Anticoagulants (e.g. warfarin)

	Examples of thrombosis risk factors for VTE
Low Risk	• None
Medium Risk	• All others e.g. • Up to 6 weeks post-partum • Previous unprovoked VTE no longer on anticoagulants • Previous travel-related VTE • Combinations of risk factors
High Risk	• Major surgery in previous 4 weeks • Active cancer undergoing chemo-radiotherapy in the previous 6 months, awaiting surgery or chemo-radiotherapy, or in palliative phase

Please note: patients will be expected to buy these products prior to travel

12. ANTICOAGULATION OUTPATIENT SERVICES IN BEDFORDSHIRE

Oral anticoagulants are generally prescribed on a shared care basis, with treatment initiated in secondary care being continued by GP practices. Safe anticoagulant therapy relies on clear communication between all parties concerned. This applies to all anticoagulation not just warfarin.

Bedfordshire patients on VKA oral anticoagulation therapy are managed by Bedford Warfarin Service, Level 4 GP surgeries or the Anticoagulation Clinic at Bedford Hospital.

Management includes arranging blood sampling for INR and dosing patients based on their results. Prescribing responsibility lies with the clinician/GP.

There are several options for getting a blood sample taken for an INR as an outpatient:

- POC testing in clinic (finger prick)
- Venous sample taken by community phlebotomist who visits the home
- Venous sample taken at outpatient clinic (i.e. Cauldwell Centre)
- Venous sample taken at GP surgery
- Self-testing (patients that do their own finger prick testing at home)

Patients can receive their dosing schedule in their yellow book or via a Postal Dosage Slip (see Appendix 7)

Bedford Warfarin Service

The Bedford Warfarin Service (01234 893413) is part of Bedfordshire Community Health Services and manages stable or largely uncomplicated patients over the age of 18. The service runs from Monday to Friday 8.30am-4pm and offers both clinic and domiciliary appointments. Access into the service is by GP referral and the patient must be registered with a Bedfordshire GP.

Level 4 GP Surgeries

GP surgeries that provide a Level 4 Local Enhanced Service for Anticoagulation monitoring to their warfarin patients. They manage their own stable or largely uncomplicated warfarin patients over the age of 18. Clinic times will vary depending on the surgery and some may offer domiciliary appointments.

***Current* Level 4 GP Surgeries in Bedfordshire** *Subject to change*			
Surgery	**Contact Tel No**	**Surgery**	**Contact Tel No**
Goldington Road	01234 351341	Queens Park Surgery	01234 213300
De Parys Medical Practice	01234 350022	Templars Way Sharnbrook	01234 781392
Pemberley Surgery	01234 351051	Ivel Medical Centre	01767 312441
Houghton Close Surgery	01525 300898	Station Road, Lower Stondon	01462 850305
Cranfield & Marston	01234 766551	Greensands Surgery Potton	01767 260340
Goldington Avenue	01234 349531	Shefford Healthcare	01462 818620
Great Barford Surgery	01234 870325	Sandy Healthcare	01767 682525
Harrold Medical Practice	01234 720225	Barton-Le-Clay Surgery	01582 528701
Putnoe Medical Practice	01234 319992		

Anticoagulation Clinic Service at Bedford Hospital

The anticoagulant service is currently based in the haematology unit of South Wing, Bedford Hospital.
Opening hours – Monday to Friday 9 – 5pm

Useful contact numbers:
General enquiries – 01234795736 (external), ext. 2207(internal)
Anticoagulation specialist nurse/pharmacist – Bleep 467
POD - 18

The target population for this service include:

- Patients who are currently on warfarin therapy in primary care and are 'unstable' in terms of target INR ('stable' is defined as having had INR readings within target range for 3 consecutive readings and considered appropriate for transfer back into GP care)
- Patients newly prescribed anticoagulation therapy
- Complex high risk patients such as:
    - Patients with alcohol dependence prone to instability in anticoagulation management
    - Patients with a known hereditary or acquired bleeding disorder
    - Patients with severe malnourishment due to absorption difficulties
    - Mentally ill with no carer support in the community
    - Dementia with no carer support in the community
    - Patients with liver failure
    - Patients with severe renal impairment
    - Patients with documented evidence of CNS haemorrhage
    - Patients with severe heart failure
    - Patients with uncontrolled hypertension
    - Patients with gastrointestinal bleeding within the last 6 months
    - Pregnant women (urgent referral to Haematologist Consultant)
    - Patients receiving chemotherapy for malignant tumours
    - Children under 16 years (this service is not provided under the outpatient service)
    - Homozygous protein C deficiency (risk of skin necrosis)

For management of outpatients in the following scenarios please see local anticoagulation clinic policies/SOPs.

- Dosing warfarin patients whilst they are abroad
- Patients self-testing INRs on Coagucheck
- Managing patients who DNA clinic appointments
- Dealing with High INRs Out of hours (Outpatients only)
- Anticoagulant clinic advice for patients leaflet and postal advice leaflets.

Responsibilities of Secondary Care

- Initiate, monitor and titrate anticoagulation treatment for appropriate patients referred into the service.
- Review and confirm patient education regarding anticoagulant therapy
- Provide urgent medical advice relating to anticoagulation.
- Accept patients who are maybe not suitable for anticoagulation monitoring in primary care (refer to Target Population)
- Ensure transfer of care from secondary to primary care is seamless in terms of patients' anticoagulant therapy.
- Provide INR testing from venous samples or POC testing (finger prick testing).
- Patients internally referred to the Anticoagulation Clinic must be risk assessed for risk of bleed by referring consultant/physician. A signed and completed 'Anticoagulation Referral Form' and signed prescription needs to also be completed.
- Referring consultant/physician assumes full overarching clinical responsibility in the care and management of the patient

Responsibilities of Bedfordshire CCG

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

- Ensuring the NPSA safety alert 18 (Action that can make anticoagulant therapy safer) March 2007 is implement in GP Practices
- Develop, update and review the Local Enhanced Service for Anticoagulation in Primary Care as necessary
- Ensure Anticoagulation Therapy Guidelines, training packs and Standard Operating Procedures to support GP Practices are implemented by Level 5 anticoagulation practices.
- Ensure anticoagulation guidelines are available for the management of under and over anticoagulation
- Ensuring regular clinical audit is undertaken.
- Ensure that adequate capacity exists in primary care for the smooth transfer of stable patients (thee INRs in target range) back into the care of their GP.

Responsibilities of Level 4 GP Practices and other Bedfordshire Anticoagulation Service Providers

To develop practice Standard Operating Procedures or detailed anticoagulation policies, which are read and signed by all relevant staff and responsibilities of staff are clear and understood.

- Ensuring appropriate training is undertaken by all staff involved in anticoagulation and evidence of this training is documented. All competencies must be satisfactory before undertaking the service.
- Training on Computerised Decision Support Software (CDSS) is completed prior to implementation, if used.
- The appropriate equipment for testing INR and vitamin K is available at the anticoagulation clinic/ GP surgery.
- Training on POC testing meters must be undertaken before testing can commence.
- Ensuring internal and external audit for the equipment used in anticoagulation is undertaken and results submitted as required.
- Perform and record clinical audit including development of action plans and re-audit.
- Ensure a GP is available at all times when anticoagulation services are offered to patients by the practice.
- Ensure reception staff are aware of the importance of patients attending within a specified period so that appointments are not delayed without guidance from appropriate clinical staff.

- Ensure transfer of care from secondary to primary care is seamless in terms of patients' anticoagulant therapy.
- Appropriate reversal medications are stored on site to deal with the management of urgent cases, such as reversal of high INR levels with Vitamin K formulations. Konakion MM paediatric is available as 2mg/0.2ml ampoules and can be given orally which licensed for oral administration

Responsibilities of Patient's GP

Overall responsibility for the care of the patients continues to reside with the registered GP who may be required to provide prescriptions for anticoagulation therapy and includes:

- Ensuring that dose recommendations and recall are guided by approved written protocols or Computerised Decision Support Software (CDSS).
- Ensuring patients receive education regarding anticoagulant therapy.
- Giving advice on duration and intensity of anticoagulation as guided by initiating clinician.
- Being aware of the potential effects of additional therapy given to a patient on anticoagulants, and arranging earlier INR testing as required.
- Acting promptly to patients with bleeding problems and/or INR > 8 or who are otherwise considered to be at risk of bleeding.
- Dosing decisions should be made by health-care professionals (e.g. GP's, registered pharmacists or registered nurses) who have undergone an approved course for practitioners undertaking anticoagulant monitoring in primary care and who are deemed competent under relevant competency frameworks.
- Arranging admission to hospital if required.
- Issuing warfarin prescriptions.
- Appropriate reversal medications are stored on site and arrangements exist with Out of Hours Services (Herts Urgent Care) to deal with the management of urgent cases, such as reversal of high INR levels with Vitamin K formulations. Konakion MM paediatric is available as 2mg/0.2ml ampoules and can be administered orally is licensed for oral administration.
- Ensuring that all patients receive appropriate monitoring, either with primary care anticoagulation service or in secondary care.
- To stop the anticoagulant when specified duration is complete, this decision can also be made by secondary care where it has been initiated by the hospital
- On initiation of therapy the patient is assessed on their ability to take warfarin safely (risk assessment of patients for oral anticoagulation)
- Ensuring that patients, who do not speak, read or write English or who have communication difficulties (including without limitation hearing, oral or learning impairments) are provided with appropriate assistance. A responsible person or carer should be identified who can assist patient with any dose alterations.

13. BEDFORDSHIRE AND LUTON JOINT PRESCRIBING COMMITTEE ADVICE

Open link to see local advice and guidance on anticoagulants from Bedfordshire CCG.

http://www.gpref.bedfordshire.nhs.uk/referrals/bedfordshire-and-luton-joint-prescribing-committee-(jpc)/jpc-advice-and-guidance.aspx

14. AUDIT

Every 2 years the parameters from the NPSA audit checklist will be audited prospectively by the Anticoagulation Outpatient Clinic at Bedford Hospital using the information on referral forms and DAWN (the Computerised Decision Support System).

Audits will be reported back to the Haemostasis and Thrombosis Committee/Drugs and Therapeutics Committee.

Patient safety incident data involving anticoagulants will be documented through the trust Datix system and reviewed by the Medicines Safety Committee. Root Cause analysis investigation report will be completed for Serious Incidents and reviewed by the Haemostasis and Thrombosis Committee.

15. EDUCATION AND TRAINING

Prescribers

All prescribers that initiate, continue or adjust dosage of anticoagulants must be competent to undertake their work safely. Any gaps in competence must be addressed through training to ensure that staff may undertake their duties safely.

The Foundation doctors' induction includes a presentation on Anticoagulation therapy. Medical prescribers are also assessed on anticoagulation as part of the National Prescribing Skills assessment and the Competency Testing for Bedford Prescribers.

All prescribers are advised to complete the BMJ E-Learning packages:
Starting patients on anticoagulants in secondary care: how to do it
Maintaining patients on oral anticoagulants: how to do it

Nursing Staff

Nursing staff (including PRPs) who are authorised to administer medications under the 'Administration of Medicines Policy (MP4)' may administer anticoagulants. Nurses who are required to prepare or administer heparin therapy must have completed the Intravenous administration competency outlined in the Administration of Medicines Policy.

It is the responsibility of line managers to ensure staff that administer or discharge patients on anticoagulants have sufficient knowledge to fulfil their responsibilities under this policy.

Pharmacy Staff

Pharmacists involved in clinically screening prescriptions for anticoagulants are advised to complete the CPPE E-Learning package Anticoagulation: initiation, management, patient support and safety.

Medicines Management technicians and ward based pharmacy technicians must have sufficient knowledge of anticoagulants to provide appropriate counselling to patients when required.

16. RESPONSIBILITIES

Haemostasis and Thrombosis Committee

It is the responsibility of the Haemostasis and Thrombosis Committee to ensure that the Trust protocols are evidence based, in line with National Guidance and up to date.

Prescribers

General responsibilities

Senior Clinicians are responsible for ensuring that all staff, particularly junior doctors, pre-op assessment staff and non-medical prescribers, keep up to date and implement the trust policy and clinical protocols. Junior doctors are responsible for implementing the protocols for all patients - as inpatients and on discharge.

Inpatient prescribing

For inpatients, VKAs should be prescribed on the 'Variable dose' tab on MedChart, unfractionated heparin on the IV Fluid Chart and other oral anticoagulants and LMWH on the Scheduled tab on MedChart.

In areas that do not use MedChart or during extended system downtime, VKAs will be prescribed on the anticoagulant paper charts which can be found in the offline charts cupboard.

The daily dose must be prescribed before 5pm wherever possible.

Dosing should not be left for the out-of-hours cover team to complete.

Prescribing on discharge

On discharge, all anticoagulants should be prescribed on the TTO. Dosing information for VKAs will be written in a Yellow book. See Appendix 9 for further information regarding referrals.

Monitoring

INR must be checked within 1-2 days of any change in other medication. Any significant change in clinical presentation in a patient on warfarin should trigger an immediate INR test and repeat INRs may be necessary whilst the patient remains unwell. Where patients on NOACs have a significant change in clinical presentation bleeding should be considered and an immediate haemoglobin check carried out. A change in renal function can also result in accumulation of active drug and NOACs and LMWHs may need to be dose reduced or withheld until renal function recovers.

Nursing Staff

Administration

VKAs should be administered on the 5-6pm drug administration round. If the dose is not prescribed by mid-afternoon the clinical team should be contacted to prescribe the dose as soon as possible.

Before administering parenteral, subcutaneous or oral anticoagulants to a patient the nurse should carry out all checks as per MP4: Administration of Medicines Policy including recent INR for VKAs.

After administering anticoagulation to a patient, the nurse should:

- Monitor for any signs of bleeding
- Manage the patients' risk of falls on the ward

Discharge

The nurse must ensure the discharge checklists in Appendix 8 have been completed.

The nurse issuing the discharge medication to the patient must check that the current anticoagulant dose (and when this dose is due to be taken) has been communicated to the patient or carer. The nurse should also confirm that the patient has understood this information. For VKA patients, the yellow book must be sent with them at discharge.

A patient requiring LMWH on discharge should be counselled on how to administer. If the patient/carer is unable to self-administer, the ward nurse should make arrangements with the appropriate community team.

Discharge checklists should be filed in the patients' medical notes once complete.

Pharmacy Staff

Medicines reconciliation

Ensure the maintenance dose of warfarin is recorded on medicines on admission. Establish which clinic the patient is under and inform them of the patients' admission to hospital.

Clinical screening of inpatient prescriptions

- Pharmacists should clinically screen all prescriptions for anticoagulants to confirm that the drug, dose and route are appropriate for the patient and therapy is safe and cost effective. **Any problems including significant drug interactions should be discussed with the prescriber and appropriate action taken.**
- Pharmacists should check that a recent, satisfactory INR test has been performed and recorded before approving a VKA prescription

Dispensing

- Patients should be provided with the minimum number of strengths of warfarin requires for them to take the prescribed dose. This will normally be 1mg and 3mg tablets but could include 500microgram and 5mg tablets if necessary. Tablets of 500micrograms may be required to prevent patients from halving tablets which can lead to inaccuracies in dosage.
- Dispensing labels for VKAs should state "Take as directed on your anticoagulant card" and should not include a specific dose.
- NPSA OAT packs and Yellow books are supplied from pharmacy and will be held as ward stock in all areas where they are commonly required. Ward stock supplies will be reordered or topped-up in the same way as stock drugs supplied from pharmacy.

Discharge

As part of the clinical screening process for TTOs, pharmacists must ensure the prescriber has completed the necessary referral forms.

The NOAC initiation checklist should be completed by either the nursing staff or pharmacy staff and filed in the patients' medical notes once complete.

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Date: 4/4/2019	Date:
Signature: Muhsin ALMUSAWY	Signature:
Print Name: MUHSIN ALMUSAWY (Chairperson of Board or Committee indicated above)	Print Name: (Chairperson of Board or Committee indicated above)

Name of Other Sub-Committee / Business Unit involved in Approval of Guideline: **Drugs and Therapeutics Committee**

Date: 10/4/19	Date:
Signature:	Signature:
Print Name: (Chairperson of Board or Committee indicated above)	Print Name: (Chairperson of Board or Committee indicated above)

Ratification Signature
Approved by Quality Board

Date:	
Signature:	
Print Name	

Consultation List

A completed list should accompany **every** guideline/policy
(This gives evidence on who has seen this Guideline and any comments made)

Name of Person	Department or Committee	Comments
Aoife McKnight	Lead Nurse Planned care	No comment
Arindam Chaudhuri	Consultant Vascular Surgeon	No comment
Cathy Pullen	Lead Nurse Integrated Medicine	No comment
Helen Friend	Associate Director of Quality Improvement	No comment
John Cooper	Consultant Cardiologist	No comment
Lia Contino	VTE coordinator	No comment
Matthew Lock	Principal Pharmacist for Integrated Medicine	Comments incorporated
Oilin Man	Lead Pharmacist Admissions	No comment
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Ruth Patrickson	Bedford Warfarin Clinic Anticoagulation Nurse	No comment
Aidan Vaughan	Deputy Director for Clinical Governance	Comments incorporated relating to policy layout
Drugs and Therapeutics Committee		Comments incorporated
Haemostasis and Thrombosis Committee		Comments incorporated