FOI REF: 26/067

East Sussex Healthcare NHS Trust

6th March 2026

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FREEDOM OF INFORMATION ACT

I am responding to your request for information under the Freedom of Information Act. The answers to your specific questions are as follows:

Please provide the current VTE prophylaxis regimen used by your organisation for the following groups of adult orthopaedic patients.

For each group, please provide the following three data items:

- **Agent (e.g., enoxaparin, DOAC, aspirin, none)**
- **Dose**
- **Duration (days)**

1. Lower-limb immobilisation (non-operative injuries)

- **Agent (e.g., enoxaparin, DOAC, aspirin, none)**

  Enoxaparin.

- **Dose**

  The dose depends on patient's weight/renal function (as per British National Formulary, BNF).

- **Duration (days)**

  For the duration of patient having been told non weight bearing/till cast removed.

2. Fragility fractures of the pelvis, hip, or proximal femur

- **Agent (e.g., enoxaparin, DOAC, aspirin, none)**

  Patients admitted with Neck of femur fractures will need Enoxaparin for 1 month (or during their inpatient hospital stay if longer).

- **Dose**

  The dose depends on patient's weight/renal function (as per BNF).

- **Duration (days)**

  28-30 days (1 month) - or whilst inpatient is they stay longer than a month as inpatient.

3. **Non-arthroplasty knee surgery (e.g., arthroscopy, ligament repair, other non-arthroplasty knee procedures)**

   - **Agent (e.g., enoxaparin, DOAC, aspirin, none)**

     If needed, Enoxaparin - depends on Consultant advice in operation note. Normally no VTE prophylaxis required unless specified.

   - **Dose**

     The dose depends on patient's weight/renal function (as per BNF).

   - **Duration (days)**

     As per operation note plan.

4. **Foot and ankle orthopaedic surgery (including operative procedures requiring immobilisation)**

   - **Agent (e.g., enoxaparin, DOAC, aspirin, none)**

     Enoxaparin (depends on what type of surgery will be required or not)- will be noted by T&O Consultant in post operative care plan.

   - **Dose**

     The dose depends on patient's weight/renal function (as per BNF).

   - **Duration (days)**

     As per operation note plan.

5. **Upper limb orthopaedic surgery**

   - **Agent (e.g., enoxaparin, DOAC, aspirin, none)**

   - **Dose**

   - **Duration (days)**

   Not applicable, no VTE prophylaxis required.

6. **Elective primary hip replacement (THR)**

- **Agent (e.g., enoxaparin, DOAC, aspirin, none)**

  THR VTE Prophylaxis Trust protocol: Enoxaparin 10 days followed by Aspirin 28 days.

- **Dose**

  Enoxaparin dose depends on patient's weight/renal function (as per BNF). Aspirin is 75 mg once a day.

- **Duration (days)**

  Duration as above.

7. **Elective primary knee replacement (TKR)**

- **Agent (e.g., enoxaparin, DOAC, aspirin, none)**

  TKR VTE Prophylaxis Trust protocol: Enoxaparin.

- **Dose**

  The dose depends on patient's weight/renal function (as per BNF).

- **Duration (days)**

  14 days duration.

If different regimens are used for "standard-risk" versus "high-risk" patients, please specify the regimen for the standard pathway.

Please see above.

If available, please also provide the relevant page(s) from your local VTE prophylaxis guideline for verification.

Please see attached the following documents:

- Clinical Guideline for Anticoagulant Use in Adults_Redacted
- Venous Thromboembolism Diagnosis, Treatment and Prevention Policy and Procedure_Redacted

Please note that East Sussex Healthcare NHS Trust also follows NICE Guideline - Venous thromboembolism in over 16s: reducing the risk of hospital-acquired deep vein thrombosis or pulmonary Embolism.

Please note that it is the Trust's FOI policy to only provide the names of staff that are grade 8a or above, therefore staff that are below that grade have been redacted from the attached policy.

Please also note that we have redacted the names of staff that no longer work for the Trust and the names of the Trust's IT Systems and are applying Sections 40(2) and 31(1)(a) respectively, please see below:

Section 40(2)

I can confirm that we hold this information, but it is exempt under Section 40(2) of the Freedom of Information Act 2000 – Personal Information of third parties. This is because this information may allow the identification of individuals and disclosure would breach the principles of the Data Protection Act.

This is an absolute exemption and there is, therefore, no requirement to consider the public interest.

Section 31(1)(a)

Section 31(1)(a) has also been applied to the names of the Trust IT systems within this document; therefore, these have also been redacted.

Under Section 31(1)(a) of the Freedom of Information Act (FOIA), the Trust can confirm that it holds information relevant to your request, however, we are unable to disclose it for the reasons explained below.

Historically, we would disclose information relevant to the Trust's IT systems, infrastructure and software as part of our transparency agenda under the terms of the Freedom of Information Act (FOIA). However, in light of the recent cyber-attacks on NHS hospitals and the serious impact these have had on patient services and the loss of patient data, we are having to reconsider this approach. Please see several links to news articles about these recent cyber incidents provided below for your information.

- *NHS England — London » Synnovis Ransomware Cyber-Attack*
- *NHS England confirm patient data stolen in cyber attack - BBC News*
- *Merseyside: Three more hospitals hit by cyber attack - BBC News*

As a result of these attacks, thousands of hospital and GP appointments were disrupted, operations were cancelled, and confidential patient data was stolen which included patient names, dates of birth, NHS numbers and descriptions of blood tests.

When we respond to a Freedom of Information request, we are unable to establish the intent behind the request. Disclosure under the FOIA involves the release of information to the world at large, free from any duty of confidence. Providing information about our systems or security measures to one person is the same as publishing it for everyone. While most people are honest and have no intention of misusing information to cause damage, there are criminals who look for opportunities to exploit system weaknesses for financial gain or to cause disruption.

In the context of the FOIA, the term ‘’public interest’’ does not refer to the private or commercial interests of a requestor; its meaning is for the “public good”. The Trust receives a significant number of requests each year regarding our IT systems, infrastructure and cyber security measures. Most of these requests are commercially driven and serve no direct public interest. Information relevant to our IT portfolio is often requested by consultancy companies who then pass on this information to their client base. Many of these requests are submitted through the FOI portal whatdotheyknow.com who publish our responses, making this information available to an even wider audience.

As a large NHS Trust we hold extensive personal data relevant to our patients and staff, much of which is considered very sensitive. A lot of this information is held electronically on various administration and clinical systems. We have a duty under the Data Protection Act 2018 and the UK GDPR to protect this personal information and take all necessary steps to ensure this data is kept safe. This means not disclosing information that could allow criminals to gain unlawful access to our systems and infrastructure. The Trust can be heavily fined should it be found to have acted in a negligent way which results in a personal data breach. We need to demonstrate that we comply with our legal obligations under data protection and freedom of information legislation, but we must be careful that too much transparency does not result in harm to our patients or staff, or cause disruption to our services.

Moreover, under the Network and Information Systems (NIS) Regulations Act 2018, operators of essential services such as NHS organisations like ours have a legal obligation to protect the security of our networks and information systems in order to safeguard our essential services. By releasing information that could increase the likelihood or severity of a cyber-attack, the Trust would fail to meet its security duties as stated in Section 10 of the Network and Information Systems Regulations 2018. Should we not comply with these requirements regulatory action can be taken against the Trust. Further information about the Network and Information Systems (NIS) Regulations Act 2018 can be found here – The Network and Information Systems Regulations 2018: guide for the health sector in England - GOV.UK

Your request asks for policy documents which unfortunately mention specific details regarding our IT Systems which, for the reasons explained above, would be inappropriate to release into the public domain. If disclosed, it is possible that patient data as well as other confidential information would be put at risk. Such disclosure could also impact on the security of our systems and result in serious disruption to the health services we deliver to the local community. Section 31(1)(a) of FOIA provides that information is exempt if its disclosure would, or would be likely to, prejudice (a) the prevention or detection of crime. In this case, disclosure would be likely to prejudice the prevention of crime by enabling or encouraging malicious acts which could compromise the Trust’s IT systems and infrastructure. The Trust’s capacity to defend itself from such acts relates to the purposes of crime prevention and therefore Section 31(a) exemption is applicable in these circumstances. For these reasons, the Trust considers disclosure of the information you are seeking to be exempt under Section 31(1)(a) [*law enforcement*] of the FOIA and the names of the IT systems within the policies are being withheld. The full wording of Section 31 can be found here: Freedom of Information Act 2000

Section 31 is a *qualified* exemption and therefore we must consider the prejudice or harm that may be caused by disclosure of the information you have requested, as well as apply

a public interest test that weighs up the factors in maintaining the exemption against those in favour of disclosure.

In considering the prejudice or harm that disclosure may cause, as explained should the Trust release information into the public domain which draws attention to any weaknesses relevant to the security of our systems or those of a supplier, this information could be exploited by individuals with criminal intent. Increasing the likelihood of criminal activity in this way would be irresponsible and could encourage malicious acts which could compromise our IT systems or infrastructure, result in the loss of personal data and/or impact on the delivery of our patient services. We consider these concerns particularly relevant and valid considering the increasing number of cyber incidents affecting NHS systems in recent years and the view by government, the ICO and NHS leaders that the threat of cyber incidents to the public sector is real and increasing.

- Organisations must do more to combat the growing threat of cyber attacks | ICO

In the Government's Cyber Security Strategy 2022-2030, the Chancellor of the Duchy of Lancaster and Minister for the Cabinet Office states on page 7:

"Government organisations - and the functions and services they deliver - are the cornerstone of our society. It is their significance, however, that makes them an attractive target for an ever-expanding army of adversaries, often with the kind of powerful cyber capabilities which, not so long ago, would have been the sole preserve of nation states. Whether in the pursuit of government data for strategic advantage or in seeking the disruption of public services for financial or political gain, the threat faced by government is very real and present.

Government organisations are routinely and relentlessly targeted: of the 777 incidents managed by the National Cyber Security Centre between September 2020 and August 2021, around 40% were aimed at the public sector. This upward trend shows no signs of abating."

With this in mind, we then considered the public interest test for and against disclosure. It should be noted that the public interest in this context refers to the public good, not what is 'of interest' to the public or the private or commercial interests of the requester. In this case we consider the public interest factors in favour of disclosure are:

- Evidences the Trust's transparency and accountability
- Provides information relevant to the IT systems and applications the Trust uses
- Reassures the public and partners that the Trust procures these systems in line with Procurement legislation
- Reassures the public and partners that the Trust's IT infrastructure and systems are secure

Factors in favour of withholding this information are:

- Public interest in crime prevention

- Public interest in avoiding disruption to our health services
- Public interest in maintaining the integrity and security of the Trust's systems
- Public interest in the Trust avoiding the costs associated with any malicious acts (e.g. recovery, revenue, regulatory fines)
- Public interest in complying with our legal obligations to safeguard the sensitive confidential information we hold

In considering all of these factors, we have concluded that the balance of public interest lies in upholding the exemption and not releasing the information requested. Although disclosure would provide transparency about our software systems and IT infrastructure, this is outweighed by the harm that could be caused by people who wish to use this information to assess any vulnerabilities in our security measures and consequently use this information for unlawful purposes. Cybercrime can not only lead to major service disruption but can also result in significant financial losses. As a publicly funded organisation, we have a duty for ensuring our public funding is protected and spent responsibly. Moreover, as a public body the Trust must demonstrate that it keeps its confidential data and IT infrastructure safe and complies with relevant legislation, but at the same time we must be vigilant that transparency does not provide an opportunity for individuals to act against the Trust. In considering the impact that recent cyber-attacks have had on NHS services, including the cancellation of thousands of patient appointments and procedures as well as the loss of confidential patient data, we consider the overriding public interest lies in withholding this information. The private or commercial interests of a requester should not outweigh the public interest in protecting the integrity of our systems and continuity of our essential patient services. Although we appreciate there may be legitimate intentions behind requesting this information, we must take a cautious approach to requests of this nature and appreciate your understanding in this matter.

If I can be of any further assistance, please do not hesitate to contact me.

Should you be dissatisfied with the Trust's response to your request, you have the right to request an internal review. Please write to the Freedom of Information Department (esh-tr.foi@nhs.net), quoting the above reference, within 40 working days. The Trust is not obliged to accept an internal review after this date.

Should you still be dissatisfied with your FOI request, you have the right of complaint to the Information Commissioner at the following address:

The Information Commissioner's Office
Wycliffe House
Water Lane
Wilmslow
Cheshire SK9 5AF

Telephone: 0303 123 1113

Yours sincerely

Freedom of Information Department
esh-tr.foi@nhs.net

East Sussex Healthcare NHS Trust

Clinical Guideline for Anticoagulant Use in Adults

Document ID Number	191
Legacy Number	876
Version:	V4.3
Ratified by:	Medicine's Optimisation Group (MOG)
Date ratified:	5th February 2025
Name of author and title:	Iwona Ward, Anticoagulation Pharmacist; Dr Richard Grace, Consultant Haematologist
Date originally written:	May 2007
Date current version was completed:	December 2024
Name of responsible committee/individual:	Dr. Richard Grace
Date issued:	
Review date:	June 2026
Target audience:	Medical, pharmacy, nursing and haematology laboratory staff involved in the management of patients with, or at risk of, venous thromboembolic disease or arterial vaso-occlusive disease.
CQC Fundamental Standard:	Regulation 9 Person Centre Care Regulation 12 Safe Care and Treatment
Compliance with any other external requirements (e.g., Information Governance):	N/A
Associated Documents:	Venous Thromboembolism Diagnosis, Treatment and Prevention Policy and Procedure. Clinical Guideline for Thromboprophylaxis and Treatment of Venous Thromboembolism in Maternity.

Did you print this yourself?
Please be advised the Trust discourages retention of hard copies of procedural documents and can only guarantee that the procedural document on the Trust website is the most up to date version.

Version Control Table

Version number and issue number	Date	Author	Reason for Change	Description of Changes Made
V1 2007055	May 2007	Dr Richard Grace		
V2 2010091	April 2010	Dr Richard Grace		
V1.0 2013119	February 2013	Dr Richard Grace	Reviewed in-line with updated Formulary, ACCP and NICE guidance	Inclusion of Apixaban, Rivaroxaban and Dabigatran
V2.0 2017232	June 2017	Iwona Ward	Reviewed in accordance with review date	Updated warfarin loading and heparin infusion protocol. Inclusion of: argatroban infusion protocol for HIT; stopping DOACs for surgery; management of bleeding with DOACs; dosing of enoxaparin in >150kg; timing of anticoagulation and neuroaxial anaesthetics.
V3.0	July 2020	Iwona Ward	Reviewed in accordance with review date	Updated target INRs for mechanical prostheses and new mechanical prostheses appendix; DOAC interactions including anticancer drugs & anti-epileptics; dosing of apixaban & rivaroxaban for VTE prophylaxis following ≥ 6 months DVT or PE treatment; suggestions for initiation of anticoagulation for AF; updated VTE guidance in line with NG158 March 2020; advice on anticoagulation in >120kg or BMI >40Kg/m^2; incorporation of 'Provision of patient information for patients newly initiated on oral anticoagulation medication' policy
V 3.1	19 March 2021	Jane Starr	Flowchart added	Balance risks of VTE and bleeding

				before VTE flow chart inserted under 7.1
V 3.2	September 2021	Iwona Ward	Updated NICE guidance for Andexanet alfa	Andexanet alfa included as reversal agent
V 3.3	November 2021	Iwona Ward	Updated in line with NICE, ESC and incident recommendations.	Revised and updated DOAC interactions including herbal medicines; advice to measure renal function within 24 hours of starting an anticoagulant.
V3.4	January 2022	Iwona Ward	Update to Appendix F	Appendix F has been updated to a new layout
V 3.5	February 2022	Iwona Ward	Updated extremes of body weight recommendations	Updated advice for prescribing DOACs at extremes of body weight; andexanet alfa administration protocol.
V3.6	March 2022	Iwona Ward	Update to Appendix F	Due to updates on ePMA, Appendix F was updated to reflect the changes.
V3.7	July 2022	Iwona Ward	Update to Appendix L	Updated bridging guidelines in mechanical heart valves.
V4.0	May 2023	Iwona Ward	Appendix M added	Addition of appendix for management of superficial vein thrombosis of the lower limb. Updated first line for NVAF suggestions in line with ICB and NHS commissioning recommendations.
V4.1	Sept 2023	Iwona Ward	Appendix N added	Appendix N added Addition of Protocol for the Management of Massive Pulmonary Embolism (PE) with Thrombolysis
V 4.2	Oct 2023	Iwona Ward	Update to Appendix M	Update to Appendix M due to further input from Cardiology
V4.3	December 2024	Iwona Ward	Updates in line with clinical guidance	Full guideline revision. Information added regarding Inhixa® enoxaparin. Updated stroke VTE algorithm. Alteplase guideline for PE thrombolysis reinstated. Argatroban therapeutic ranges updated. Reversal

				of life-threatening bleed with dabigatran protocol updated. HAS-BLED changed to ORBIT – bleeding risk calculator.

Consultation Table

This document has been developed in consultation with the groups and/or individuals in this table:

Name of Individual or group	Title	Date
Dr. Joel Newman	Consultant Haematologist	October 2020
[redacted]	Medical Director / Consultant Cardiologist	October 2020
[redacted]	Consultant Cardiologist	October 2020
[redacted]	Deputy Chief Pharmacist	October 2020
Medicines Optimisation Group		November 2020
Medicines Optimisation Group		September 2021
Medicines Optimisation Group		November 2021
Medicines Optimisation Group		January 2022
Medicines Optimisation Group		June 2023
Medicines Optimisation Group		September 2023
Medicines Optimisation Group		February 2025

This information may be made available in alternative languages and formats, such as large print, upon request. Please contact the document author to discuss.

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Abbreviations

AF	Atrial Fibrillation
APTT	Activated Partial Thromboplastin Time
BD	Twice Daily
BMI	Body Mass Index
BNF	British National Formulary
BCRP	Breast Cancer Resistance Protein
CKD	Chronic Kidney Disease
CrCl	Creatinine Clearance
DIC	Disseminated Intravascular Coagulation
DOAC	Direct Oral Anticoagulant
DVT	Deep Vein Thrombosis
eGFR	estimated Glomerular Filtration Rate
FBC	Full Blood Count
FFP	Fresh Frozen Plasma
GI	Gastrointestinal
H_2B	H2-Blocker
HIT	Heparin Induced Thrombocytopenia
INR	International Normalised Ratio
LFT	Liver Function Test
LMWH	Low Molecular Weight Heparin
MI	Myocardial Infarction
NICE	National Institute for Health and Care Excellence
NSAIDs	Non-Steroidal Anti-Inflammatory Drugs
NVAF	Non-valvular Atrial Fibrillation
OD	Once Daily
PE	Pulmonary Embolism
P-gp	P-Glycoprotein
PCC	Prothrombin complex concentrate
PPI	Proton Pump Inhibitor
SVT	Superficial venous thrombosis

UFH	Unfractionated Heparin
ULN	Upper Limit of Normal
VKA	Vitamin K Antagonist
VTE	Venous Thromboembolic Event

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1. Introduction

This document is designed to provide support for staff in the safe prescribing, administration and monitoring of anticoagulant therapies including the management of adverse events.

2. Purpose

2.1. Rationale

To highlight issues surrounding the safe initiation, administration and monitoring of anticoagulant therapy to prevent and treat venous thromboembolic disease and arterial vaso-occlusive conditions.
The use of agents in relation to acute coronary syndromes is not included in this guidance.

2.2. Scope

- The document applies to Medical, Pharmaceutical, Podiatry, Nursing and Midwifery, and Operating Department Practitioners involved in the care of patients receiving anticoagulant therapies.

- Please read this in conjunction with the Venous Thromboembolism Diagnosis, Treatment and Prevention Policy and Procedure 01152_P.pdf (esht.nhs.uk).

- LMWH, UH, VKAs and DOACs are all licensed for the treatment of VTEs. Refer to Table 35 for the most suitable choice in specific clinical circumstances.

- Follow Figure1 Process for initiation of anticoagulant therapy and document the outcome of the patient discussion, before initiating anticoagulation to ensure that NICE standards are met.

2.3. Accountability Statement

- Doctors and Non-Medical Prescribers are responsible for the safe and appropriate prescribing of the drugs referenced within this document. They are also responsible for ensuring that patients are monitored appropriately, patients are provided with relevant information, counselling, and that all discussions and outcomes are documented.

- Registered Nurses, Pharmacists, Podiatrists, Midwives and Operating Department Practitioners are responsible for the implementation of monitoring arrangements, safe administration of medicines and for ensuring that any adverse effects are escalated and acted upon to maintain patient safety.

3. Process for Initiation of Anticoagulant Therapy

- The following provides a summary of the process that initiators of therapy must follow in order to fulfil expectations of NICE guidelines [1, 2].
- To aid decision making and patient discussion, further details regarding the indications, interactions and contraindications for anticoagulant therapy can be found in section 4. Starting Oral Anticoagulant Therapy (hyperlink) of the guidelines.

Figure 1**:** Process for initiation of anticoagulant therapy

Perform Baseline Assessment:

- Full blood count, renal function, liver function, coagulation screen - within 24 hours.
- Calculate CrCl using Cockcroft – Gault equation https://www.mdcalc.com/creatinine-clearance-cockcroft-gault-equation.
- If out of range results obtained, discuss with Haematology prior to initiating treatment.

For patients with AF- assessing suitability for anticoagulation:

- If considering Anticoagulation in patients with AF NICE guidance requires:

1. CHA_2DS_2-VASc ≥2 or CHA_2DS_2-VASc ≥1 in men
   Calculate: https://www.mdcalc.com/cha2ds2-vasc-score-atrial-fibrillation-stroke-risk
2. ORBIT score
   Calculate: https://www.mdcalc.com/calc/10227/orbit-bleeding-risk-score-atrial-fibrillation
   - Score ≥4 = high risk for major bleeding

- Review risk factors for bleeding and modify as able, including:
  - Uncontrolled hypertension, poor INR control in patients on warfarin, concurrent medication (such as antiplatelets, SSRIs and NSAIDs), harmful alcohol consumption and reversible anaemia.
- Do not withhold anticoagulation solely because of age or risk of falls.

Patient Discussion:

- NICE guidelines require discussion with patient to include:
  - Risk and benefits of treatment options and alternatives to anticoagulation
  - Advantages and disadvantages of each therapy in context of individual clinical circumstances.

  Assess:
    - Risk of bleeding
    - Likelihood of person maintaining consistent anticoagulation
    - Renal and hepatic functions
    - Potential drug interactions
    - Patient experience and treatment preference

Education:

Once patient has agreed a treatment option, organise **ABC** – **A**lert Card, **B**ook & **C**ounselling.
Refer to counselling policy Appendix C

Follow-up:

- **New warfarin patients should be seen within 3 days of discharge by their GP** – to check INR, medication management, bleeding / thromboembolic events and other side effects.
- **New DOAC patients should be seen 1 month post discharge by their GP** – to check on adherence, bleeding / thromboembolic events / other side effects and renal function.

Documentation:

- Document:
  - Indication for treatment
  - Discussion with patient
  - Risk assessment including baseline laboratory assessments
  - Patient treatment preference
  - CHA_2DS_2-VASc and ORBIT for patients requiring anticoagulation for AF
  - Complete mandatory Anticoagulation section of e-Discharge Summary Letter

References [2,3]

4. Starting Oral Anticoagulant Therapy

- The following section provides further information regarding anticoagulant therapy options to guide physician and patient treatment selection.
- For each anticoagulant option guidance is given regarding indications, contraindications, interactions and treatment initiation.
- Oral anticoagulant therapy can be divided into vitamin K antagonists (VKAs) & direct oral anticoagulants (DOACs). Warfarin is the most commonly used VKA.
- DOACs are further divided into direct anti Xa-inhibitors (rivaroxaban, apixaban and edoxaban) and the direct thrombin inhibitor dabigatran.

4.1. Vitamin K Antagonists

- Warfarin is the most commonly prescribed VKA.
- See Appendix B1 Warfarin for product summary.
- Warfarin takes 48 to 72 hours for its anticoagulant effect to develop and when stopped, the effect declines over 24-48hrs.
- Acenocoumarol (Sinthrome®) and phenindione are also occasionally used.

4.1.1. Indications

Table 1: Indications for VKA-Oral Anticoagulant Therapy and target INR (including mechanical heart valve targets)

Indication	Target INR	
Pulmonary embolus	2.5	
Proximal deep vein thrombus	2.5	
Calf vein thrombus	2.5	
Recurrence of venous thromboembolism when no longer on warfarin	2.5	
Recurrence of venous thromboembolism whilst on warfarin	3.5	
Symptomatic inherited thrombophilia	2.5	
Antiphospholipid syndrome	2.5	
Non-rheumatic atrial fibrillation	2.5	
Atrial fibrillation due to rheumatic heart disease, congenital heart disease and thyrotoxicosis	2.5	
Cardioversion	2.5 - 3.0	
Mural thrombus	2.5	
Cardiomyopathy	2.5	
Mechanical prosthetic heart valve – Prosthesis thrombogenicity[a,c]	Patient risk factors[b]	
	Absent	≥1 Present
Low	2.5	3.0
Medium	3.0	3.5
High	3.5	4.0
Bioprosthetic valve	Aortic position – anticoagulation not indicated; current recommendation is for antiplatelet treatment e.g. aspirin for 3 months post-	

	surgery, provided no other risk factors Mitral & Tricuspid position - 2.5 for 3 months post-surgery provided no other risk factors for continued anticoagulation
Ischaemic stroke without atrial fibrillation	Not indicated
Retinal vessel occlusion	Not indicated
Peripheral arterial thrombosis	Not indicated
Arterial grafts	2.5 if anticoagulated
Coronary artery thrombosis	2.5 if anticoagulated
Coronary artery graft	Not indicated
Coronary angioplasty and stents	Not indicated

[a] **Mechanical heart valve prosthesis thrombogenicity** [4]			[b] **Patient risk factors:**
Low (most current valves)	Carbomedics (aortic position)		Mitral, tricuspid or pulmonary position
	Medtronic Hall		Previous arterial thromboembolism
	Medtronic Open –Pivot		Atrial fibrillation
	ATS		Left atrium diameter > 50 mm
	St Jude Medical		Mitral stenosis of any degree
	On-X		Left ventricular ejection fraction < 35%.
	Sorin Bicarbon		Left atrial dense spontaneous echo contrast
Medium	Other bileaflet valves with insufficient data		
High	Starr-Edwards (ball cage)		
	Omniscience		
	Lillehei-Kaster		
	Bjork-Shiley and other tilting-disc valves		

[c] Recent randomised trials supported lower target INRs for aortic prostheses, however limited statistical power, certain methodological concerns and the restriction to certain prostheses and/or the use of INR self-management led the European Society of Cardiology Guidelines not to change recommendations for target INR.
Median INR values are recommended rather than range to avoid considering extreme values in the target range as valid target INR.[4]

For further information regarding anticoagulation in patients with valvular heart disease and prosthetic valves refer to Appendix L.
For duration of anticoagulation treatment – VTE, bioprosthetic valves and cardioversion refer to Table 33.

4.1.2. Contraindications

- Known hypersensitivity to warfarin / other vitamin K antagonists or to any excipients
- Haemorrhagic stroke
- Clinically significant bleeding
- Within 72 hours of major surgery with risk of severe bleeding
- Within 48 hours postpartum
- Pregnancy

- Drugs where interactions may lead to a significantly increased risk of bleeding [5]

4.1.3. Cautions

- Bacterial endocarditis
- Previous gastrointestinal bleeding
- Active peptic ulceration
- Recent ischaemic stroke (hold for 14 days if large embolic stroke or uncontrolled hypertension)
- Recent surgery
- Uncontrolled hypertension (systolic >200mmHg or diastolic > 120mmHg)
- Concomitant NSAID
- Poor adherence
- Lactose intolerance [5,6]

4.1.4. Interactions in patients on VKA-Oral Anticoagulant Therapy

- Vitamin K antagonists have multiple drug interactions. These need to be considered prior to prescribing warfarin. Refer to the following link for information https://bnf.nice.org.uk/interaction/warfarin.html.
- Stopping smoking is likely to cause an increase in INR and increase the risk of bleeding. Monitor closely and be prepared to reduce the dose of warfarin if necessary.
- The following vitamin K rich sources may reduce INR levels and may require an increase in warfarin dose: some enteral feeds (containing vitamin K); foods: liver, broccoli, Brussels sprouts, green leafy vegetables, chick peas, egg yolks, cereals containing wheat bran & oats, mature cheese, blue cheese, avocado, olive oil - **advise patients to eat small portions if occasional intake, otherwise eat regularly to achieve steady INR levels.**
- Your clinical / ward pharmacist may be contacted for further advice.

4.1.5. Side effects

4.1.5.1. Bleeding

Most common side effect. People who take usual doses of warfarin have a:

- 2–4% risk per year of having a bleeding episode that requires a transfusion
- 0.2% risk per year of having a fatal haemorrhage
- Bleeding risk for patients taking anticoagulants for AF can be calculated using ORBIT as per NICE ORBIT Bleeding Risk Score for Atrial Fibrillation (mdcalc.com)
- Bleeding risk is compounded by concomitant anti-platelet therapy.

4.1.5.2. Other side effects

- Alopecia
- Diarrhoea
- Hepatic dysfunction
- Nausea and vomiting
- Pancreatitis
- 'Purple toes'
- Purpura
- Rash
- Skin necrosis:
    - Rare but serious adverse effect of warfarin.

- Stop warfarin if warfarin related skin necrosis is suspected.
- Skin necrosis is more likely in people with pre-existing congenital protein C or protein S deficiency.
- It presents as painful, localized skin lesions (due to thrombosis of capillaries) within subcutaneous fat. Lesions can occur in areas of fatty tissue such as the breasts, abdomen or in the extremities.

4.1.6. Initiating Warfarin Treatment- New Patients

- The following provides guidance regarding initiating warfarin in patients where the INR target is 2-3.
- In some circumstances a higher INR target may be appropriate, and a regime will need to be individualized.
- If there are any concerns, please discuss such patients with a Haematology Consultant.

4.1.6.1. Warfarin tablet supply – minimising risk

- Supplying warfarin tablets of more than one strength, may increase the risk of accidental overdose and requires additional patient education.
- Particular consideration should be given to those with learning disabilities and/or other communication needs.
- **Request a supply of only 1 mg tablets for patients who may become confused about their medication.**

4.1.6.2. Warfarin administration

- Warfarin is prescribed in the evening to allow time for INR monitoring before administration.
- The tablets contain minimal amounts of lactose.
- Warfarin tablets can be crushed & mixed with water and administered via a gastric tube, or a suspension can be used; the latter is considerably more expensive.
- Some enteral feeds contain vitamin K which will antagonise the effect of warfarin.
- Warfarin should NOT be put into monitored dosage systems (blister packs) as these are commonly prepared in advance for patients and do not accommodate warfarin dose changes.

Figure 2: Algorithm to guide initiation of warfarin in new patients

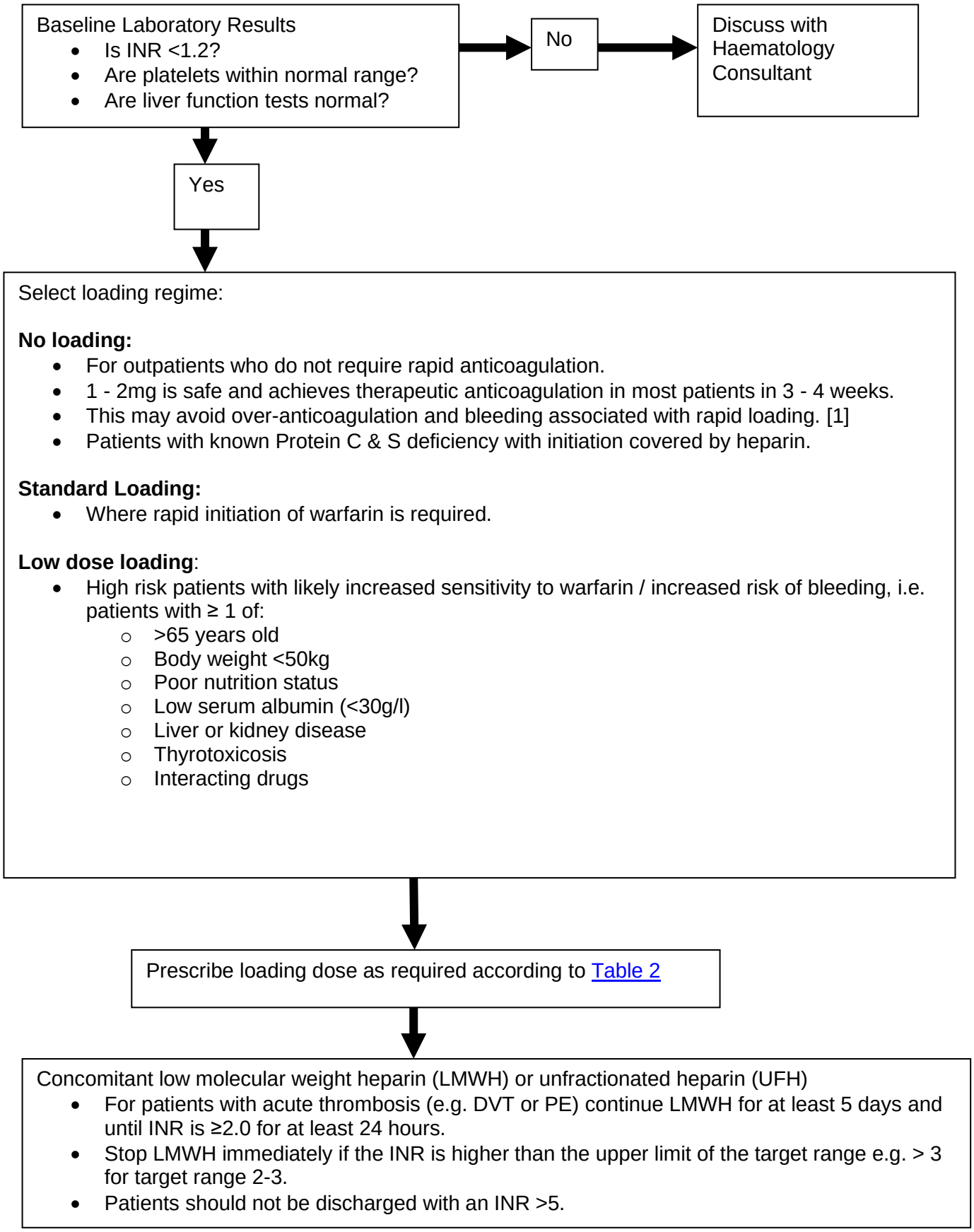


Table 2: Warfarin loading dose and maintenance [7]

<table>
<tr><th colspan="3">Day 1 Loading</th><th colspan="3">Day 2 Loading</th><th colspan="3">Day 3 Loading</th><th colspan="3">Day 4 Predicted maintenance</th></tr>
<tr><td>Baseline INR</td><td>Standard</td><td>Low dose</td><td>INR</td><td>Standard</td><td>Low dose</td><td>INR</td><td>Standard</td><td>Low dose</td><td>INR</td><td>Standard</td><td>Low dose</td></tr>
<tr><td><1.4</td><td>10mg</td><td>5mg</td><td><1.8</td><td>10mg</td><td>5mg</td><td><2.0</td><td>10mg</td><td>5mg</td><td><1.4</td><td>10mg</td><td>5mg</td></tr>
<tr><td colspan="3" rowspan="6">a) *Use low dose loading for high-risk patients with likely increased sensitivity to warfarin / increased risk of bleeding: e.g. > 65 years old, body weight <50kg, poor nutritional status, low serum albumin (<30g/l), liver or kidney disease, heart failure, thyrotoxicosis &/or on interacting drugs</td><td>1.8</td><td>1mg</td><td>1mg</td><td>2.0 - 2.5</td><td>4mg</td><td>2mg</td><td>1.4</td><td>8mg</td><td>4mg</td></tr>
<tr><td>>1.8</td><td>0.5mg</td><td>0.5mg</td><td>2.6 - 3.0</td><td>3mg</td><td>2mg</td><td>1.5 - 1.7</td><td>7mg</td><td>4mg</td></tr>
<tr><td colspan="3" rowspan="5">b) Patients with protein C deficiency (& possibly protein S deficiency) are at risk of developing skin necrosis when starting warfarin – initiate without a loading dose and cover with heparin until INR therapeutic</td><td>3.1 - 3.4</td><td>2mg</td><td>1mg</td><td>1.8 - 2.0</td><td>6mg</td><td>3mg</td></tr>
<tr><td>3.5 - 4.0</td><td>1mg</td><td>1mg</td><td>2.1 - 2.6</td><td>5mg</td><td>3mg</td></tr>
<tr><td>>4.0</td><td>Nil</td><td>Nil</td><td>2.7 - 3.0</td><td>4mg</td><td>2mg</td></tr>
<tr><td colspan="3" rowspan="3"></td><td>3.1 - 3.5</td><td>3mg</td><td>2mg</td></tr>
<tr><td>3.6 - 4.0</td><td>2mg</td><td>1mg</td></tr>
<tr><td>>4.0</td><td colspan="2">Omit & recheck following day</td></tr>
</table>

[Adapted from Fennerty algorithm and King's College Hospital protocol]

4.1.7. Monitoring and Maintaining Target INR 2-3

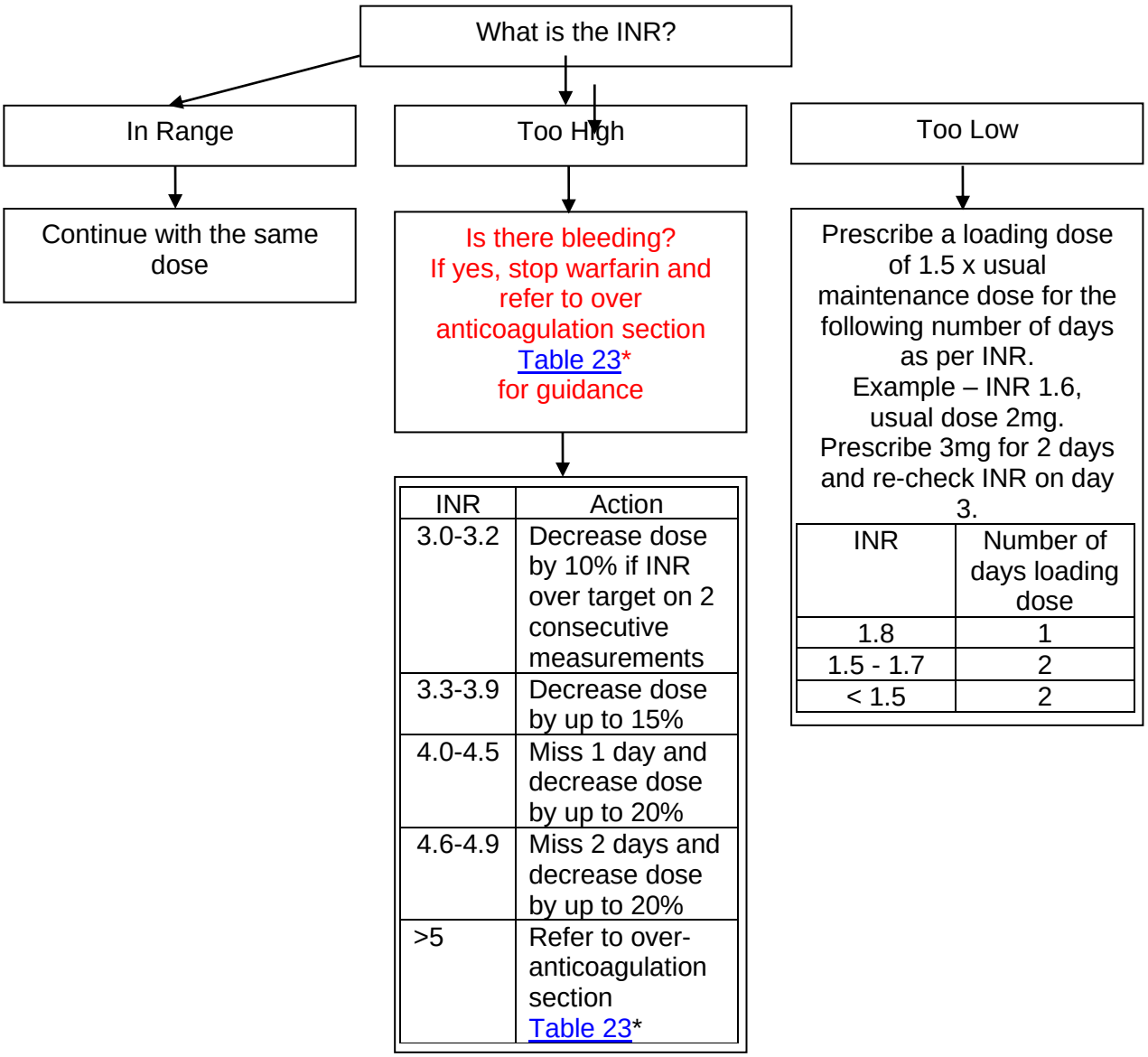
- Warfarin (VKA) therapy is monitored by means of the prothrombin time. To allow standardisation and to facilitate safe dosing the prothrombin time is expressed as the INR (International Normalised Ratio).
- Once within the therapeutic range, monitor the INR at least twice weekly until control is stable. Increase monitoring frequency if any changes are made to medication such as the initiation or withdrawal of antibiotics or other interacting drugs.
- Thereafter monitoring can be gradually extended up to a maximum of 12 weeks provided the INR remains therapeutic and there are no changes made to medication or lifestyle.
- Refer to Figure 3 for guidance on maintenance dose adjustment to achieve INR 2-3.

4.1.8. Discharge and Follow-up on Warfarin

- Prior to discharge patients need to be educated and counselled. For detailed information please refer to:

    - Figure 4 Summary of process guiding patient counselling and discharge - warfarin
    - Appendix C 'The provision of patient information for patients newly initiated on oral anticoagulation medication'.
- A VKA counselling checklist is available in Appendix D1 Warfarin checklist.
- Patient counselling should include the offer of appropriate translation, interpreting and reformatting as per Trust policy.
- Patients should be counselled on the following:
    - How and when to take warfarin, how to manage dose changes and what to do if a dose is missed.
    - The importance of regular INR monitoring and attendance at INR monitoring appointments.
    - The signs and symptoms of bleeding and what to do about them.
    - Awareness that warfarin interacts with other medication both prescribed and purchased over the counter (e.g. NSAIDs & herbal remedies).
    - Interactions with food and awareness of alcohol limits.
    - The need to inform their dentist that they are on an anticoagulant.
    - The need for contraception to prevent pregnancy.
- Patients should be advised that they should seek medical advice if they experience any problems in relation to bleeding or warfarin therapy with their primary care service.
- They must seek urgent medical attention if:
    - They are involved in a major trauma
    - Suffer a significant blow to the head
    - Are unable to stop bleeding

Figure 3: Algorithm guiding dose adjustment of warfarin dose based on target INR of 2-3
*Click here for Table 23 hyperlink



INR	Action
3.0-3.2	Decrease dose by 10% if INR over target on 2 consecutive measurements
3.3-3.9	Decrease dose by up to 15%
4.0-4.5	Miss 1 day and decrease dose by up to 20%
4.6-4.9	Miss 2 days and decrease dose by up to 20%
>5	Refer to over-anticoagulation section Table 23*

INR	Number of days loading dose
1.8	1
1.5 - 1.7	2
< 1.5	2

Figure 4: Summary of process guiding patient counselling and discharge – warfarin

Patients on warfarin or other VKA **MUST** (in working hours) be seen by a Clinical Pharmacy team member to receive **ABC** - **A**lert Card, completed Yellow **B**ook (anticoagulation Information Pack) & **C**ounselling.
For **out of hours** see below *.

Referring Consultant team to:

- Complete Section 1 of VKA Discharge Advice form (Appendix E) at earliest opportunity & leave at front of patient's notes.
- Contact ward Pharmacist or Technician at earliest opportunity to arrange warfarin or other VKA **ABC** – **A**lert Card, Yellow **B**ook (completed) and **C**ounselling.

If unable to contact the ward Pharmacy team, ring the Dispensary to request urgent warfarin counselling on: **EDGH** [redacted] **or Conquest** [redacted]
Dispensary staff will contact the Lead Medicines Management Technician to organise counselling.

Pharmacist / Pharmacy Technician to:

- Use the information on the Anticoagulation Discharge Advice form (left at the front of the patient's notes) to complete the Yellow Book & Alert Card (both sides) & personalise counselling information. **Ensure patient understands that any previous anticoagulant has been stopped & warfarin (or other VKA) started**.
- Explain Anticoagulation Discharge Advice form to the patient, highlighting:
  - Patient will be contacted by GP surgery to arrange an INR blood test appointment by date shown on form (patient to contact GP surgery directly if they do not hear from them).
  - The form must be shown to the person managing their warfarin at the INR appointment.
- File Anticoagulation Discharge Advice form in the Yellow Book in the patient's POD locker.
- Complete Appendix D1 Warfarin counselling checklist & file in the patient's notes.
- Annotate the Anticoagulation section on [redacted] to document that the patient has received **ABC** –**A**lert Card, **B**ook & **C**ounselling

Referring Consultant team - on day of discharge to:

- Complete e-Discharge Summary letter requesting an **URGENT INR within 3 days of discharge,** including:
  - Anticoagulant Discharge Information section. For NVAF CHA_2DS_2-VASc, ORBIT & weight values are mandatory requirements.
  - Changes to Medication section.
- **Complete dosing information, INR due date & INR on discharge, on Anticoagulation Discharge Advice form** (in Yellow Book in patient's POD locker).

Pharmacist – on day of discharge – checks e-Discharge Summary, INR due date and discharge dose.

Ward staff – on day of discharge to:

- Check that Anticoagulation Discharge Advice form (in Yellow Book in patient's locker) is **fully** completed & given to patient;
- Confirm that the patient understands the discharge dose, when their INR blood test is due, what to expect regarding follow up & understands the importance of attending.
- Ensure patient understands that any previous anticoagulant has been stopped & a VKA started.

*** If out of hours, the referring Consultant team** are responsible for anticoagulation counselling & providing /completing the Anticoagulation Information Pack (Yellow Book), including the Alert Card (both sides) - available in the Emergency Drug Cupboards on each site via the Clinical Site Manager. Ensure patient understands that any previous anticoagulant has been stopped & a VKA started.
Click link here for Appendix D1 Warfarin counselling checklist.

4.1.9. Restarting Warfarin in previously stable patients with target INR 2-3

- In a patient who has had warfarin treatment temporarily stopped, for example to allow for surgery, they can be restarted at their previous dose.
- If warfarin loading is necessary, Table 3 below provides guidance on dosing.

Table 3: Re-loading warfarin in previously stable patient

- Prescribe a loading dose of 1.5 x usual maintenance dose for the following number of days:

INR	Number of days of loading dose
1.8	1
1.5 – 1.7	2
<1.5	3

- For example, if the INR prior to re-starting is 1.4, and the patient is usually stable on a dose of 2mg, warfarin 3mg should be prescribed for 3 days as per the algorithm, with an INR check on day 3.
- It would be anticipated that in patients with a previously stable INR that their on-going maintenance dose would be the same as before: in this case 2mg.

4.2. Direct Oral Anticoagulant Drugs (DOACs)

- The following section provides guidance regarding the selection and initiation of the currently available DOAC drugs:
  - Direct Thrombin Inhibitor: dabigatran
  - Direct Factor Xa Inhibitors: rivaroxaban, apixaban and edoxaban
  - Summary information sheets can be found in B2 (dabigatran), B3 (rivaroxaban), B4 (apixaban), and B5 (edoxaban).
- Dabigatran, rivaroxaban, apixaban and edoxaban can be used for primary thromboprophylaxis in relation to orthopaedic surgery. Please see additional details regarding thromboprophylaxis in section 7.
- When calculating DOAC dosages use:
  - Actual body weight as per clinical trials
  - Cockcroft and Gault equation to determine creatinine clearance

4.2.1.1. DOACs at extremes of body weight

- Any DOAC is appropriate for patients weighing 50kg to 120kg **or** BMI up to 40 kg/m^2**.**
- In BMI> 40 kg/m^2 or weight <50kg or >120kg there is limited data.
- In patients with **obesity requiring VTE treatment** where warfarin is inappropriate [8,9]:
  - Rivaroxaban can be used at standard doses regardless of high BMI and weight.
  - Apixaban can be used as an alternative to rivaroxaban; however, there is less supportive data.

  - When using rivaroxaban or apixaban in obese patients, be aware that there is a paucity of data at weight > 150kg and BMI > 50 kg/m^2.
  - Do NOT measure peak or trough levels as there is insufficient data to influence management decisions.
  - Do NOT use dabigatran (unconvincing data) or edoxaban (lack of PK/PD data) in patients with weight > 120kg or BMI > 40 kg/m^2.
  - Alternatives to DOACs include warfarin or weight-based enoxaparin.
- In patients with **obesity and AF** extrapolation of the above guidance is currently less certain.
- In patients who are < 50kg, discuss anticoagulation options with Haematology. DOACs, in particular, dose adjusted rivaroxaban and edoxaban can be considered. [10,11]

4.2.2. Indications, contraindications and cautions for DOACs

Table 4: Summary of licensed indications for DOACs
[10, 12, 13, 14]

Indication	Post elective total hip or total knee replacement surgery – VTE prophylaxis	Treatment of DVT & PE ; Prevention of recurrent DVT / PE	Stroke & systemic embolism prevention in non-valvular AF & ≥1 of 1. Previous stroke, TIA or systemic embolism 2. Left ventricular ejection fraction <40% 3. Symptomatic heart failure ≥NYHA Class 2 4. Age ≥75 years 5. Age ≥65 years associated with diabetes, coronary heart disease or hypertension	Prevention of athero-thrombotic events post Acute Coronary Syndrome	Prophylaxis of athero-thrombotic events in patients with coronary artery disease or symptomatic peripheral artery disease at high risk of ischaemic events
Dabigatran	√	√ following at least 5 days of parenteral anticoagulant treatment	√	X	X
Rivaroxaban	√	√	√	√ in combination with aspirin or aspirin and clopidogrel	√ in combination with aspirin
Apixaban	√	√	√	X	X
Edoxaban	X	√ following at least 5 days of parenteral anticoagulant treatment	√	X	X

4.2.3. Contraindications

- Moderate to severe mitral stenosis
- Mechanical prosthetic heart valves
- Antiphospholipid syndrome - in particular patients that are triple positive (for lupus anticoagulant, anticardiolipin antibodies and anti-beta 2-glycoprotein I antibodies)
- Hypersensitivity to active substance or excipients
- Bleeding

  - Active clinically significant bleeding
  - Lesion or condition considered a significant risk factor for bleeding
- Renal function calculated using the Cockcroft-Gault method
  - Dabigatran contraindicated at CrCl <30mL/min
  - Apixaban, edoxaban & rivaroxaban contraindicated at CrCl <15mL/min
- Hepatic disease associated with coagulopathy and clinically relevant bleeding risk including cirrotic patients with Child Pugh B and C
- Concomitant anticoagulation EXCEPT when switching anticoagulant therapy or with UFH locks to maintain an open central venous or arterial catheter
- Pregnancy / breast feeding
- Dabigatran - Concomitant treatment with the following strong P-gp inhibitors: systemic ketoconazole, cyclosporine, itraconazole, dronedarone and the fixed-dose combination glecaprevir / pibrentasvir
- Dabigatran for DVT/ PE inpatients with active cancer

4.2.4. Cautions

- Lactose intolerance – apixaban & rivaroxaban
- Weight < 50kg or >120kg or BMI >40kg/m^2 refer to 4.2.1.1 – DOACs at extremes of bodyweight

4.2.5. DOAC Drug Interactions

- There are a number of clinically significant drug interactions with strong inducers and inhibitors of CYP3A4 and P-glycoprotein (P-gp). In such cases concurrent use is contraindicated.
- With moderate to weak inducers and inhibitors the clinical significance of the interaction is based on other patient factors such as age, renal function and concurrent drugs.
- Table 5 is to be used as a guide to significant interactions but application to specific patients may require a degree of clinical judgement.

Table 5: DOAC general drug interactions
– anticipated effects on DOAC plasma levels
Please be aware that the information below is current at the time of writing, however interactions are constantly being updated and so pharmacy should be consulted for further advice if required.
Colour coding is based on the respective DOAC SPC, drug interaction databases, or expert opinion.
The hatched colour coding indicates no clinical or PK data available.
Some of the colour codes will require adaptation as more data becomes available over time.
White: No relevant drug–drug interaction anticipated.
Yellow: Caution required, especially in case of polypharmacy or in the presence of >_2 yellow/bleeding risk factors.
Orange: Lower dose (dabigatran) or dose reduction (edoxaban) recommended by manufacturer.
Red: Contraindicated/not advisable due to increased plasma levels.
Dark blue: Contraindicated due to reduced NOAC plasma levels.
Light blue: Caution required, especially in case of polypharmacy or in the presence of >_2 light blue interactions due to reduced NOAC plasma levels.
AUC, area under the curve; BCRP, breast cancer resistance protein; BD, twice daily; CrCl, creatinine clearance; NSAID, non-steroidal anti-inflammatory drug; PK, pharmacokinetic; PPI, proton pump inhibitor.

Drug	Mechanism	Apixaban	Dabigatran	Edoxaban	Rivaroxaban
Antiarrhythmics					
Amiodarone	Moderate P-gp competition	No PK data	+12 to 60% Dose ↓ only necessary in VTE prevention post hip / knee replacement. **a) 1- 4 hrs post surgery:** ↓ dose from 110mg to 75mg stat. **b) Main-tenance:** ↓ dose to 150 mg OD (from 220mg OD).	+40%	Minor effect - use with **caution** if CrCl <50ml/min
Digoxin	P-gp competition	No effect			
Diltiazem	Weak P-gp competition & CYP3A4 inhibition	+40%	No effect	No data	No effect
Dronedarone	P-gp & CYP3A4 inhibition	With caution	+70 to 100% Concurrent treatment **contra-indicated**	+85% Dose reduction to 30 mg OD advised by manufacturer	**Moderate effect, should be avoided**
Quinidine	P-gp inhibition	No data	+53%. Dose ↓ only necessary in VTE prevention post hip / knee replacement. **a) 1- 4 hrs post surgery:** ↓ dose from 110mg to 75mg stat. **b) Main-tenance:** ↓ dose to 150 mg OD (from 220mg OD).	+77%. No dose reduction required by manufacturer	Extent of increase unknown
Drug	**Mechanism**	**Apixaban**	**Dabigatran**	**Edoxaban**	**Rivaroxaban**
Verapamil	P-gp competition	No PK data	+12 to 180%	+53%.	+40%

	& weak CYP3A4 inhibition		if taken simul-taneously. **Stroke / DVT / PE**: ↓ to 110mg BD (from 150mg BD). In **VTE prevention post hip/ knee replacement** **a) 1- 4 hrs post surgery:** ↓ dose from 110mg to 75mg stat. **b) Main-tenance with normal renal function**: ↓ to 150 mg OD (from 220mg OD). **c) Main-tenance with moderate renal impairment (30-50 mL/min)**: consider ↓ to 75 mg OD from 220mg OD.	No dose reduction required by manufacturer	(probably not relevant)
Other cardiovascular drugs					
Atorvastatin	P-gp inhibition & CYP3A4 competition	No data	No relevant interaction	No effect	No effect
Ticagrelor	P-gp inhibition	No data – carefully monitor	+24% to 65% Give loading dose 2h after dabigatran	No data – carefully monitor	No data – carefully monitor
Drug	**Mechanism**	**Apixaban**	**Dabigatran**	**Edoxaban**	**Rivaroxaban**
Antibiotics					
Clarithromycin Erythromycin	P-gp inhibition & strong CYP3A4 inhibition	Clarithromycin + 60% AUC +30% C_{max}	Clarithromycin + 19% AUC +15% C_{max} Manufacturer advises to monitor closely for signs of	Erythromycin +85% AUC +68% C_{max} Dose reduction to 30 mg OD advised by	Clarithromycin +50% AUC +40% C_{max} Erythromycin +30% AUC; +30% C_{max}

			bleeding **especially in renal impairment.**	manufacturer.	
Rifampicin	P-gp / BCRP & CYP3A4 induction	- 54% AUC - 42% C_{max}	- 66% AUC - 67% C_{max}	-35% AUC but with compensatory increase in active metabolites. Manufacturer advises to use with caution.	- 50% AUC - 22% C_{max}
Antiviral drugs					
HIV protease inhibitors (e.g. Ritonavir)	P-gp & BCRP inhibition or induction; CYP3A4 inhibition	Strong increase Manufacturer advises **avoid.**	Variable increase / decrease	No data	+153% AUC +55% Cmax (with Ritonavir 600 BID) Manufacturer advises **avoid.**
Fungostatics					
Fluconazole	Moderate CYP3A4 inhibition	No data	No data	No data	+42% AUC +30% C_{max} if systemically administered
Itraconazole Ketoconazole	Potent P-gp and BCRP competition; strong CYP3A4 inhibition	+100% AUC +64% C_{max} with ketoconazole	+140 to 150% with ketoconazole Concurrent treatment contra-indicated.	+87% AUC +89% C_{max} with ketoconazole. Dose reduction to 30 mg OD advised by manufacturer.	+160% AUC +72% C_{max} with ketaconazole
Voriconazole	Strong CYP3A4 inhibition	SPC	No Data	No data	SPC
Posaconazole	Mild to moderate P-gp inhibition; strong CYP3A4 inhibition	SPC	SPC		SPC
Drug	**Mechanism**	**Apixaban**	**Dabigatran**	**Edoxaban**	**Rivaroxaban**
Other drugs					
Naproxen	P-gp competition; **pharmaco-dynamically increased bleeding time**	+55% AUC +61% C_{max}	No data	No difference in AUC	No relevant increase of AUC
H_2 antagonists PPIs Aluminium hydroxide Magnesium	GI absorption	No effect	Minor effect, not clinically relevant	Minor effect, not clinically relevant	No effect

hydroxide					
SSRIs; SNRIs	Pharmacodynamic effect on platelets	SPC	SPC	SPC	SPC
St. John's wort	P-gp/BCRP and CYP3A4 induction				
Other factors					
Age ≥ 80 years	Potential for ***increased*** plasma levels		110mg BD SPC		
Age ≥ 75 years	Potential for ***increased*** plasma levels				
Weight ≤60kg	Potential for ***increased*** plasma levels			Dose reduction to 30mg OD advised by manufacturer	
Weight ≥ 120 kg	Potential for ***decreased*** plasma levels				
Chronic kidney disease	Potential for ***increased*** plasma levels				
Other increased bleeding risk		Pharmacodynamic interactions: Antiplatelet drugs NSAIDs Other anticoagulants Systemic steroids History of GI bleeding Recent surgery on critical organ: Brain, Eye Predisposition to bleeding - thrombocytopenia, anaemia HAS-BLED ≥3 Frailty / falls risk			

Table 6: DOAC interactions with antiepileptic drugs – anticipated effects on DOAC plasma levels

	Mechanism	Apixaban	Dabigatran	Edoxaban	Rivaroxaban
P-gp substrate		**Yes**	**Yes**	**Yes**	**Yes**
CYP3A4 substrate		**≈25%**	**No**	**<4%**	**≈18%**
Drug					
Brivaracetam		No relevant interaction known/assumed			
Carbamazepine	Strong CYP3A4/P-gp induction; CYP3A4 competition	**-50%** SPC	**-29%** SPC	SPC	SPC
Ethosuximide	CYP3A4 competition.	No relevant interaction known/assumed			
Gabapentin		No relevant interaction known/assumed			
Lacosamide		No relevant interaction known/assumed			
Lamotrigine	P-gp competition	No relevant interaction known/assumed			
Levetiracetam	P-gp induction; P-gp competition				
Oxcarbazepine	CYP3A4 induction; P-gp competition				
Phenobarbital	Strong CYP3A4/ possible P-gp induction	SPC		SPC	SPC
Phenytoin	Strong CYP3A4/ P-gp induction; P-gp competition	SPC	SPC	SPC	SPC
Pregabalin		No relevant interaction known/assumed			
Topiramate	CYP3A4 induction; P-gp competition				
Valproic acid	CYP3A4/P-gp induction/ inhibition				
Zonisamide	CYP3A4 competition; weak P-gp inhibition	No relevant interaction known/assumed			

Colour coding is based on the respective DOAC SPC, drug interaction databases, or expert opinion.
The hatched colour coding indicates no clinical or PK data available.
Some of the colour codes will require adaptation as more data becomes available over time.
White: No relevant drug–drug interaction anticipated.
Dark blue: Contraindicated due to *reduced* DOAC plasma levels.
Light blue: Use with caution or avoid—either the label for the respective DOAC mentions that co-administration is possible despite a *decreased* plasma level, which are deemed not clinically relevant (nevertheless, since not tested prospectively, such concomitant use should be used with caution, and avoided when possible) or expert opinion.

Where no data or SmPC instructions were available, expert opinion was based on the following principles:
• Strong CYP3A4 and/or P-gp inducer—should not be used (**dark blue**).
• Moderate CYP3A4 or P-gp inducer—use with caution or avoid (light blue).
• Strong CYP3A4 and/or inhibitor—should not be used (**red**).
• Moderate CYP3A4 or P-gp inhibitor—use with caution, consider dose reduction or different DOAC (**orange**).
• Mild CYP3A4 and/or P-gp inducers or inhibitors—caution is needed with polypharmacy or in the presence of >_2 bleeding risk factors (yellow).

Table 7: DOAC drug interactions with anticancer drugs – anticipated effects on DOAC plasma levels

Drug	**Mechanism**	**Apixaban**	**Dabigatran**	**Edoxaban**	**Rivaroxaban**
P-gp substrate		**Yes**	**Yes**	**Yes**	**Yes**
CYP3A4 substrate		**≈25%**	**No**	**<4%**	**≈18%**
Antimitotic agents					
Paclitaxel	Moderate CYP3A4 induction; CYP3A4/P-gp competition				
Vinblastine	Strong P-gp induction; CYP3A4/P-gp competition				
Docetaxel, Vincristine	Mild CYP3A4 induction; CYP3A4/P-gp competition				
Vinorelbine	CYP3A4/P-gp competition				
Antimetabolites					
Methotrexate	P-gp competition	No relevant interaction anticipated			
Pemetrexed, Purine analogs, Pyrimidine analogs		No relevant interaction anticipated			
Topoisomerase inhibitors					
Topotecan		No relevant interaction anticipated			
Irinotecan	CYP3A4/P-gp competition.	No relevant interaction anticipated			
Etoposide	Mild CYP3A4 inhibition; CYP3A4/P-gp competition				
Anthracyclines / Anthracenediones					
Doxorubicin	Strong P-gp induction, mild CYP3A4 inhibition; CYP3A4/P-gp competition				

Idarubicin	Mild CYP3A4 inhibition; P-gp competition				
Daunorubicin	P-gp competition.	No relevant interaction anticipated			
Mitoxantrone		No relevant interaction anticipated			
Alkylating agents					
Ifosfamide	Mild CYP3A4 inhibition; CYP3A4 competition				
Drug	**Mechanism**	**Apixaban**	**Dabigatran**	**Edoxaban**	**Rivaroxaban**
Cyclo-phosphamide	Mild CYP3A4 inhibition; CYP3A4 competition				
Lomustine	Mild CYP3A4 inhibition				
Busulfan	CYP3A4 competition	No relevant interaction anticipated			
Bendamustine	P-gp competition	No relevant interaction anticipated			
Chlorambucil Melphalan Carmustine Procarbazine Dacarbazine Temozolomide		No relevant interaction anticipated			
Platinum based agents					
Cisplatin Carboplatin Oxaliplatin		No relevant interaction anticipated			
Intercalating agents					
Bleomycin Dactinomycin		No relevant interaction anticipated			
Mitomycin C		No relevant interaction anticipated			
Tyrosine kinase inhibitors					
Imatinib Crizotinib	Strong P-gp inhibition; moderate CYP3A4 inhibition; CYP3A4/P-gp competition				
Nilotinib Lapatinib	Moderate to strong P-gp inhibition; mild CYP3A4 inhibition; CYP3A4/P-gp competition				
Vemurafenib	Moderate CYP3A4 induction;				

	CYP3A4/P-gp competition				
Dasatinib	Mild CYP3A4 inhibition; CYP3A4/P-gp competition				
Vandetanib Sunitinib	Strong P-gp induction; CYP3A4 competition				
Drug	**Mechanism**	**Apixaban**	**Dabigatran**	**Edoxaban**	**Rivaroxaban**
Erlotinib Gefitinib	CYP3A4 competition.	No relevant interaction anticipated			
Monoclonal antibodies					
Brentuximab	CYP3A4 competition.	No relevant interaction anticipated			
Rituximab Alemtuzumab Cetuximab Trastuzumab Bevacizumab		No relevant interaction anticipated			
Hormonal agents					
Abiraterone	Moderate CYP3A4 inhibition, strong P-gp inhibition; CYP3A4/P-gp competition				
Enzalutamide	Strong CYP3A4 induction, strong P-gp inhibition; CYP3A4/P-gp competition				
Bicalutamide	Moderate CYP3A4 inhibition				
Tamoxifen	Strong P-gp inhibition, mild CYP3A4 inhibition; CYP3A4 competition				
Anastrozole	Mild CYP3A4 inhibtion				
Flutamide	CYP3A4 competition;	No relevant interaction anticipated			
Letrozole Fluvestrant	CYP3A4 competition	No relevant interaction anticipated			
Raloxifene Leuprolide Mitotane		No relevant interaction anticipated			
Immune-modulating agents					

Ciclosporin	Strong to moderate P-gp inhibition, moderate CYP3A4 inhibition; CYP3A4/P-gp competition	SPC	SPC	+73% AUC Dose reduction to 30 mg OD advised by manu-facturer	
Dexamethasone	Moderate CYP3A4 induction; CYP3A4 competition				
Drug	**Mechanism**	**Apixaban**	**Dabigatran**	**Edoxaban**	**Rivaroxaban**
Tacrolimus	Strong to moderate P-gp inhibition, mild CYP3A4 inhibition; CYP3A4/P-gp competition	Consider avoiding	SPC	Consider avoiding	Consider avoiding
Prednisolone	Moderate CYP3A4 induction; CYP3A4 competition				
Temsirolimus, Sirolimus	Mild CYP3A4 inhibition; CYP3A4/P-gp competition				
Everolimus	CYP3A4 competition	No relevant interaction anticipated			

Purine analogues: Mercaptopurine, Thioguanine, Pentostatin, Cladribine, Clofarabine, Fludarabine.
Pyrimidine analogues: Fluorouracil, Capecitabine, Cytarabine, Gemcitabine, Azacitadine, Decitabine

Colour coding is based on the respective DOAC SPC, drug interaction databases, or expert opinion.
The hatched colour coding indicates no clinical or PK data available.
Some of the colour codes will likely require adaptation as more data become available over time.
White: No relevant drug–drug interaction anticipated.
Yellow: Caution required, especially in case of polypharmacy or in the presence of >_2 yellow/bleeding risk factors.
Orange: Consider avoiding concomitant use, careful monitoring required if combined. Dose reduction (edoxaban) recommended by manufacturer.
Red: Contraindicated/not advisable due to increased plasma levels.
Dark blue: Contraindicated/not advisable due to reduced NOAC plasma levels.
Light blue: Caution required, especially in case of polypharmacy or in the presence of >_2 light blue interactions due to reduced NOAC plasma levels

Where no data or SPC instructions were available, expert opinion was generally based on the following principles:

- Strong CYP3A4 and/or P-gp inducer—should not be used (**dark blue**).
- Moderate CYP3A4 or P-gp inducer—use with caution or avoid (light blue).
- Strong CYP3A4 and/or inhibitor—should not be used (**red**).
- Moderate CYP3A4 and/or P-gp inhibitor—use with caution or avoid (orange).
- Mild CYP3A4 and/or P-gp inducers or inhibitors—caution required especially with polypharmacy or in the presence of >_2 bleeding risk factors (yellow)

Table 8: DOAC drug interactions with common herbal medicines - anticipated effects on DOAC plasma levels

Drug	**Mechanism**	**Apixaban**	**Dabigatran**	**Edoxaban**	**Rivaroxaban**
P-gp substrate		**Yes**	**Yes**	**Yes**	**Yes**
CYP3A4 substrate		**Yes (≈25%)**	**No**	**No (<4%)**	**Yes (≈18%)**
Drug					
Curcumin	P-gp inhibition				
Echinacea purpurea	Mild CYP3A4 inhibition				
Garlic	Mild CYP3A4 inhibition; anticoagulation / antiplatelet effect				
Ginger	Anticoagulation / antiplatelet effect				
Ginkgo biloba	P-gp inhibition; anticoagulation / antiplatelet effect				
Ginseng	Anticoagulation / antiplatelet effect				
Green Tea	P-gp inhibition; anticoagulation / antiplatelet effect				
Horse chestnut	Anticoagulation / antiplatelet effect				
St. John's wort	P-gp/ BCRP and CYP3A4 induction	With caution SPC	Should be avoided SPC	With caution SPC	Should be avoided SPC
Valerian	Mild CYP3A4 inhibition				

Colour coding is based on the respective DOAC SPC, drug interaction databases, or expert opinion.
The hatched colour coding indicates no clinical or PK data available.
Some of the colour codes will require adaptation as more data becomes available over time.
Major limitations regarding the assessment of DOACs—herbal drug interactions include the possibility of several hypothetical pharmacokinetic and pharmacodynamic pathways, unknown mechanisms of interaction, and the inherent variation in composition.
White: No relevant drug–drug interaction anticipated.
Yellow: Caution required, especially in case of polypharmacy or in the presence of >_2 yellow/bleeding risk factors.

Dark blue: Contraindicated/not advisable due to reduced DOAC plasma levels. Where no data or SPC instructions were available, expert opinion was generally based on the following principles:

- Strong CYP3A4 and/or P-gp inducer—should not be used (**dark blue**).
- Mild CYP3A4 and/or P-gp inducers or inhibitors or pharmacodynamic interaction—caution is needed especially with polypharmacy or in the presence of >_2 bleeding risk factors (yellow).

References: [10,12,13,14,15].

4.2.6. Initiating and Dosing DOACs

4.2.6.1. Baseline assessments prior to initiation of DOACs

- Check FBC, liver and renal function, and establish bleeding risk for individual patient; review weight and BMI.
- If the blood results are out of range or there are additional bleeding risks, discuss treatment with a Haematology Consultant prior to initiating treatment.
- Renal function should be measured **within 24 hours of starting a DOAC**.
- The creatinine clearance (CrCl) should be calculated using the Cockcroft and Gault equation. Calculator: http://www.mdcalc.com/creatinine-clearance-cockcroft-gault-equation/
- Dosing should be adjusted according to creatinine clearance (CrCl) as per the tables below.

4.2.6.2. Dabigatran dosing

Table 9: Dosing table for dabigatran in VTE and NVAF

- with one or more risk factors such as prior stroke or TIA; age ≥ 75, heart failure (NYHA Class ≥II); diabetes mellitus; hypertension

For VTE treatment & prevention (following 5 days treatment with a parenteral anticoagulant) **For NVAF**	**Recommended dose**	**Comments**
Adults 18-79 years	150mg BD	**Reduce dose** to 110mg BD if **on concomitant verapamil**
		Consider dose reduction to 110mg BD if 1 or more below after individual assessment of thromboembolic risk and risk of bleeding: - 75-79 years Moderate renal impairment (CrCl 30-50 mL/min) Gastritis, oesophagitis or gastro-intestinal reflux High bleeding / increased bleeding risk
Adults ≥ 80 years	110mg BD	
In reduced renal function dose as below:		
CrCl > 50mL/minute	150mg BD	Consider 110mg BD if: - High bleeding / increased bleeding risk and/or

CrCl 30-50mL/minute	150mg BD	Gastritis, oesophagitis or gastro-intestinal reflux (particularly if CrCl <50mL/min and / or body weight <50kg)
CrCl < 30mL/minute	**Do not use**	
Hepatic impairment	**Do not use**	If ALT > 2 x ULN - do not use

4.2.6.3. Dabigatran Administration

- Dabigatran capsules **must be swallowed whole**, with or without food.
- The capsules **must not be opened** as oral bioavailability may be increased by 75% after a single dose and 37% at steady state when the pellets are taken without the capsule shell, and this may increase bleeding risk. Patients should be advised **NOT** to open the capsules e.g. to sprinkle over food or put into beverages.
- Dabigatran must **NOT** be put down an NG tube as opening the capsules is likely to increase bleeding risk.
- Dabigatran must be stored in the original container and must **NOT** be put into monitored dosage systems (e.g. blister packs, etc.).
- If concomitant verapamil or amiodarone is prescribed, dose at the same time as dabigatran.

4.2.6.4. Changing to or from Dabigatran treatment

Table 10: Switching TO dabigatran in DVT / PE and NVAF

From	**To dabigatran**
LMWH	Stop LMWH. Start dabigatran 0-2 hours prior to time next dose of LMWH due.
UFH	Stop UFH. Start dabigatran immediately.
Warfarin	Stop warfarin. Start dabigatran when INR <2.0.

Table 11: Switching FROM dabigatran in DVT / PE and NVAF

To	**From dabigatran**	
LMWH	Stop dabigatran. Start LMWH 12 hours after the last dose of dabigatran.	
UFH	Stop dabigatran. Start UFH 12 hours after the last dose of dabigatran.	
Warfarin *NB. Because dabigatran can ↑ INR, a true INR value will only be obtained 2 days after stopping dabigatran. Until then interpret INR values with caution.* ***Measure INR immediately pre-dabigatran dose (trough).***	Starting time of warfarin is based on CrCl:	
	CrCl ≥ 50 mL/min	Continue dabigatran. Give dabigatran + warfarin for **3** days then stop dabigatran & continue warfarin alone.
	CrCl ≥ 30-<50mL/min	Continue dabigatran. Give dabigatran + warfarin for **2** days then stop dabigatran & continue warfarin alone.

4.2.6.5. Dabigatran- Missed dose

- A missed dose can be taken up to 6 hours prior to the next scheduled dose.
- If there are fewer than 6 hours till the next due dose, omit the missing dose and give the next dose at the normal scheduled time.

4.2.6.6. Rivaroxaban dosing

Table 12: Dosing table for rivaroxaban in VTE and NVAF
- with one or more risk factors, such as congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, prior stroke or transient ischaemic attack

For NVAF	Dose	Comments
CrCl ≥50mL/min	20mg OD	With food
CrCl 30-49mL/min	15mg OD	With food
CrCl 15-29mL/min	15mg OD	With food Limited trial data: **caution** - increased blood levels and bleeding risk.
CrCl <15mL/min	Do not use	
Hepatic impairment associated with coagulopathy	Do not use	

DVT & PE treatment & prevention	Recommended dose	Comments
Initial treatment of acute DVT or PE (Days 1-21)	15mg **BD** for **3 weeks** followed by	Should always be taken with food. No dose reduction in renal impairment. **If a dose is missed during initial 21-day phase**: take immediately to ensure dose = 30mg/day - in this case **2 x 15mg may be taken together**
Day 22 onwards (including patients switched from alternative anticoagulation >21 days after acute event)	20mg OD	Should always be taken with food. Consider 15mg OD if CrCl 15 – 49 mL/min and bleeding risk outweighs risk of recurrent DVT or PE. [10,16] If dose is missed during once daily treatment phase do not double up dose to catch up
Prevention of recurrent DVT and PE	Following completion of at least 6 months therapy for DVT or PE	10 mg once daily Consider 20mg once daily (with food) where risk of recurrent DVT or PE is considered high, e.g. complicated comorbidities or recurrent DVT or PE with 10 mg daily
Renal impairment – DVT/PE		

CrCl <30ml/minute	No dose reduction recommended however consider 15mg once daily from day 22	Limited trial data. Use with caution: increased blood levels and bleeding risk. The recommendation for the 15 mg once daily dose from day 22 is based on PK modelling and has not been studied in this clinical setting.
CrCl <15mL/min	**Do not use**	
Hepatic impairment: associated with coagulopathy	**Do not use**	

4.2.6.7. Rivaroxaban- Administration

- 15mg - 20mg doses must be taken with food. With food oral bioavailability of 100% will be achieved, without food only 66% bioavailability will be achieved.
- 2.5mg -10mg doses can be taken with or without food.
- Can be put into a blister pack.
- Tablets may be crushed & mixed with water or apple puree immediately before administration; 15mg and 20mg doses should be immediately followed by food.
- Can be administered via gastric tube, followed immediately by enteral feeding.

4.2.6.8. Rivaroxaban - Missed dose

- Prevention of stroke and systemic embolism:
  - If a dose is missed, the patient should take the missing dose immediately and then continue with intake as before.
  - The dose should not be doubled within the same day to make up for a missed dose.

- Treatment of DVT, treatment of PE and prevention of recurrent DVT and PE:
  - If a dose is missed during the 15 mg twice daily treatment phase (day 1 - 21), the patient should take the missing dose immediately to ensure an intake of 30 mg rivaroxaban per day.
  - In this case two 15mg tablets may be taken at once.
  - The patient should continue with the regular 15 mg twice daily intake as recommended on the following day.

4.2.6.9. Changing to or from Rivaroxaban treatment

Table 13: Switching TO rivaroxaban in DVT / PE and NVAF

From	To rivaroxaban
LMWH	Stop LMWH. Start rivaroxaban 0-2 hours prior to time next dose of LMWH due.
UFH	Stop UFH. Start rivaroxaban immediately.
Warfarin – for stroke prevention in AF	Stop warfarin. Start rivaroxaban when INR ≤3.0. **When converting patients from warfarin to rivaroxaban, INR values will be falsely elevated after the intake of rivaroxaban. INR should not be used to measure the anticoagulant activity of rivaroxaban.**
Warfarin – for DVT, PE & prevention of recurrence	Stop warfarin. Start rivaroxaban when INR ≤2.5. **When converting patients from warfarin to rivaroxaban, INR values will be falsely elevated after the intake of rivaroxaban. INR should not be used to measure the anticoagulant activity of rivaroxaban.**

Table 14: Switching FROM rivaroxaban in DVT / PE and NVAF

To	**From rivaroxaban**
LMWH	Stop rivaroxaban. Start LMWH when next dose of rivaroxaban due.
UFH	Stop rivaroxaban. Start UFH when next dose of rivaroxaban due.
Warfarin	Continue rivaroxaban and start warfarin. Continue both anticoagulants until INR is ≥ 2.0, and then stop rivaroxaban. *For the first two days of the conversion period, use standard initial warfarin dosing, thereafter, adjust warfarin dose as per INR.* *While patients are on both rivaroxaban & warfarin the INR should only be tested immediately prior to the next dose of rivaroxaban (trough - to minimize its influence on the INR; rivaroxaban can contribute to an elevated INR).* *Once rivaroxaban is discontinued INR testing may be done reliably at least 24 hours after the last dose.*

4.2.6.10. Apixaban dosing

Table 15: Dosing table for apixaban in VTE and NVAF

- with one or more risk factors, such as prior stroke or TIA; age ≥ 75 years; hypertension; diabetes mellitus; symptomatic heart failure (NYHA Class ≥ II)

For NVAF	Recommended dose	Comments
CrCl≥ 30mL/min	5mg BD	
CrCl 15-29mL/min	2.5mg BD	Limited trial data: caution
CrCl < 15mL/min	**Do not use**	
If 2 or more of: **A**ge ≥ 80 years **B**ody mass (wt)≤ 60kg **C**reatinine ≥ 133µmol/l	2.5mg BD	Low body weight (<60kg) may increase haemorrhagic risk
Hepatic disease associated with coagulopathy Severe hepatic impairment	**Do not use**	Limited data in liver disease. AST/ALT > 2xULN or bilirubin >1.5x ULN excluded from trials – use with caution. Check liver function prior to prescribing

For treatment and prevention of VTE	Recommended dose	Comments
Treatment of VTE	10mg BD for **7 days** followed by 5mg BD thereafter	Avoid in patients on concomitant systemic treatment with strong inducers of both CYP3A4 and P-gp, e.g. rifampicin, carbamazepine, phenytoin, phenobarbital, primidone or St John's Wort as likely to reduce apixaban levels and efficacy. See DOAC drug interactions for more complete list.
Prevention of recurrence of VTE	2.5mg BD	Use with caution in patients on concomitant drugs as above
Renal impairment –DVT/PE		
CrCl 15-29 ml/min	No dose reduction recommended but manufacturer advises use with caution. Limited trial data shows apixaban concentrations are raised in severe renal impairment which may increase bleeding risk	
CrCl <15ml/min or on dialysis	**Do not use**	No clinical experience - avoid
Hepatic disease associated with coagulopathy Severe hepatic impairment	**Do not use**	Limited data in liver disease. AST/ALT > 2xULN or bilirubin >1.5x ULN excluded from trials – use with caution. Check liver function prior to prescribing

4.2.6.11. Apixaban- Administration

- Can be administered with or without food.
- Can crush tablets and suspend in water or 5% dextrose in water or apple juice, or mix with apple puree and administer immediately orally.
- Can administer through an enteral tube immediately after crushing and suspending tablet in 60 mL of water or 5% dextrose.
- Crushed apixaban tablets are stable in water, 5% dextrose, apple juice and apple puree for up to 4 hours.
- Can be put in a blister pack.

4.2.6.12. Apixaban- Missed dose

- If a dose is missed, the patient should take the missing dose immediately and then continue with intake as before.
- Two doses should not be taken at the same time to make up for a missed dose.

4.2.6.13. Switching to or from Apixaban Treatment

Table 16: Switching TO apixaban in DVT / PE and NVAF

From	**To apixaban**
LMWH	Stop LMWH. Start apixaban when next dose of LMWH due.
UFH	Stop UFH. Start apixaban immediately.
Warfarin	Stop warfarin. Start apixaban when INR <2.0.

Table 17: Switching FROM apixaban in DVT / PE and NVAF

To	**From apixaban**
LMWH	Stop apixaban. Start LMWH when next dose of apixaban due.
UFH	Stop apixaban. Start UFH when next dose of apixaban due.
Warfarin	Continue apixaban and start warfarin. Continue both apixaban + warfarin for 2 days. After 2 days measure INR immediately prior to next apixaban dose (trough). Continue both anticoagulants until INR is ≥ 2.0, and then stop apixaban.

4.2.6.14. Edoxaban dosing

Table 18: Dosing table for Edoxaban in VTE and NVAF
- in adult patients with one or more risk factors, such as congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, prior stroke or TIA.

For NVAF & **VTE treatment** (following 5 days treatment with a parenteral anticoagulant**) &** **VTE prevention**	Recommended dose	Comments
CrCl > 50mL/min	60mg OD	Caution: Decreased efficacy in patients with CrCl>95mL/min
If one or more of: **B**ody Weight ≤ 60 kg **C**rCl 15-50mL/min **D**rugs: Concomitant ciclosporin, dronedarone, erythromycin, or ketoconazole	30mg OD	
CrCl < 15mL/min	**Do not use**	
Hepatic disease associated with coagulopathy Severe hepatic impairment	**Do not use**	Limited data in liver disease. ALT > 2xULN or bilirubin >1.5x ULN excluded from trials. Check liver function prior to prescribing.

4.2.6.15. Edoxaban Administration

- Edoxaban can be taken with or without food.
- Can be crushed and mixed with water or apple puree and administered orally immediately.
- Can be crushed and suspended in a small amount of water and immediately delivered through a gastric tube which should then be flushed with water.
- Can be put into a monitored dosage system, e.g. blister pack.

4.2.6.16. Edoxaban - Missed dose

- If a dose is missed, the patient should take the missing dose immediately and then continue with intake as before.
- The dose should not be doubled within the same day to make up for a missed dose.

4.2.6.17. Switching to or from Edoxaban Treatment

Table 19: Switching TO edoxaban in DVT / PE and NVAF

From	**To edoxaban**
LMWH or fondaparinux	Stop LMWH or fondaparinux Start edoxaban when next dose of LMWH due.
UFH	UFH. Stop infusion and start edoxaban 4 hours later.
Warfarin	Stop warfarin. Start edoxaban when INR ≤ 2.5.
DOAC (rivaroxaban, apixaban or dabigatran)	Stop DOAC. Start edoxaban when next dose of DOAC is due.

Table 20: Switching FROM edoxaban in DVT / PE and NVAF

To	**From edoxaban**
LMWH e.g. enoxaparin	Stop edoxaban. Start LMWH when next dose of edoxaban due.
UFH	Stop edoxaban. Start UFH when next dose of edoxaban due.
DOAC (rivaroxaban, apixaban or dabigatran)	Stop edoxaban. Start DOAC when next dose of edoxaban due.
Warfarin	**Patients should not take a loading dose of warfarin.** **Oral option**: For patients currently on 60 mg edoxaban: Give 30mg edoxaban + 1-2mg warfarin (slow loading). For patients currently on 30 mg edoxaban: Give 15mg edoxaban + 1-2mg warfarin (slow loading). Once INR is ≥ 2.0, stop edoxaban. This should occur within 14 days using the above method. During the first 14 days of warfarin + edoxaban, measure the INR at least 3 times **immediately prior to edoxaban dose** (trough) to minimise the influence of edoxaban on INR measurements. Concomitant edoxaban + warfarin can increase the INR post edoxaban dose by up to 46%. **Parenteral option**: Stop edoxaban and give a LMWH + warfarin when next dose of edoxaban is due. Once a stable INR of ≥ 2.0 is achieved, stop the LMWH and continue warfarin.

4.2.7. Discharge on DOACs

- Prior to discharge patients need to be educated and counselled. Refer to Figure 5 Summary of process guiding patient counselling and discharge process – DOACs.
- A DOAC counselling checklist is available in Appendix D2 DOAC counselling checklist. For full information see Appendix C 'The provision of patient information for patients newly initiated on oral anticoagulation medication'.
  DOAC counselling videos are available on:
  Anticoagulation (AF) Atrial Fibrillation - YouTube
- Patient counselling and information should include the offer of appropriate translation, interpreting and reformatting as per Trust policy.
- Patients should be counselled on the following:
  - How and when to take medication and what to do if a dose is missed.
  - The signs and symptoms of bleeding and what to do about them.
  - The need to inform their dentist that they are on an anticoagulant.
  - The need for contraception to prevent pregnancy.
- Patients should be advised that they should seek medical advice if they experience any problems in relation to bleeding on DOAC therapy with their primary care service.
- They must seek urgent medical attention if:
  - They are involved in a major trauma.
  - Suffer a significant blow to the head.
  - Are unable to stop bleeding.

Figure 5: Summary of process guiding patient counselling and discharge - apixaban, dabigatran, edoxaban or rivaroxaban (DOACs)

Patients on DOACs **MUST** (in working hours) be seen by a Clinical Pharmacy team member to receive **ABC** - completed **A**lert Card, patient information **B**ook from the manufacturer and **C**ounselling.
For **out of hours** see below *.

↓

Referring Consultant team to:

- Ensure indication of DOAC & duration is clearly documented on the patient's ePMA record.
- Contact Ward Pharmacist or Technician at earliest opportunity to arrange **ABC** - **A**lert Card, **B**ook and **C**ounselling.

↓

If unable to contact the ward Pharmacy team, ring the Dispensary to request urgent DOAC counselling on:
EDGH [redacted] or Conquest [redacted].
Dispensary staff will contact the Lead Medicines Management Technician to organize counselling.
Alternatively, Trust counselling videos are available at Anticoagulation (AF) Atrial Fibrillation - YouTube

↓

Pharmacist / Pharmacy Technician to:

- Refer to ePMA drug record to complete the 'DOAC Alert Card', provide the specific patient information booklet & personalise counselling information.
- **Ensure patient understands that any previous anticoagulant has been stopped & a DOAC (specify which one) started.**
- Put Alert Card in the patient's medication locker (unless placed directly with the patient's belongings).
- Complete Appendix D2 DOAC counselling checklist & file in the patient's notes.
- Annotate the Anticoagulation section of [redacted] to document that the patient has received **ABC**- **A**lert Card, **B**ook and **C**ounselling.

↓

Referring Consultant team - on day of discharge to:

- Complete e-Discharge Summary letter including:
  - Anticoagulant Discharge Information section – specifying indication & duration for DOAC. For NVAF, CHA_2DS_2-VASc, ORBIT, CrCl & weight values are mandatory requirements.
  - Changes to Medication section.

↓

Pharmacist – on day of discharge – check e-Discharge Summary, ensuring Anticoagulant Discharge Information section is fully completed.

↓

Ward staff – on day of discharge to:

- Confirm that the patient has a 'DOAC Alert Card' and written information.
- Ensure patient understands that any previous anticoagulant has been stopped & a DOAC (specify which one) started.

↓

*** If out of hours, the referring Consultant team are responsible for ABC:**

- Providing /completing the 'DOAC **A**lert Card**'.
- Providing the appropriate patient information **B**ook**.
- Anticoagulation **C**ounselling – Appendix D2 DOAC counselling checklist or via video at Anticoagulation (AF) Atrial Fibrillation - YouTube
- Ensuring the patient understands that any previous anticoagulant has been stopped & a DOAC (specify which one) started.

**Available in the Emergency Drug Cupboards on each site via the Clinical Site Manager.

4.3. Follow-up and Monitoring DOACs

- Routine monitoring of coagulation is not required.
- The discharge summary should recommend that new DOAC patients should be seen 1 month post discharge by their GP – to check on adherence, bleeding / thromboembolic events, other side effects and renal function.

5. Stopping Oral Anticoagulant Therapy

5.1. Planned Surgery

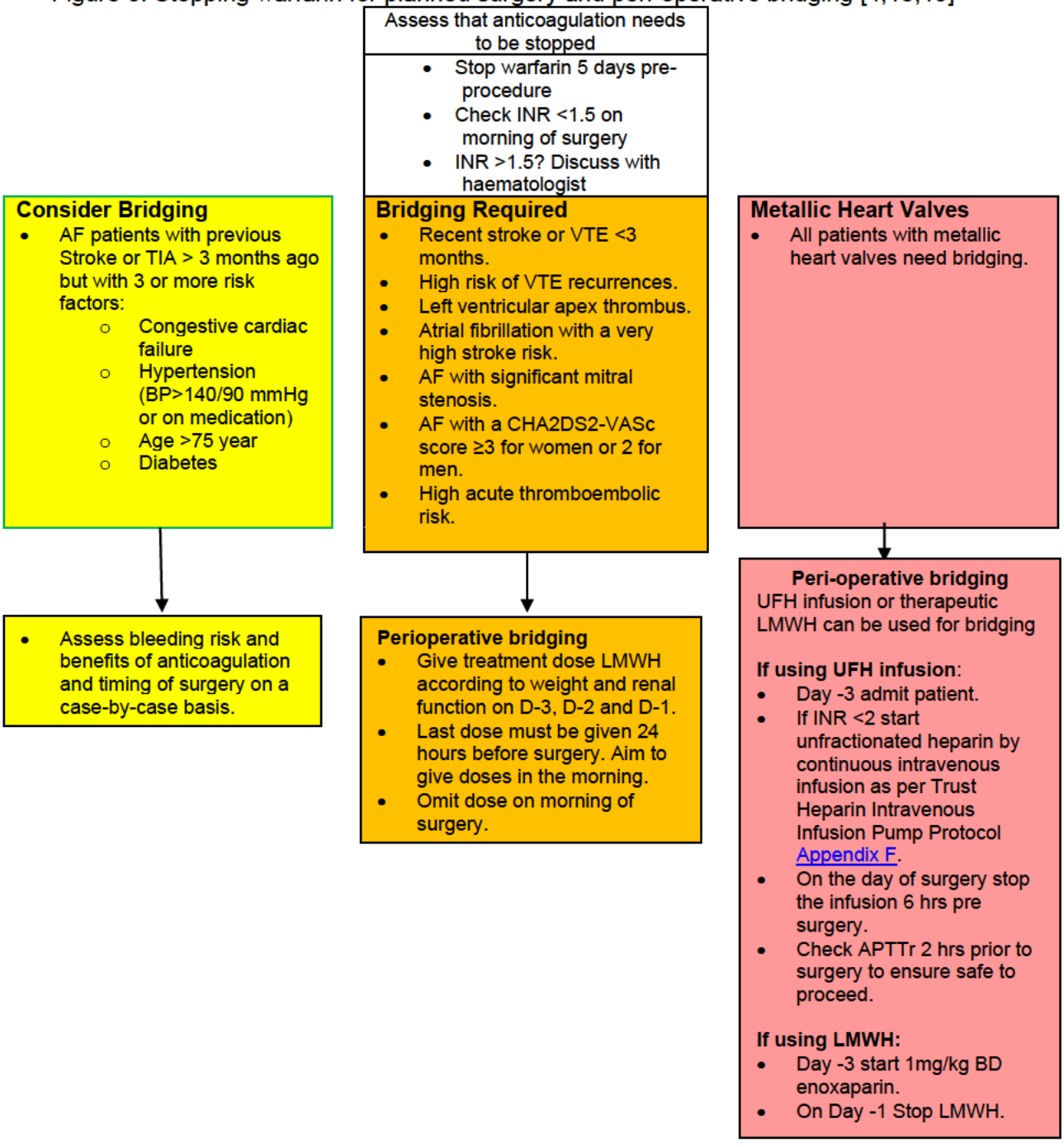
5.1.1. Does Anticoagulation need to be stopped?

- For dermatology procedures INR should be taken three days pre-procedure and the level reviewed by the dermatologist carrying out the procedure to ascertain whether warfarin can be safely continued.
- For some procedures (e.g. dental, joint injections, cataract surgery, and some endoscopic procedures) anticoagulation may not need to be stopped.
- Operating surgeon, dentist or radiologist should assess risk of bleeding for the individual patient and the need to stop anticoagulation for the planned intervention [13].
- The following provides guidance only and each individual patient's bleeding and thrombotic risks need to be individually evaluated.

5.1.2. Stopping Warfarin for planned surgery

- Figure 6 provides guidance regarding stopping warfarin and recommendations for bridging with heparin [4,17].
- Patients with mechanical heart valves:
  - Should have their warfarin discontinued and heparin substituted as per the protocol below.
- Patients with VTE within the preceding 3 months (especially within the last 6 weeks):
  - Should be considered at high risk of recurrence of their event.
  - Consideration should be given to the urgency of the surgery and whether or not this can be delayed.
  - The use of heparin and IVC filters should be considered and discussed with the Haematology Consultant.
- Please see additional guidance regarding Neuroaxial anaesthesia and anticoagulation.

Figure 6: Stopping warfarin for planned surgery and peri-operative bridging [4,18,19]



5.1.3. Stopping DOACs for planned surgery

- Figure7 provides guidance regarding stopping DOACs prior to surgery [15, 17].
- Patients with VTE within the preceding 3 months (especially within the last 6 weeks):
  - Should be considered at high risk of recurrence of their event.
  - Consideration should be given to the urgency of the surgery and whether or not this can be delayed.
  - The use of heparin and IVC filters should be considered and discussed with the Haematology Consultant.
- Please see additional guidance and cautions regarding anticoagulation and neuraxial anaesthetics.

5.1.4. Neuraxial anaesthesia and anticoagulation for planned procedures

- The risk of spinal haematoma with spinal/epidural anaesthesia is greatest at times of needle/catheter insertion and removal.
- Table 21 summarises recommendations from Royal College of Anaesthetists regarding the timing of anticoagulation in the context of neuraxial anaesthesia [20].

Figure 7: Stopping DOACS for planned surgery

Pre-operative assessment
- Does DOAC need to be stopped?
- Assess renal function and stop according to following table:

	Stopping time pre-surgery	
CrCl (ml/min)	High bleeding risk	Low bleeding risk
Dabigatran		
≥ 80	48 hours	24 hours
≥ 50 - <80	72 hours	48 hours
≥ 30 - <50	96 hours	48 - 72 hours
Rivaroxaban		
> 30	48 hours	24 hours
< 30	72 hours	48 hours
Apixaban		
> 30	48 hours	24 hours
< 30	72 hours	48 hours
Edoxaban		
> 30	48 hours	24 hours
< 30	72 hours	48 hours

Postoperative: Restarting a DOAC

Minor Surgery/ Low Bleeding Risk
- Resume DOAC 6 - 12 hours post procedure if adequate haemostasis
- Restart at patient's normal dose

Major Surgery/ High Bleeding Risk
- Delay starting DOAC for at least 48 hours post operation
- Restart at patient's normal dose

High Risk Thrombosis?
In high risk patients consider thromboprophylaxis prior to starting DOAC.

VTE
- VTE within previous 3 months.

AF
- Patients with Stroke or TIA in last 3 months.
- Patients with previous Stroke or TIA > 3 months ago, but with 3 or more risk factors:
  - Congestive cardiac failure.
  - Hypertension (BP >140/90 mmHg or on medication).
  - Age > 75 years.
  - Diabetes.

Table 21: Timing of anticoagulation and neuraxial anaesthetics

Drug	Minimum time between last dose and inserting epidural or spinal catheter		Administration of drug whilst epidural or spinal catheter in place?	Minimum time between removing epidural or spinal catheter and re-starting anticoagulation
UFH				
Prophylaxis-Subcutaneous	4hrs		With caution	1 hour
Treatment-intravenous	4hrs		Not advised	4 hours Consider not re-starting for 24hrs if traumatic procedure
LMWH				
Prophylaxis-Subcutaneous	12hrs	For patients with CrCl 15-30 ml/min, consider doubling the timing of puncture/ catheter placement or removal [21]	With caution	4 hours
Treatment-Subcutaneous	24hrs		Not advised	4 hours Consider not re-starting for 24hrs if traumatic procedure
Warfarin	When INR ≤ 1.4		Not advised	After catheter removal
Dabigatran				
CrCl (mL/min) ≥ 80	48 hours		Not advised	6 hours Consider not re-starting for 24hrs if traumatic procedure
CrCl (mL/min) ≥ 50 - <80	72 hours		Not advised	6 hours Consider not re-starting for 24hrs if traumatic procedure
CrCl (mL/min) ≥ 30 - <50	96 hours		Not advised	6 hours Consider not re-starting for 24hrs if traumatic procedure
Rivaroxaban, Apixaban, Edoxaban				
CrCl (mL/min) ≥30	48 hours		Not advised	6 hours Consider not re-starting for 24hrs if traumatic procedure
CrCl (mL/min) <30	72 hours		Not advised	6 hours. Consider not re-starting for 24hrs if traumatic procedure

Reference [20, 21]

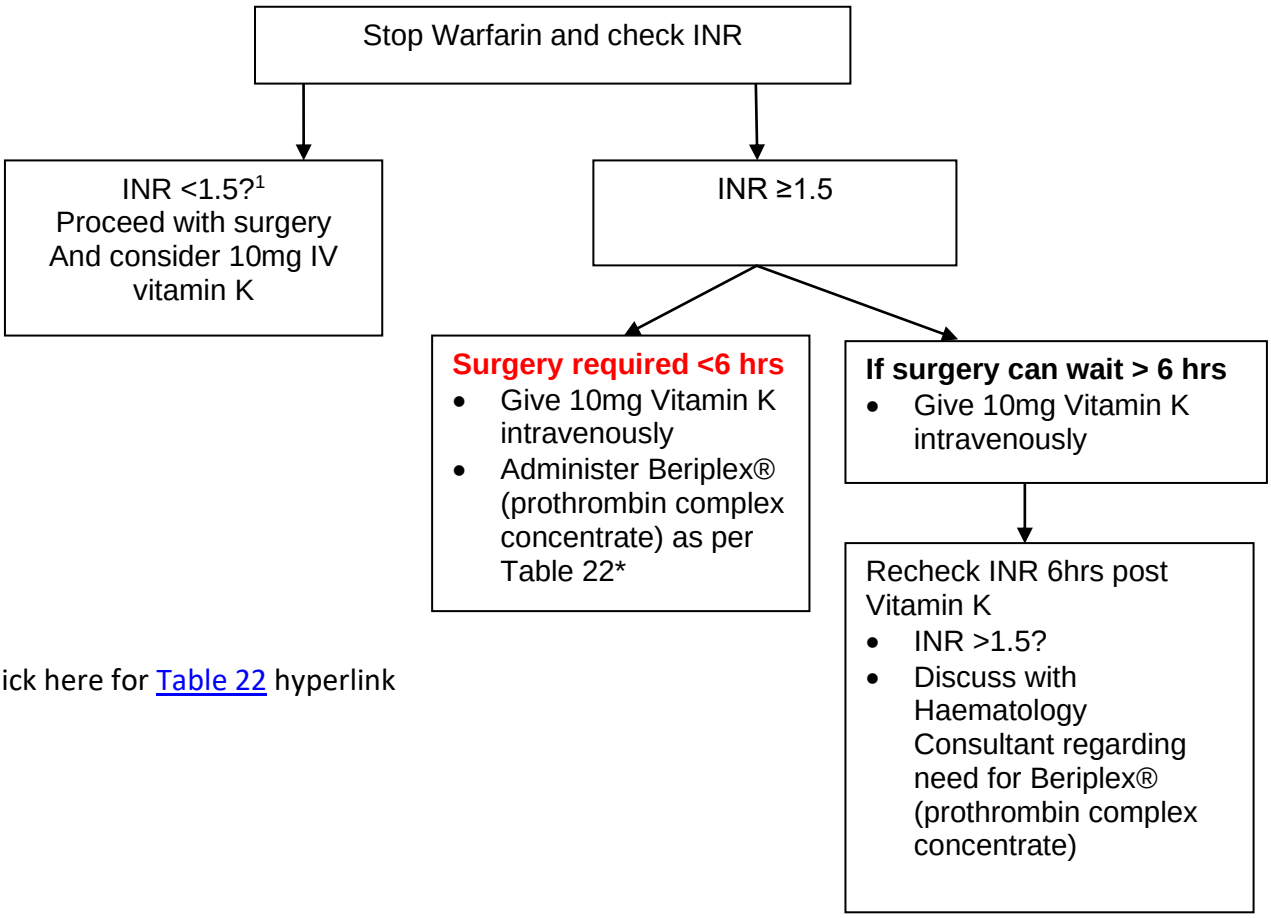
Please also refer to Guidelines for Epidural Analgesia. http://nww.esht.nhs.uk/wp-content/uploads/2018/08/00741_P.pdf

5.2. Emergency Surgery

5.2.1. Stopping warfarin for emergency surgery

- Warfarin can be reversed to allow for emergency surgery
- The following provides guidance regarding timing and methods of reversal

Figure 8: Reversing warfarin for emergency surgery
Reference [22]



*Click here for Table 22 hyperlink

5.2.1.1. Vitamin K (Phytomenadione)

- Vitamin K may be given intravenously (IV) or orally.
- IV vitamin K will reverse anticoagulation more rapidly & reliably than oral vitamin K.
- IV vitamin K will have a significant effect on the INR in 4-6 hours but requires up to 24 hours for a full effect.
- In the presence of bleeding use IV vitamin K [1].
- In patients not bleeding use oral vitamin K [1].

- Intravenous vitamin K injections must be given very slowly [23].
  - Administer by IV infusion in 50ml glucose 5%, given over 20 - 30minutes. Refer to: Injectable Medicines Guide - Display - Phytomenadione - Intravenous - Version 13 - IVGuideDisplayMain.asp [24].
  - Do not dilute with sodium chloride as precipitation may occur [24].

5.2.1.2. Fresh Frozen Plasma

- The use of fresh frozen plasma is not recommended for the reversal of warfarin.

5.2.1.3. Prothrombin complex concentrate (PCC)

- Beriplex® is a virally inactivated prothrombin complex concentrate containing vitamin K dependent clotting factors (II, VII, IX and X) and Protein C and Protein S.
- It provides instant (< 30 minutes) reversal of the effects of warfarin which will last for 8-12 hours.
- The dose of Beriplex® is based upon the patient's INR and weight as in Table 22.
- The pre-treatment INR should be measured as close as possible to the time of dosing to calculate the appropriate dose of Beriplex®.
- IV vitamin K should also be given to maintain effect.
- Recovery and the duration of effect may vary, therefore monitoring of INR during treatment is mandatory.
- Beriplex® is prothrombotic so is only suitable for emergency use.
- Patients' religious preferences and other beliefs must be considered before prescribing blood products in line with the Trust transfusion guidance.
- **Beriplex® is a blood product and is available from blood bank.**

5.2.1.4. Dosing Prothrombin complex (PCC) for the reversal of warfarin

Table 22: Dosing PCC (Beriplex®) for reversal of warfarin

Body Weight	INR 2.0-3.9	INR 4.0-6.0	INR > 6.0
30 kg	750 units	1000 units	1500 units
35 kg	750 units	1000 units	1750 units
40 kg	1000 units	1500 units	2000 units
45 kg	1000 units	1500 units	2250 units
50 kg	1250 units	1750 units	2500 units
55 kg	1250 units	2000 units	2500 units
60 kg	1500 units	2000 units	3000 units
65 kg	1500 units	2000 units	3000 units
70 kg and above	1750 units	2500 units	3500 units

- **Beriplex® is a blood product and is available from blood bank.**
- Recheck INR approximately 30 minutes after the infusion to ensure the INR is < 1.5.
- Further doses may be needed if an adequate level of correction has not been achieved. **Advice should be sought from a Consultant Haematologist**.

5.2.2. Stopping DOACs for emergency surgery

- If the surgery is urgent the risk of bleeding must be weighed against the risk of a delay in operating.
- If urgent reversal of apixaban, rivaroxaban or edoxaban is required Beriplex® should be considered, following discussion with a Consultant Haematologist.
- If possible, surgery should be delayed for at least 24 hours as per Figure 7: Stopping DOACS for planned surgery
- The half-life of:
  - rivaroxaban is 5 - 13 hours
  - apixaban is 12 hours
  - dabigatran is 12 - 17 hours
  - edoxaban is 10 -14 hours

5.2.3. Dabigatran

- Surgery / intervention should be delayed if possible until at least 12 hours after the last dose. If surgery cannot be delayed the risk of bleeding may be increased [14].
- In the event of a patient requiring emergency surgery or other invasive procedure that cannot be delayed for at least 8 hours dabigatran can be reversed using Idarucizumab (Praxbind®) [25].
- Idarucizumab is a humanized monoclonal antibody fragment that is a specific reversal agent for adult patients treated with dabigatran only.
- Idarucizumab will not reverse the effects of other anticoagulants.
- See Appendix H for guidance regarding the administration of Idarucizumab (Praxbind®).

5.3. Stopping anti-platelet therapy for planned and emergency surgery

5.3.1. Aspirin or Clopidogrel Monotherapy

- Aspirin monotherapy for secondary prophylaxis of cardiovascular disease can be continued for most low-risk procedures.
- If there is a high risk of bleeding aspirin should be omitted for 7 days and clopidogrel for 10 days prior to surgery [17].

5.3.2. Dual anti-platelet therapy

- In patients with recent stents or acute coronary syndrome, procedures at low risk of bleeding should proceed on dual anti-platelet therapy.
  Elective procedures with a high risk of bleeding should be postponed if possible.
- If surgery cannot be postponed, aspirin should continue and clopidogrel be postponed for 5 days pre-procedure [17].
- Discuss with cardiology for further advice.

5.3.3. Urgent surgery and anti-platelet therapy

- For urgent high-bleeding risk surgery consider the use of tranexamic acid pre-operatively.
- If bleeding risk is considered to be very high, consider platelet transfusion following discussion with a Consultant Haematologist.

5.4. Over-anticoagulation and bleeding

5.4.1. Managing over-anticoagulation and bleeding with warfarin

- Assess the cause of over-anticoagulation.
- Document the decision regarding the risks and benefits of further treatment.

Table 23: Managing over-anticoagulation and bleeding patients on warfarin [27, 28]

Clinical Situation	Guidance
Major bleeding	Stop warfarin. Give 10 mg vitamin K **by slow intravenous injection**. Give Beriplex® Table 22. Recheck INR following administration of Beriplex® to ensure adequate reversal.
INR > 8.0 - minor bleeding	Stop warfarin. Give vitamin K **by slow intravenous injection**. Repeat dose of vitamin K if INR still too high after 24 hours. Resume warfarin therapy at a lower dose in due course.
INR > 8.0 – no bleeding	Stop warfarin. Give vitamin K **by mouth** using the IV preparation orally (unlicensed use). Use Konakion MM Paediatric 2mg/0.2ml solution for injection of 1 - 2mg doses. Repeat dose of vitamin K if INR still too high after 24 hours. Resume warfarin therapy at a lower dose in due course.
INR 5.0 – 8.0 – minor bleeding	Stop warfarin. Give vitamin K by **slow intravenous injection**. Resume warfarin therapy at a lower dose in due course.
INR 5.0 – 8.0 – no bleeding	Stop warfarin for 1 - 3 days and resume therapy at a lower dose.
Bleeding at therapeutic levels	Investigate possibility of underlying cause e.g. renal or gastro-intestinal tract pathology as in non-anticoagulated patients.

5.4.2. Managing over-anticoagulation and bleeding with DOACs

5.4.2.1. Dabigatran

- Dabigatran can be reversed using idarucizumab (Praxbind®), a humanized monoclonal antibody fragment that is a specific reversal agent for adult patients treated with dabigatran.
- Idarucizumab will not reverse the effects of other anticoagulants. It is used for the emergency reversal of dabigatran in the following circumstances:
  - Life –threatening bleed defined as one or more of: symptomatic intracranial bleeding, reduction in haemoglobin of at least 5g/dl, transfusion of ≥ 4 units of blood, bleeding associated with hypotension requiring use of IV inotropic agents and/or bleeding necessitating surgical intervention [29].
  - Emergency surgery or other invasive procedure that cannot be delayed for at least 8 hours, requiring urgent reduction of dabigatran anticoagulation effect [29].
  - Refer to Appendix G for Adult Patient Receiving Dabigatran Therapy: Haemorrhage Protocol.
  - Refer to Appendix H for Idarucizumab (Praxbind®) Protocol.

5.4.2.2. Rivaroxaban, Apixaban, Edoxaban

- Andexanet alfa, the specific antidote to rivaroxaban and apixaban has been approved by NICE for **GI bleeds ONLY** [30]. Discuss with a Haematology consultant to consider if andexanet alfa is appropriate. Andexanet alfa **CANNOT** be issued without Haematology consultant approval.
- Andexanet alfa is kept in the cold store in Pharmacy on each site.
- There is no specific licensed antidote to edoxaban.
- The role of blood products to reverse the effects of anti-Xa inhibitors is uncertain, discussion with a Consultant Haematologist is recommended in this situation.

5.4.2.3. Andexanet alfa

Table 24: Andexanet alfa dosing and administration

Andexanet alfa administration			
Dose	Initial IV dose	Continuous IV infusion	No. 200mg vials
Low dose	400mg over 15 mins (rate 30mg/min)	4 mg/min for 120 mins (480mg)	**5**
High dose	800mg over 30 mins (rate 30mg/min)	8 mg/min for 120 mins (960mg)	**9**
Fxa inhibitor	Last dose	<8 hours or unknown	≥ 8 hours
Apixaban	≤ 5 mg	Low dose	Low dose
	> 5 mg/ unknown	High dose	
Rivaroxaban	≤ 10mg	Low dose	Low dose
	> 10mg / unknown	High dose	

Refer to Appendix I Andexanet Alfa Administration Protocol for further information.

Figure 9: Managing bleeds in patients on apixaban, rivaroxaban or edoxaban

Bleeding in patients taking APIXABAN or RIVAROXABAN or EDOXABAN

Document time of last intake and dosing regimen.
Discontinue treatment

Consider 50g activated charcoal (in Emergency Drug Cupboard) if ingestion <1 hour

- Assess clinical effects of bleeding and resuscitate patient as appropriate.
- Use local haemostatic measures to control bleeding.
- Check FBC and U&E's.
- Send Group and Save sample.

MILD BLEED
Bleeding that does not meet criteria for major or life-threatening bleeding

- Mechanical compression
- Consider dose reduction OR discontinue treatment

MAJOR BLEED

- Symptomatic bleeding in a critical area or organ such as intracranial, intraspinal, intraocular, retroperitoneal, intra-articular, pericardial or intramuscular with compartment syndrome
- Bleeding causing a fall in Hb level of ≥ 20 g/L or requiring transfusion of ≥ 2 units of blood

- Give fluid replacement to maintain urine output
- Optimise tissue oxygenation
- Control haemorrhage
  - Mechanical compression
  - Surgical / radiological intervention
- Tranexamic acid 1g IV over 10 minutes & repeat if bleeding persists – up to TDS; in renal impairment check SPC
- Red cell transfusion
  - Aim Hb > 70 g/L
- Platelet transfusion
  - Aim Plt > 50 x 10^9/l or
  - If CNS bleed aim Plt > 100 x 10^9/l
- Identify bleeding source, e.g. surgery, endoscopy, interventional radiology

LIFE THREATENING BLEED
1 or more of:

- Symptomatic intracranial bleeding
- Reduction in haemoglobin of at least 50 g/L
- Transfusion of ≥ 4 units of blood
- Bleeding associated with hypotension requiring use of IV inotropic agents
- Bleeding necessitating surgical intervention

- **All bleeds with Apixaban, Rivaroxaban or Edoxaban** - Prothrombin Complex Concentrate (Beriplex) – contact Haematology via switchboard for advice.
- **GI bleed with Apixaban** or **Rivaroxaban** – discuss with Haematology consultant to consider if Andexanet Alfa appropriate. Andexanet Alfa **CANNOT be issued without Haematology consultant approval.**
- **Note:** Andexanet alfa is NOT licensed for the reversal of edoxaban.

References [15, 30–35]

6. Heparin Anticoagulant Therapy

- Heparins are available in unfractionated (UFH) and low molecular weight (LMWH) forms.
  - UFHs are administered intravenously (IV) and subcutaneously (S/C).
  - LMWHs are only administered S/C.

- LMWHs are preferred over UFH as:
  - Bioavailability is greater and more predictable.
  - Half-life is longer enabling once daily administration for both treatment and prophylaxis, although twice daily administration is used in some circumstances.
  - Monitoring is not routinely required.

- Enoxaparin is the preferred LMWH in the Trust.
  It is expressed both in milligrams (mg) and in international units (IU) of anti-Xa activity: 1 mg of enoxaparin sodium is equivalent to 100 IU anti-Xa activity.

- Dosing needs to be adjusted in the following patient groups: -
  - Renal impairment Table 26 - **renal function should be measured within 24 hours of starting heparin.**
  - Raised BMI Table 26
  - Pregnancy (refer to separate guideline - Clinical Guideline for Thromboprophylaxis and Treatment of Venous Thromboembolism in Maternity - http://nww.esht.nhs.uk/wp-content/uploads/2018/08/00419_P.pdf.

The following are not included in this guidance and advice should be sought from the appropriate units:

- UFH and LMWH in acute coronary syndromes.
- The use of heparin to support hemofiltration in the Intensive Therapy Units.

6.1. Cautions and contraindications to heparins

Contraindications:

- Anaesthesia - spinal or epidural - with treatment doses of UFH or LMWH within 24 hours
- Bacterial endocarditis (acute)
- Cerebral haemorrhage (recent)
- Haemophilia (untreated) and other haemorrhagic disorders
- History of/suspected HIT
- Hypersensitivity
- Hypertension (severe)
- Liver disease (severe)
- Major trauma
- Oesophageal varices
- Gastrointestinal ulcer
- Surgery – recent neurosurgery or recent eye surgery
- Thrombocytopenia with platelets $<60 \times 10^9$/l –seek advice from a Consultant Haematologist.
- Active tuberculosis (heparin calcium) [36]

Cautions:

- Concomitant drugs that increase risk of bleeding
- Elderly
- Hepatic and renal impairment - **renal function should be measured within 24 hours of starting heparin.**
- LMWH and UFH are porcine derived which may be incompatible with some patients' religious beliefs, other beliefs or preferences e.g. veganism. In these patients fondaparinux may be used as an alternative anticoagulant but this should be discussed with a Consultant Haematologist.

- Long term heparin use (LMWH & UFH) can cause:
  - Osteoporosis - LMWH is preferred for long-term use over UFH.
  - Hyperkalaemia - caused by inhibition of aldosterone secretion. The risk appears to increase with duration of therapy. Patients with the following conditions seem to be more susceptible and will require additional monitoring:
    - Diabetes mellitus
    - Chronic renal failure
    - Acidosis
    - Taking potassium-sparing drugs

6.1.1. LMWH treatment in VTE:

- In the acute phase, whilst a VTE is being confirmed (but treatment is deemed appropriate) consider LMWH.
- Where VKAs are used for the treatment of VTE, LMWH should be introduced at the same time and continued for at least 5 days and until the INR is ≥ 2.0 for at least 24 hours [3,21].
- The DOACs dabigatran and edoxaban require treatment with at least 5 days of a parenteral anticoagulant prior to their initiation.
- Enoxaparin is available in prefilled syringes for subcutaneous injection. See Appendix J for details.

6.1.2. Enoxaparin:

Treatment doses for VTE - choosing the right regimen

- The dosing regimen of enoxaparin for the treatment of DVT and PE is dependent on a number of factors including thromboembolic risk, bleeding risk and renal function.
- The appropriate dosing regimen should be selected from Table 25:

Table 25: Enoxaparin: Treatment doses for VTE – choosing the right regime

Patient group	Comment	Enoxaparin dosing regimen
Uncomplicated patients	• Low risk of VTE recurrence • CrCl ≥30mL/min	**Once daily** injection of 1.5 mg/kg (150 IU/kg)
More complex patients e.g. with symptomatic PE, cancer, recurrent VTE or proximal (iliac vein) thrombosis, weight >150kg	• CrCl ≥30mL/min	**Twice daily** injections of 1 mg/kg (100 IU/kg)
Patients with severe renal impairment (CrCl 15-29mL/min)		**Once daily** injection of 1 mg/kg (100 IU/kg)

- See Table 26 for dose bandings according to weight and dosage regime.

Table 26: Enoxaparin dose bandings according to weight and dosing regime

Patient weight (kg)	1.5mg/kg ONCE DAILY for un-complicated patients with low risk of VTE recurrence and CrCl ≥30mL/min	Volume to admini-ster	Suggested pre-filled syringe(s) to be used	1mg/kg TWICE DAILY for all other patients with CrCl ≥30mL/min e.g. >150kg, with symptomatic PE, cancer, recurrent VTE or proximal (iliac vein) thrombosis ONCE DAILY For all patients (complex or uncomplicated) with severe renal impairment CrCl 15-29mL/min *		
				Dose	Volume	Suggested pre-filled syringe
40-46 kg	60mg	0.6ml	60mg/0.6ml Enoxaparin	40mg	0.4ml	40mg/0.4ml Enoxaparin
47-59 kg	80mg	0.8ml	80mg/0.8ml Enoxaparin	50mg	0.5ml	60mg/0.6ml Enoxaparin
60-74 kg	100mg	1.0ml	100mg/1ml Enoxaparin	60mg	0.6ml	60mg/0.6ml Enoxaparin
75-89 kg	120mg	0.8ml	120mg/0.8ml Enoxaparin	80mg	0.8ml	80mg/0.8ml Enoxaparin
90-110 kg	150mg	1.0ml	150mg/1.0ml Enoxaparin	100mg	1.0ml	100mg/1.0ml Enoxaparin
111-119 kg	180mg	1.0ml using 100mg/1.0ml Enoxaparin + 0.8ml using 80mg/0.8ml Enoxaparin		120mg	0.8ml	120mg/0.8ml Enoxaparin
120-130 kg	190mg	1.0ml using 100mg/1ml Enoxaparin + 0.9ml using 100mg/1ml Enoxaparin		120mg	0.8ml	120mg/0.8ml Enoxaparin
131 - 139 kg **	200 mg	2.0ml using 2 x 100mg/1.0ml Enoxaparin		140mg	1.0ml of 100mg/1.0ml Enoxaparin + 0.4ml of 40mg/0.4ml Enoxaparin	
140 - 150 kg **	220mg	1.0ml using 100mg/1.0ml Enoxaparin + 0.8ml using 120mg/0.8ml Enoxaparin		150mg	1.0ml of 150mg/1.0ml Enoxaparin	

Check renal function within 24 hours of initiation.

***In patients with end stage kidney disease (CrCl <15mL/min) unfractionated heparin should be used – obtain advice from Haematology where possible.**

**In patients weighing 131 - 150kg:

- Take a peak anti Xa level (4 hours post dose) after the 3rd dose.
- Adjust the dose as per Table 27.
- Speak to a Consultant Haematologist for further advice regarding ongoing treatment.

6.1.3. Dosing enoxaparin in patients >150kg

Dose of enoxaparin for treatment of DVT / PE / AF bridging in patients >150kg

- Dose at 1mg/kg twice a day.
- Take a peak anti Xa level (4 hours post dose) after the 3rd dose.
- Adjust the dose as per Table 27.
- Speak to a Consultant Haematologist for further advice regarding ongoing treatment.

6.1.4. Monitoring of low molecular weight heparin

- Monitoring is not routinely required for thromboprophylaxis or treatment with LMWHs.
- Monitoring may be indicated in the following patient groups; the need for possible monitoring should be discussed with a Consultant Haematologist:
  - Severe renal failure
  - The obese
  - Pregnant women
  - Neonates
  - Infants

  Reference [21]
- An anti-Xa assay may be used for monitoring.
- Measure peak LMWH levels for anti-Xa assay 4 hours post S/C injection.

6.1.5. Requesting and interpreting anti-Xa levels

- Anti-Xa levels are measured via the haematology labs
- Take a peak anti Xa level (4 hours post dose) after the 3rd dose.
- Send samples as early in the day as possible.
- Adjust the dose as per Table 27.
- Speak to a Consultant Haematologist for further advice regarding ongoing treatment.

Table 27: Anti-Xa levels and dose adjustments

Enoxaparin dose adjustment after peak anti-Xa monitoring for patients 1.5mg/kg ONCE daily dosing			
Anti-Xa level (IU/ml)	Hold next dose	Dose change	Next **peak** anti-Xa level (always take level 4 hours after dose)
<0.5	No	Increase by 50%	48 hours
0.51 – 0.99	No	Increase by 25%	48 hours
1 – 2	No	No	1 week
2.1 – 3	No	Decrease by 30%	48 hours
>3	Until anti-Xa <0.5 IU/ml (check every 6 hours)	Decrease by 50%	48 hours after next dose, consider changing to UFH

Enoxaparin dose adjustment after peak anti-Xa monitoring for patients >150kg on initial 1mg/kg TWICE daily dosing			
Anti-Xa level (IU/ml)	Hold next dose	Dose change	Next **peak** anti-Xa level (always take level 4 hours after dose)
<0.25	No	Increase by 50%	48 hours
0.25 – 0.49	No	Increase by 25%	48 hours
0.5 – 1.2	No	No	1 week
1.21 – 1.5	No	Decrease by 25%	48 hours
1.51 – 2	For 3 hours	Decrease by 30%	48 hours after next dose
>2	Until anti-Xa <0.5 IU/ml (check every 6 hours)	Decrease by 50%	48 hours after next dose, consider changing to UFH

6.1. Unfractionated heparin (UFH)

- UFH is available in a concentration of 1000 units/ml for the treatment of venous thromboembolic events (please note other concentrations are available for other indications). Infusions should be made up as per Trust Heparin Infusion Pump Protocol Appendix F.

- LMWH is the preferred heparin for the treatment of venous thromboembolic events.

6.1.1. Heparin Induced Thrombocytopenia (HIT): Monitoring the platelet count during heparin therapy

- Both UFH and LMWH can cause heparin induced thrombocytopenia (HIT).
- The risk is greater with UFH.
- Measure baseline platelet count in all patients to receive heparin - on day of starting treatment.
- Recheck platelet count 24 hours after starting heparin.
- Monitor platelet count at least every other day from days 4 to 14 or until heparin stopped, whichever is longer in patients receiving UFH.
- Routine monitoring of platelets in patients receiving LMWH is not required unless they have been exposed to UFH in the previous 100 days.

- An accurate diagnosis of HIT is based on the presence of clinical features [37], including:
  - A fall of ≥ 30% in platelet count
  - Appropriate timing of thrombocytopenia (day 4 -14 following exposure)
  - Development of new thrombosis despite thrombocytopenia and heparin therapy
  - The absence of a more likely cause of thrombocytopenia [24].
  - A pre-test probability score should be calculated using Table 28.
  - If the pretest probability score is ≤3, no further laboratory investigation is recommended for the majority of patients, except rarely for patients treated in the intensive care unit.
- If the pretest probability of HIT is ≥4, heparin should be stopped, and an alternative anticoagulant started at therapeutic intensity while laboratory tests are performed. **Testing and alternative anticoagulant therapy should be discussed with a Consultant Haematologist.**
- After a consultation with consultant Haematologist, if deemed appropriate, administer IV argatroban until platelet count recovers [37,38].
- Argatroban is non-formulary, for hospital use only.
- Click here for Argatroban Protocol – Appendix K

Table 28: Pre-test probability scoring for heparin induced thrombocytopenia
Reference [37]

	Points (0,1 or 2 for each of four categories: Max possible score = 8)		
	2	**1**	**0**
Thrombocytopenia	>50% fall and platelet nadir ≥20 x 10^9/L	30% - 50% fall or platelet nadir 10-19 x 10^9/L	Fall <30% or platelet nadir <10 x 10^9/L
Timing[a] of platelet count fall or other sequelae	Clear onset between days 5 and 10; or ≤1 day (if heparin exposure within past 30 days)	Consistent with immunisation but not clear (e.g., missing platelet counts) or onset of thrombocytopenia after Day 10; or fall ≤1 day (if heparin exposure 30-100 days ago)	Platelet count fall ≤4 days (without recent heparin exposure
Thrombosis or other sequalae (e.g., skin lesions)	New thrombosis; skin necrosis; post-heparin bolus acute systemic reaction	Progressive or recurrent thrombosis; erythematous skin lesions; suspected thrombosis not yet proven	None
Other cause for thrombocytopenia not evident	No other cause for platelet count is evident	Possible other cause is evident	Definite other cause is present

Pretest probability score:
6-8 = High 4-5 = Intermediate 0-3 = Low
[a]First day of immunising heparin exposure considered Day 0. The day the platelet count begins to fall is considered the day of onset of thrombocytopenia, (it generally takes 1-3 days more until an arbitrary threshold that defines thrombocytopenia is passed).

6.1.2. Monitoring of potassium levels during heparin therapy

- In the following patient groups measure plasma potassium concentration before starting heparin, and monitor at least weekly thereafter, particularly if treatment is to be continued for longer than 7 days:-
  - Diabetes mellitus
  - Chronic renal failure
  - Acidosis
  - Raised plasma potassium
  - Concomitant potassium-sparing drugs.

6.2. Bleeding and heparin anticoagulation

- In the bleeding patient it is possible to neutralise heparin anticoagulation, although 100% neutralisation of LMWHs is not achievable.
- UFH given intravenously has a short half-life such that its anticoagulant effect disappears relatively rapidly on discontinuation of administration thus, reversal of UFH may be unnecessary.
- If reversal is deemed necessary protamine sulfate may be used. Discussion with a Consultant Haematologist is recommended prior to the use of protamine.

6.2.1. Protamine for neutralisation of unfractionated heparins

- Protamine sulfate should not be given when bleeding occurs without prior heparin use.
- Protamine sulfate is not suitable for reversing the effects of oral anticoagulants.
- Protamine sulfate can cause severe hypotension, cardiovascular collapse, non-cardiogenic pulmonary oedema, catastrophic pulmonary vasoconstriction, and pulmonary hypertension. Risk factors include: -
    - High dose or overdose
    - Rapid administration
- Use caution when administering protamine sulfate to patients who may be at increased risk of allergic reaction to protamine. These include: -
    - Patients who have previously undergone procedures such as coronary angioplasty or cardiopulmonary by-pass which may include the use of protamine.
    - Diabetics who have been treated with protamine insulin.
    - Patients allergic to fish.
    - Men who have had a vasectomy or are infertile and may have antibodies to protamine.

- In patients with any of these risk factors, carefully consider the risk /benefit of protamine sulfate administration. Vasopressors and resuscitation equipment should be immediately available in case of a severe reaction to protamine.
- No more than 50mg of protamine sulfate should be given in any one dose.
- In excess, protamine itself acts as an anticoagulant.

Neutralisation of UFH administered by IV infusion – in bleeding patients only:

- Stop the UFH infusion.
- Give 25 - 50mg of protamine sulfate by slow IV injection - max rate 5mg/minute (refer to Medusa Injectable Medicines Guide - Display - Protamine sulfate - Intravenous - Version 5 - IVGuideDisplayMain.asp
- Preferably administer via a central venous access device to avoid potential venous irritation as the preparation has a low pH.
- If given peripherally, choose a large vein and monitor the injection site closely using a recognised infusion phlebitis scoring tool.

Neutralisation of UFH administered subcutaneously - in bleeding patients only:

- Give 1mg of protamine sulfate per 100 units of UFH by slow IV injection (max rate 5mg/minute) up to a maximum of 50mg protamine in any one dose. Usual dose required: 25-50mg protamine sulfate, i.e. to neutralise 5,000 units of UFH give 25-50mg protamine over 5-10 minutes.

For patients receiving doses of UFH > than 5,000 units, i.e. patients >100kg and so requiring more than 50mg of protamine for neutralisation, give the initial 50mg of protamine by slow IV injection as above and the balance by intravenous infusion over 8 -16 hours (see example below).

- The last UFH S/C dose is used to calculate the dose of protamine sulfate required.

Example:
A patient has been receiving UFH 7,500 units three times a day S/C. He is now bleeding and requires protamine for heparin neutralisation.

1mg of protamine sulfate will neutralise 100 units of heparin.
7,500 units of heparin will require 75mg of protamine sulfate to achieve neutralisation.

BUT
No more than 50mg of protamine sulfate can be given in any one dose.

Therefore:
Give 50mg of protamine sulfate by slow IV injection (max 5mg/min) – this will neutralise 5000 units of heparin.

Then administer the balance - 25mg protamine sulfate- by IV infusion over 8 – 16 hours, this will neutralise the remaining 2,500 units of heparin.

Neutralisation of LMWH enoxaparin - in bleeding patients only:

- If neutralisation of LMWH is being considered, discuss with Haematology Consultant.
- The anticoagulant effects of enoxaparin can be largely neutralised by slow IV protamine sulfate injection BUT even with high doses of protamine sulfate, the anti-Xa activity of enoxaparin is never completely neutralised (maximum about 60%).
- The initial dose of protamine sulfate depends on the dose and the timing of the last enoxaparin dose.

Table 29: Protamine administration to neutralise enoxaparin

Time of last enoxaparin dose	**Dose of protamine sulfate**	**Maximum dose of protamine**	**Comment**
0 – 8 hours	1mg per 1mg of enoxaparin	50mg	**Protamine can exert its own anticoagulant effect if used in larger doses**.
>8 - ≤ 12 hours	0.5mg per 1mg of enoxaparin		
>12 hours	Protamine may not be required – discuss with Haematology Consultant		

- Refer to a Consultant Haematologist if there is ongoing bleeding.
- The anti-Xa activity of enoxaparin may not be completely reversed with protamine sulfate and may persist for up to 24 hours after administration.

7. Thromboprophylaxis

[26]

- Hospitalised patients (medical or surgical) are at risk of venous thromboembolic events (VTE).
- Risk factors for VTE are well established (see Table 30).
- LMWHs are preferred over UFH because of the reduced risk of HIT and the usual once daily administration (although twice daily regimens are used for some indications).
- Where pharmacological VTE prophylaxis is indicated, it should be started as soon as possible and within **14 hours of admission** unless otherwise stated and continued until the patient is no longer at increased risk of VTE. Reassess all medical, surgical and trauma patients at consultant review or if their clinical condition changes. [26]
- Please refer to the Venous Thromboembolism Diagnosis, Treatment and Prevention Policy and Procedure 01152_P.pdf (esht.nhs.uk).
- The Trust risk assessment tool and ePMA should be used to assess the need for thromboprophylaxis in all patients.
- For patients already on antiplatelet therapy (e.g. aspirin, clopidogrel) for other conditions who are assessed to be at increased risk of VTE:
    - Consider offering pharmacological VTE prophylaxis according to the reason for admission, if the risk of VTE outweighs the risk of bleeding.
    - Offer mechanical VTE prophylaxis if the risk of bleeding outweighs the risk of VTE.

- **Do not offer additional pharmacological or mechanical VTE prophylaxis to patients therapeutically anticoagulated.**
- Consider VTE prophylaxis for people at increased risk of VTE who are interrupting anticoagulant therapy [26].

Table 30: Risk factors for VTE

Patient related factors		Admission related factors
Active cancer or cancer treatment (hormonal, chemotherapy or radiotherapy)		Significantly reduced mobility for 3 days or more; paresis
Age >60		Hip or knee replacement
Dehydration		Hip fracture
Inherited or acquired thrombophilic factors		Total anaesthetic + surgery time >90 minutes
Known thrombophilias		Critical care admission
Obesity (BMI >30kg/m^2)		Surgery with a significant reduction in mobility
One or more significant medical co-morbidities (e.g. heart disease; metabolic endocrine or respiratory pathologies; acute infectious diseases; inflammatory conditions)		Surgery involving pelvis or lower limb with a total anaesthetic + surgery time > 60 minutes
Personal history or first degree relative with a history of VTE		Acute surgical admission with inflammatory or intra-abdominal condition
Use of hormone replacement therapy		
Use of oestrogen containing contraceptive therapy		
Varicose veins with phlebitis		
Pregnancy or < 6 weeks postpartum (see NICE for specific risk factors)		

Reference [39]

7.1. Prophylaxis against VTE in general medical patients

- Pharmacological VTE prophylaxis should be offered for a minimum of 7 days (throughout hospital admission) in acutely ill medical patients where risk of VTE outweighs bleeding risk.
- Enoxaparin should be used first line.
- Where enoxaparin is contraindicated (except in renal impairment) use Fondaparinux [26].
- In patients where pharmacological VTE prophylaxis is contraindicated, consider offering mechanical VTE prophylaxis, i.e. anti-embolism stockings, intermittent pneumatic compression devices or foot impulse devices, as available.

7.1.1. Dosing heparin thromboprophylaxis in medical patients

Table 31: Dosing heparin thromboprophylaxis
References [21, 26, 40-43] **Check renal function within 24 hours of initiating**

	Pharmacological thromboprophylaxis - administered subcutaneously			
Renal Function	<50kg	50-99kg	100-150kg	>150kg
CrCl > 30mL/min	Enoxaparin 20mg once daily	Enoxaparin 40mg once daily	Enoxaparin 40mg twice daily	Enoxaparin 60mg twice daily
CrCl 15-29mL/min	Enoxaparin 20mg once daily	Enoxaparin 20mg once daily	UFH 7500 units three times daily	UFH 7500 units three times daily
CrCl <15mL/min	UFH 5000 units twice daily	UFH 5000 units twice daily	UFH 7500 units three times daily	UFH 7500 units three times daily

7.1.2. Thromboprophylaxis in Acute Coronary Syndromes (ACS)

- Patients receiving anticoagulant drugs as part of their treatment for ACS do not usually need VTE prophylaxis [26].

7.1.3. Thromboprophylaxis in Cancer patients

- Do NOT offer VTE prophylaxis to people receiving cancer-modifying treatments such as radiotherapy, chemotherapy or immunotherapy who are mobile, except as below, unless they are also at increased risk of VTE for reasons other than cancer.
- Consider pharmacological VTE prophylaxis:
    - For people with myeloma who are receiving chemotherapy with thalidomide, pomalidomide or lenalidomide. Consider either:
        - Aspirin (75mg or 150mg) or
        - LMWH
        - Rivaroxaban 10mg
    - For people with other malignancies, an assessment of risk of VTE should be made using the Khorana risk score https://www.mdcalc.com/khorana-risk-score-venous-thromboembolism-cancer-patients.
- If giving VTE prophylaxis to people with cancer, continue for as long as they are perceived to be at risk. [26]

7.1.4. Thromboprophylaxis in Palliative Care

- Consider offering pharmacological VTE prophylaxis to patients in palliative care who have potentially reversible acute pathology. Take into account potential risks and benefits and the views of patients and their families and/or carers. Review regularly.
    - Use LMWH as first line treatment.
    - If LMWH is contraindicated (except in renal impairment) use fondaparinux.
- Do not offer VTE prophylaxis to people in the last days of their life. [26]

7.1.5. Dosing fondaparinux thromboprophylaxis in medical patients

- In patients for whom porcine products are inappropriate, subcutaneous fondaparinux can be used (see Table 32 for dosing guidance). However:

- Patients with body weight <50 kg are at increased risk of bleeding as elimination of fondaparinux decreases with weight. Fondaparinux should be used with caution in these patients.
- There is insufficient evidence to make firm dosage recommendations for use of fondaparinux in morbidly obese patients (BMI > 40 kg/m^2).

Table 32: Dosing fondaparinux thromboprophylaxis

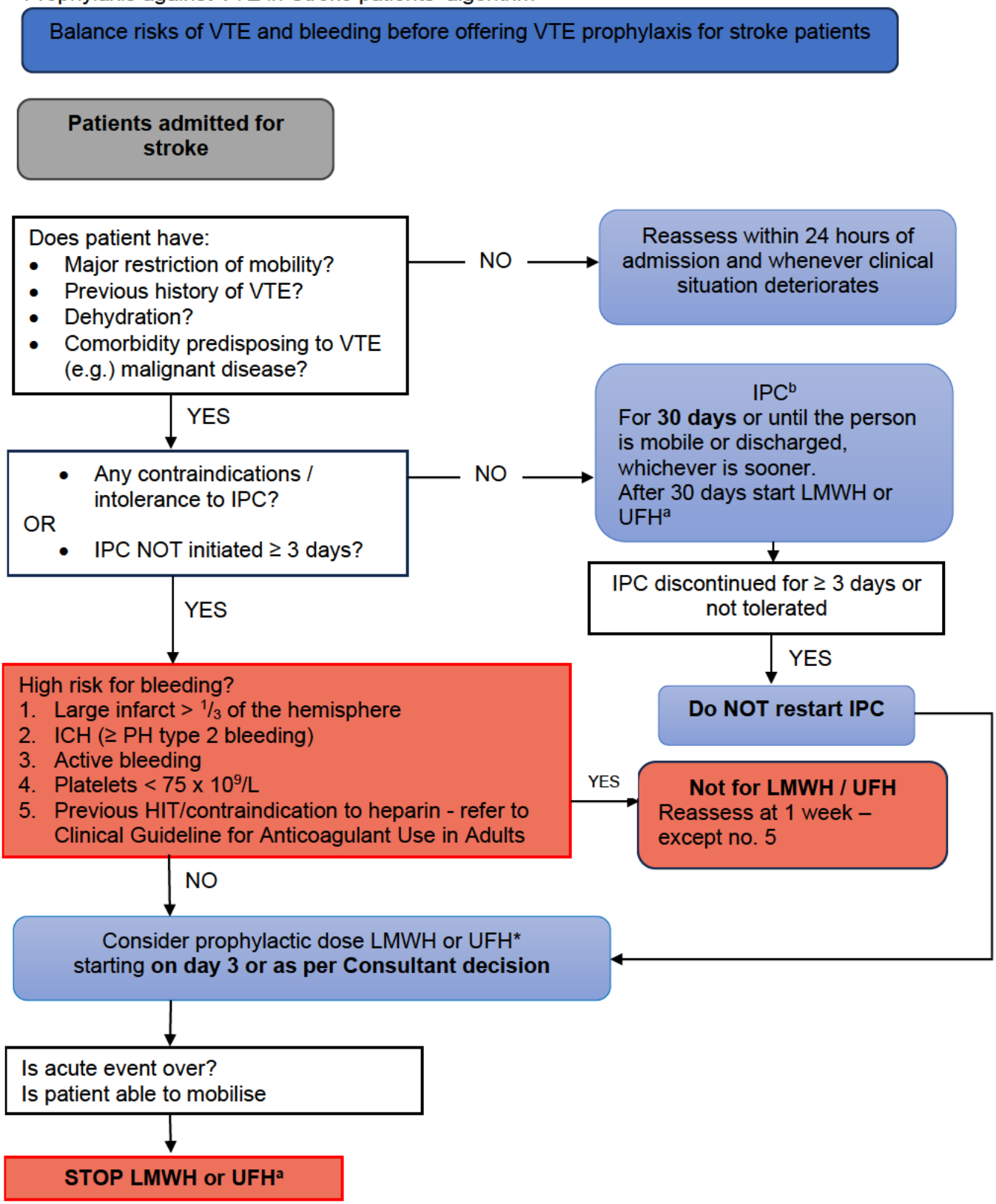
Creatinine clearance	**Fondaparinux dose for prophylaxis against VTE**
>50 mL/min	2.5 mg daily
20 - 50 mL/min	1.5mg daily
<20 mL/min	**Avoid**

7.1.6. Prophylaxis against VTE in Stroke patients

- Intermittent pneumatic compression (IPC) for VTE prophylaxis should be considered in immobile patients admitted with acute stroke and started **within 3 days** of acute stroke.
- Explain to the patient or family members / carers (as appropriate) that:
  - It reduces the risk of deep vein thrombosis and may provide an increase in survival.
  - It will not help them recover from stroke, and there may be an associated increased risk of surviving with severe disability.
- Intermittent pneumatic compression for patients who are admitted for stroke, should be provided for 30 days or until the patient is mobile or discharged, whichever is sooner.
- Patients admitted for stroke must NOT be given anti-embolism stockings for VTE prophylaxis.

- Enoxaparin or UFH (for patients with severe renal impairment or established renal failure) should only be considered if the following criteria are met – **see following flow-chart** for further guidance:
  - Diagnosis of haemorrhagic stroke has been excluded, AND
  - Risk of bleeding (haemorrhagic transformation of stroke or bleeding into another site) is assessed to be low, AND
  - Patient has >1 of:
    - Major restriction of mobility
    - Previous history of VTE
    - Dehydration
    - Comorbidities (such as malignant disease).
- Continue until the acute event is over and the patient's condition is stable.

Prophylaxis against VTE in Stroke patients' algorithm



[a]For patients with renal failure
[b]IPC initiated as soon as possible but **within 3 days** of acute stroke

Prophylaxis against VTE in surgical patients

7.1.7. General recommendations

- Advise patients to consider stopping oestrogen-containing oral contraceptives or hormone replacement therapy 4 weeks before elective surgery. If stopped, provide advice on alternative contraceptive methods.
- Assess the risks and benefits of stopping pre-existing established antiplatelet therapy 1 week before surgery. Refer to section 5.3 'Stopping anti-platelet therapy for planned and emergency surgery (Stopping antiplatelets for surgery) for more information.
- Do not routinely offer pharmacological or mechanical VTE prophylaxis to patients undergoing a surgical procedure with local anaesthesia by local infiltration with no limitation of mobility [26].

7.1.8. Specific surgical recommendations

- Consider extending pharmacological VTE prophylaxis to 28 days postoperatively for patients who have had major cancer surgery in the abdomen or pelvis.
- Do not offer pharmacological VTE prophylaxis to patients with ruptured cranial or spinal vascular malformations (for example, brain aneurysms) or acute traumatic or non-traumatic haemorrhage until the lesion has been secured or the condition is stable.
- Do not routinely offer VTE prophylaxis to patients undergoing upper limb surgery unless assessed to be at increased risk of VTE.
- Consider offering pharmacological VTE prophylaxis to patients with lower limb plaster casts after evaluating the risks and benefits based on clinical discussion with the patient. Offer LMWH (or UFH for patients with severe renal impairment or established renal failure) until lower limb plaster cast removal.

7.1.9. Dosing and duration of pharmacological thromboprophylaxis in orthopaedic surgery

- If pharmacological thromboprophylaxis is required, doses need to be adjusted according to weight and renal function.
- Table 33 provides general guidance regarding dosing and duration of treatment in orthopaedic surgery but please refer to specific orthopaedic recommendations.

Table 33: Thromboprophylaxis post-orthopaedic surgery

Treatment	**Post elective hip replacement**	**Post elective knee replacement**	**Post fragility fractures of pelvis, hip and proximal femur**
1st line	LMWH (enoxaparin) for 10 days followed by aspirin (75mg or 150mg) for a further 28 days OR LMWH (enoxaparin) for 28 days combined with anti-	Aspirin (75mg or 150mg) for 14 days OR LMWH (enoxaparin) for 14 days combined with anti-	LMWH (enoxaparin) OR Fondaparinux, providing there is a low risk of bleeding

	embolism stockings (until discharge) OR Rivaroxaban	embolism stockings (until discharge) OR Rivaroxaban	
2nd line if none of 1st line options can be used	Apixaban Or Dabigatran	Apixaban Or Dabigatran	N/A
3rd line if pharmacological interventions contraindicated	Anti-embolism stockings until discharge	Intermittent pneumatic compression (IPC) until person mobile	Intermittent pneumatic compression (IPC) until no longer has significantly reduced mobility relative to normal or anticipated mobility

Treatment	**Dose and starting time post-surgery**	**Duration post elective hip replacement**	**Duration post elective knee replacement**	**Duration post fragility fractures of pelvis, hip and proximal femur**
Enoxaparin **	Started 6 - 12 hours* post-surgery. **Avoid** in CrCl <15mL/min See Table 31 for dosing	28 days	14 days	1 month
Unfractionated heparin - in patients with severe renal impairment or established renal failure	Started 6 - 12 hours post-surgery. See Table 31 for dosing	28 days	14 days	1 month
Rivaroxaban	10mg OD started 6 - 10 hours post-surgery, provided haemostasis has been established. Use with **caution** in CrCl 15 - 29 mL/min. **Avoid** in CrCl < 15	35 days	14 days	N/A

	mL/min.			
Apixaban	2.5mg BD started 12 - 24 hours post-surgery. **Avoid** in CrCl < 15 mL/min.	32 – 38 days	10 - 14 days	N/A
Dabigatran	110mg stat started 1 - 4 hours post-surgery, then 220mg OD thereafter. **Reduce dose to 75mg stat** started 1 - 4 hours post-surgery, **then 150mg OD** thereafter in: a) CrCl 30-50 mL/min b) Concomitant verapamil, amiodarone, quinidine c) Age >75 **Avoid** in CrCl < 30 mL/min.	28 - 35 days	10 days	N/A
Fondaparinux sodium**	Started 6 hours after surgical closure provided haemostasis has been established. See Table 32 for dosing	Not recommended by NICE	Not recommended by NICE	1 month

* This recommendation is as per NICE rather than the product licence, which recommends starting enoxaparin pre-operatively [26].

** Consider pre-operative VTE prophylaxis for people with fragility fractures of the pelvis, hip or proximal femur if surgery is delayed beyond the day of admission. Give the last dose no less than 12 before surgery for LMWH or 24 hours before surgery for Fondaparinux sodium.

Additional Information

8.1. Duration of Oral Anticoagulation

- The duration of anticoagulation treatment varies depending on the treatment indication.

Table 34: Duration of anticoagulation treatment - VTE, bioprosthetic valves (including TAVI) and cardioversion
[3, 18, 28, 43-45, 62]

<table>
<tr><th>Diagnosis</th><th>Duration</th><th>Comments</th></tr>
<tr><td colspan="3">VTE: DVT/ PE</td></tr>
<tr><td>Isolated calf vein DVT*</td><td>6 weeks</td><td rowspan="4">* If treated with warfarin, consider bridging therapy if INR <1.7 during 1st month of an acute VTE

Consider stopping anticoagulation after 3 months if provoking factor is no longer present and the clinical course has been uncomplicated.

If stopping anticoagulation, give advice about risk of recurrence and provide:

• Written information on signs and symptoms to look out for

• Direct contact details of healthcare professional/team with whom can discuss new signs or symptoms, or concerns

• Information about out of hours services they can contact when healthcare team unavailable*</td></tr>
<tr><td>Proximal (involvement of popliteal vein or above) DVT &/or PE*</td><td>3 months (at least)</td></tr>
<tr><td>VTE provoked by surgery*</td><td>3 months</td></tr>
<tr><td>VTE with non-surgical recent (within 3 months) transient provoking risk factor

e.g. trauma, significant immobility (plaster cast, bedbound, unable to walk unaided or likely to spend a substantial proportion of the day in bed or in a chair), combined oral contraceptive pill or hormone replacement therapy, pregnancy or puerperium *</td><td>3 months</td></tr>
<tr><td>Unprovoked DVT or PE*</td><td>Minimum 3 months.</td><td rowspan="2">Consider continuing anticoagulation long term.

Base decision on predicted risk of recurrence (do not rely solely on predictive risk tools) and the risk of bleeding. Discuss risks and benefits of long-term anticoagulation with the patient and consider their preferences.

For patients with low bleeding risks - benefits of continuing anticoagulation are likely to outweigh risks.

Use ORBIT score to assess bleeding risk. Discuss stopping anticoagulation if ORBIT score ≥4 and cannot be modified.</td></tr>
<tr><td>Active cancer associated VTE*

Active cancer defined as: receiving active antimitotic treatment; or diagnosed within the past 6 months; or recurrent or metastatic, or</td><td>3 - 6 months.

Anti-coagulation therapy includes treatment with apixaban or rivaroxaban 1st line or LMWH or</td></tr>
</table>

inoperable. Excludes squamous skin cancer or basal cell carcinoma. *	warfarin 2nd line. See Table 36	When deciding on long term anticoagulant consider patient's preferences and clinical situation: • For patients **without** renal impairment, active cancer, established triple positive antiphospholipid syndrome or <50kg or >120kg: o Continue on current anticoagulant if well tolerated. o Consider switching to apixaban if current treatment not tolerated or clinical situation or person's preferences changed • For patients **with** renal impairment, active cancer, established triple positive antiphospholipid syndrome or <50kg or >120kg: o Continue on current anticoagulant if well tolerated. For people who decline continued anticoagulation treatment, consider aspirin 75mg or 150mg daily. Evidence shows aspirin reduces DVT/PE recurrence for up to 2 years but there is no difference in recurrence between aspirin and no treatment at 4 years. Review general health, risk of VTE recurrence, bleeding risks and treatment preferences at least annually for people on long term anticoagulation. If anticoagulation is stopped, consider testing for antiphospholipid antibodies. May need to restart anticoagulation if present.
Bioprosthetic heart valves (as directed by cardiothoracic unit)		
Bioprosthesis in mitral or tricuspid position – surgical implantation or repair	3 months	Treat with warfarin (INR target 2.5) [62]
Bioprosthesis in aortic position – surgical implantation or valve-sparing aortic surgery	3 months	Treat with low dose aspirin 75mg daily (Class IIa recommendation) or oral anticoagulation (Class IIb recommendation)
Bioprosthetic valve & history of systemic embolism	3 months (at least)	Treat with warfarin (INR target 2.5)

Bioprosthetic valve & left atrial thrombus at surgery	Until clot has resolved	Treat with warfarin (INR target 2.5) and/or UFH
TAVI	Lifelong single antiplatelet therapy where anti-coagulation not required for other reasons	
Cardioversion		
Cardioversion	Anticoagulate for at least 3 weeks prior to and 4 weeks post cardioversion. If warfarin rather than a DOAC is used, aim for a target INR of 2.5.	Although an INR target of 2.5 is recommended with warfarin, an INR target of 3.0 can be used prior to the procedure to minimize cancellations due to low INR.

8.2. Investigation of Venous Thromboembolic Events

Reference [3]

- **Investigations for cancer**
  - For patients with an **unprovoked DVT or PE** who are not already known to have a cancer, review the medical history and baseline blood test results including full blood count, renal and hepatic function, PT and APTT and review any findings found on physical examination.
  - Do not offer further investigations for cancer to people with unprovoked DVT or PE unless they have relevant clinical symptoms or signs.

- **Thrombophilia testing**
  - Do not offer testing for hereditary thrombophilia to people who are continuing anticoagulation treatment.
  - Do not offer thrombophilia testing to patients who have had a provoked DVT or PE.
  - Consider testing for antiphospholipid antibodies (anticardiolipin antibodies, and anti-beta 2-glycoprotein 1 antibodies) in patients who have had an unprovoked DVT or PE if it is planned to stop anticoagulant therapy or if there are clinical features of concern. Lupus anticoagulant testing is not possible on anticoagulated patients. Discuss with Consultant Haematologist for further information.
  - Consider testing for hereditary thrombophilia in patients who have had unprovoked DVT or PE and who have a first-degree relative with a history of unprovoked VTE if it is planned to stop anticoagulant therapy but be aware that these tests can be affected by anticoagulants. Discuss with Consultant Haematologist for further information. In this case, a positive result may change the perceived risks and benefits of ongoing anticoagulation.

- Do not routinely offer thrombophilia testing to first-degree relatives of people with a history of DVT or PE and thrombophilia.

8.3. Graduated compression stockings post DVT

- NICE does not recommend offering elastic graduated compression stockings to prevent post-thrombotic syndrome or VTE recurrence after a proximal DVT.
- Elastic stockings for the management of leg symptoms after DVT may be used. Information should be given on their application, use, duration and replacement.

8.4. Inferior Vena Cava Filters

Reference [3]

- Inferior vena cava (IVC) filters are inserted to prevent pulmonary embolus in patients with deep vein thrombosis.
- IVC filters may be indicated:
  - In patients with thrombosis who have a contraindication to anticoagulation
  - Selected patients with pulmonary emboli despite therapeutic anticoagulation – only after steps have been taken to resolve treatment failure, see Table 36, Treatment failure.
  - Surgical patients with recent thromboembolic disease (<12 weeks) in whom anticoagulation must be interrupted.
- The appropriateness of their use should be discussed with a Consultant Haematologist and Radiologist.
- Before fitting an IVC filter, ensure there is a strategy in place for it to be removed at the earliest opportunity. Document the strategy and review it if the clinical situation changes.
- Where anticoagulation can be restarted, remove the IVC filter when anticoagulation treatment has been **established**.

8.5. Mechanical thromboprophylaxis

Mechanical VTE prophylaxis is appropriate for patients for whom bleeding risk outweighs the risk of VTE [26]. Options include:

- Anti-embolic stockings
- Foot impulse devices
- Intermittent pneumatic compression devices

Note that anti-embolic stockings are not recommended in patients with:

- Suspected or proven peripheral arterial disease
- Peripheral arterial bypass grafting
- Peripheral neuropathy or other causes of sensory impairment
- Any local conditions in which stockings may cause damage, for example fragile 'tissue paper' skin, dermatitis, gangrene or recent skin graft
- Known allergy to material of manufacture
- Cardiac failure
- Severe leg oedema or pulmonary oedema from congestive heart failure
- Unusual leg size or shape
- Major limb deformity preventing correct fit
- Stroke - no significant reduction in DVT is seen but skin breaks, ulcers and skin necrosis are more common.

  Detailed guidance on the appropriate use of mechanical thromboprophylaxis is provided in the Venous Thromboembolism Diagnosis, Treatment and Prevention Policy and Procedure. Please refer to this policy for more information: 01152_P.pdf (esht.nhs.uk).

9. Summary: Which anticoagulant?

- Within these guidelines, extensive information has been given regarding the individual risks and benefits of the anti-coagulant drugs available.
- The following table summarises the recommended first choice anticoagulant according to clinical setting [3, 40-42, 46-61].

Table 35: Suggestions for choice of anticoagulant for atrial fibrillation

Indication	Anticoagulant	Pros	Cons
First line use for NVAF	Apixaban	**Apixaban** • Reversal agent andexanet alfa - recommended for life-threatening GI bleeding only • Good efficacy vs safety profile • Particularly suitable for low body weight patients • Good choice in renal impairment – least renally cleared (27%) • Suitable if CrCl ≥15ml/min • Suitable for blister packs	**Apixaban** • Twice daily dosing
NVAF after ischaemic stroke on apixaban	Dabigatran 150mg	• Good for high stroke risk with low bleeding risk	• Twice daily dosing • CrCl must be greater than 30mls/min • Unsuitable for ≥ 80 years • Must be swallowed whole • Unsuitable for most blister packs • Unsuitable for patients with GI bleeding risk or gastritis / indigestion
NVAF after bleeding on apixaban	Edoxaban 30mg	• Once daily dosing • Good for high bleeding risk and low stroke risk • Less indigestion side effects than rivaroxaban	• Efficacy worse than warfarin • No reversal agent

Indication	Anticoagulant	Pros	Cons
		• Suitable for low body weight patients (weight ≤ 60 kg) • Suitable if CrCl is in the range 15 – 50 ml/min • Suitable for blister packs	
NVAF for patient requiring once daily dosing	Edoxaban 30mg /60mg Or Rivaroxaban 15mg/20mg	• Once daily dosing • Edoxaban less likely to cause indigestion side effects than rivaroxaban • Rivaroxaban remains efficacious with increased CrCl >95mls/min • Rivaroxaban has a reversal agent – andexanet alfa – recommended for life-threatening GI bleeding only • Both edoxaban and rivaroxaban suitable for blister packs	• Reversal agent not available for Edoxaban • Edoxaban 60mg most suitable if CrCl is between 50-95 ml/min. Trend towards decreasing efficacy with increasing CrCl >95 ml/min • Rivaroxaban more likely to cause indigestion side effects
NVAF with previous haemorrhagic stroke	Dabigatran 110mg	• Low ICH bleeding risk so good for patients with poor HTN control, previous haemorrhagic stroke, cerebral micro-haemorrhages or amyloid • In patients > 75 years the benefits of dabigatran over apixaban and edoxaban 30mg is lost	• Twice daily dosing • CrCl must be greater than 30mls/min • Must be swallowed whole • Unsuitable for most blister packs • May cause GI side effects
AF with renal impairment - CrCl <15mls/min	Warfarin	• Once daily dosing • Metabolised in the liver. Minimal renal excretion	• Requires monitoring • Unsuitable for blister packs
AF with concomitant epilepsy being treated with carbamazepine, phenytoin or	Warfarin	• Dose can be adjusted for CYP1A2, CYP3A4 and CYP2C9 enzyme inducer effects. • Note: Phenytoin can initially cause a transient	

Indication	Anticoagulant	Pros	Cons
phenobarbital		**increase** in anticoagulant effect following displacement of warfarin by phenytoin from protein binding sites. Subsequent CYP2C9 enzyme induction reduces the anticoagulant effect of warfarin.	
AF with concomitant antiphospholipid syndrome	Warfarin	• Anticoagulant of choice in antiphospholipid syndrome	
AF with concomitant metal heart valve	Warfarin	• Only oral anticoagulant that can be used in prosthetic heart valves	
AF and on HIV protease inhibitors e.g. Ritonavir	Warfarin	• Dose can be adjusted for CYP2C9, CYP1A2, CYP2C19 and CYP3A4 activity.	

Abbreviations: EHRA –European Heart Rhythm Association; ESC – European Society of Cardiology; DOAC – direct oral anticoagulant; HTN – hypertension; ICH – intra-cerebral haemorrhage; GI – gastro-intestinal CrCl – Creatinine clearance NVAF – non-valvular atrial fibrillation

Table 36: Suggestions for choice of anticoagulant for acute VTE treatment

Characteristic	Drug choice	Rationale / comment
Access issues		
Limited access to anticoagulation clinic because of impaired mobility or geographical inaccessibility	DOAC	Given in fixed doses without monitoring.
Acute coronary syndrome (recent)		
Recent acute coronary syndrome	Rivaroxaban Apixaban Edoxaban Warfarin	Small risk of myocardial infarction with dabigatran.
Antiphospholipid syndrome		
Triple positive	Warfarin with LMWH bridging	

antiphospholipid syndrome	for at least 5 days or until INR ≥ 2.0 for 2 consecutive readings	
Bleeding		
High initial risk of bleeding	UFH infusion	Enables dose titration; rapid offset and availability of protamine as an antidote simplify management should bleeding occur.
Recent gastrointestinal bleed	Apixaban Warfarin	More gastrointestinal bleeding with dabigatran, rivaroxaban, and edoxaban.
Cancer		
Active cancer Defined as receiving active antimitotic treatment; or diagnosed within the past 6 months; or recurrent or metastatic; or inoperable. Excludes squamous skin cancer or basal cell carcinoma.	1st line consider a DOAC: Apixaban Rivaroxaban Edoxaban 2nd line consider: LMWH or Warfarin with LMWH bridging for at least 5 days or until INR ≥ 2.0 for 2 consecutive readings	When choosing anticoagulation treatment consider tumour site, drug interactions including cancer treatment drugs and bleeding risk. Less bleeding than LMWH Caution GI malignancies. More bleeding than LMWH Where apixaban or rivaroxaban unsuitable Particularly useful if vomiting, have reduced oral intake or poor appetite. May be preferable in patients with gastrointestinal or genitourinary cancers. Indicated where DOACs are unsuitable but oral treatment preferred long term. Less clinically effective than LMWH.
Cancer in remission	As per DVT / PE without other factors	
Compliance		
Poor compliance with long-term twice daily dosing	Rivaroxaban Edoxaban Warfarin	OD regimens for long-term use.
Dyspepsia / Upper GI symptoms		
Dyspepsia or upper	Apixaban	Dyspepsia / abdominal pain is common (≥ 1/100 to <1/10) in patients given

gastrointestinal symptoms	Warfarin	dabigatran, edoxaban or rivaroxaban.
DVT / PE without other factors		
Proximal DVT or PE	Apixaban or Rivaroxaban	Causes fewest bleeds If neither suitable offer: • LMWH for at least 5 days followed by dabigatran or edoxaban or • LMWH with warfarin for at least 5 days or until INR is ≥2.0 in 2 consecutive readings followed by warfarin on its own.
Extensive DVT or massive PE	Heparin Warfarin	Such patients were excluded from trials with the DOACs.
Extremes of body weight		
Weight <50kg or >120kg/ BMI>40 kg/m^2	Warfarin Or Rivaroxaban 2nd line Apixaban	Such patients require regular monitoring of therapeutic levels to ensure effective anticoagulation. For obese patients >120kg/ BMI>40 kg/m^2: • Rivaroxaban can be used at standard doses regardless of high BMI and weight. • Apixaban = alternative to rivaroxaban; however less supportive data. • For rivaroxaban & apixaban there is a paucity of data at weight > 150kg and BMI > 50 kg/m^2. • Do NOT measure peak or trough levels - insufficient data to influence management decisions. • Do NOT use dabigatran (unconvincing data) or edoxaban (lack of PK/PD data. • (Extrapolation of this guidance in AF is less certain). In patients who are < 50kg, discuss anticoagulation options with Haematology. DOACs, in particular, dose adjusted rivaroxaban and edoxaban can be considered.
Liver dysfunction		
Liver dysfunction with increased prothrombin time/ INR at baseline	LMWH (Warfarin*)	DOACs contraindicated if INR raised because of liver disease (such patients were excluded from the trials because DOACs undergo hepatic metabolism).

		(*VKA difficult to control and INR may not reflect antithrombotic effect.)
Oral therapy only		
All-oral therapy	Rivaroxaban Apixaban	VKA, dabigatran, and edoxaban require initial parenteral therapy.
PE & haemodynamic instability		
PE & haemodynamic instability	UFH	Consider thrombolytic therapy.
Pregnancy		
Pregnancy	LMWH	Warfarin and DOACs cross the placenta.
Renal impairment		
Creatinine clearance 30 - 50 mL/min	Apixaban Rivaroxaban LMWH for ≥ 5 days then edoxaban Warfarin	Less affected by renal impairment than dabigatran; use renal doses as appropriate.
Creatinine clearance 15 - 29 mL/min	Warfarin LMWH Caution: Apixaban LMWH for ≥ 5 days then edoxaban Rivaroxaban	Dabigatran contraindicated with severe renal impairment.
Creatinine clearance < 15 mL/min	UFH Warfarin	DOACs contraindicated with severe renal impairment LMWH – increased risk of bleeding. Consider UFH.
Treatment failure*		
Treatment failure		• Check adherence • Address other sources of hypercoagulability • Increase dose of anticoagulant OR • Change to an anticoagulant with

		a different **mode** of action
Venous access difficulty		
Venous access or monitoring difficulties e.g. patients with certain impairments and intravenous drug users	LMWH DOACs	

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11. Monitoring Compliance with the Document Monitoring Table

Element to be Monitored	Lead	Tool for Monitoring	Frequency	Responsible Individual/Group/ Committee for review of results/report	Responsible individual/ group/ committee for acting on recommendations/action plan	Responsible individual/group/ committee for ensuring action plan/lessons learnt are Implemented
Guidance document content	Dr Richard Grace	Review	Every 3 years	Dr Richard Grace	Document Authors	Document Authors
Incidence Occurring	Jane Starr (MSO)	Regular review of incidents	Monthly	Medicines Safety Group	Medicines Safety Group	Medicines Safety Group

Appendix A - EHRA Form

A Due Regard, Equality & Human Rights Analysis form must be completed for all procedural documents used by East Sussex Healthcare NHS Trust. Guidance for the form can be found here on the Equality and Diversity Extranet page.

Due Regard, Equality & Human Rights Analysis

Title of document: Clinical Guideline for Anticoagulation Use in Adults
Who will be affected by this work? Staff and patients
Please include a brief summary of intended outcome: This guidance is designed to provide support for staff in the safe prescribing, administration and monitoring of anticoagulants and management of adverse effects to minimise risk and optimise patient safety.

		Yes/No	Comments, Evidence & Link to main content
1.	**Does the work affect one group less or more favourably than another on the basis of:** (Ensure you comment on any affected characteristic and link to main policy with page/paragraph number)		
	• Age	No	This guidance is for adults only.
	• Disability (including carers)	No	
	• Race	No	
	• Religion & Belief	No	LMWH and UFH are porcine derived which may be incompatible with some patients' religious or other beliefs (e.g. vegetarianism or veganism). **See section 6.1, page 63**. Prothrombin complex concentrate is a blood product which may be incompatible with some patients' religious or other beliefs. **See section 5.2.1.3, page 56.**
	• Gender	No	
	• Sexual Orientation (LGBT)	No	
	• Pregnancy & Maternity	No	Warfarin and DOACs cross the placenta and so need to be avoided in pregnancy. DOACs further need to be avoided in breast feeding **See section 4.1.2, page 17; section 4.2.3, page 28; section 4.2.7 page 48; section 6.0, page 62; section 9, page 88.** LMWH or UFH can be used in these circumstances however

			dosing needs adjusting in these patients. This is addressed in a separate guideline - Clinical Guideline for Thromboprophylaxis and Treatment of Venous Thromboembolism in Maternity. **See section 6, page 62.**
	• Marriage & Civil Partnership	No	
	• Gender Reassignment	No	
	• Other Identified Groups	No	
2.	**Is there any evidence that some groups are affected differently and what is/are the evidence source(s)?**		Age: Older patients are at higher risk of bleeding when prescribed anticoagulants and doses used often need to be reduced. This policy ensures that patients are treated with age-appropriate doses and age is taken into consideration when assessing bleeding risk. **See Table 2, page 21; Table 5, page 28; Table 8, page 38; Table 14, page 43; Table 27, page 66.** Disability: Patients with learning difficulties, those that are unable to communicate verbally and those with hearing/sensory impairment will need communication to be delivered in a way that is understandable to them. **See Appendix C, section 7, page 107.** Pregnancy and breastfeeding: Warfarin and DOACs cross the placenta and are contraindicated in pregnancy. feeding **See section 4.1.2, page 17; section 4.2.3, page 28; section 4.2.7 page 48; section 6.0, page 62; section 9, page 88.** LMWH or UFH can be used in these circumstances however dosing needs adjusting in these patients. This is addressed in a separate guideline - Clinical Guideline for Thromboprophylaxis and Treatment of Venous Thromboembolism in Maternity. **See section 6,**

			page 62. Race: where language barriers are seen to be a factor which prevents comprehension of the information being provided, staff should be mindful of this and offer appropriate translation, interpreting and re-formatting of information as per Trust Policy. **See section 4.1.8, page 22; section 4.2.7, page 48; Appendix C, section 7, page 108.**
3.	**What are the impacts and alternatives of implementing / not implementing the work / policy?**	Anticoagulants are considered high risk drugs that are associated with significant bleeding risks. If inappropriately prescribed, administered or monitored, anticoagulants can result in patient death. Application of this guidance ensures the safe prescribing, administration and monitoring of anticoagulants and management of adverse effects to minimise risk and optimise patient safety.	
4.	**Please evidence how this work / policy seeks to "eliminate unlawful discrimination, harassment and victimisation" as per the Equality Act 2010?**	Age: Older patients are at higher risk of bleeding when prescribed anticoagulants and doses used often need to be reduced. This policy ensures that patients are treated with age-appropriate doses. **See Table 2, page 21; Table 5, page 28; Table 8, page 38; Table 14, page 43; Table 27, page 66.** Disability: Patients with learning difficulties, those that are unable to communicate verbally and those with hearing/sensory impairment will need communication to be delivered in a way that is understandable to them. **See Appendix C, section 7, page 107.** Pregnancy and breastfeeding: Warfarin and DOACs cross the placenta and are contraindicated in pregnancy. **See section 4.1.2, page 17; section 4.2.3, page 28; section 4.2.7 page 48; section 6.0, page 62; section 9, page 88.** LMWH or UFH can be used in these circumstances however dosing needs adjusting in these patients. This is addressed in a separate guideline - Clinical Guideline for Thromboprophylaxis and Treatment of Venous Thromboembolism in Maternity. **See section 6, page 62.**	

		Race: where language barriers are seen to be a factor which prevents comprehension of the information being provided, staff should be mindful of this and offer appropriate translation, interpreting and re-formatting of information as per Trust Policy. **See section 4.1.8, page 22; section 4.2.7, page 48; Appendix C, section 7, page 108.**
5.	**Please evidence how this work / policy seeks to "advance equality of opportunity between people sharing a protected characteristic and those who do not" as per the Equality Act 2010?**	Age: Older patients are at higher risk of bleeding when prescribed anticoagulants and doses used often need to be reduced. This policy ensures that patients are treated with age-appropriate doses. **See Table 2, page 21; Table 5, page 28; Table 8, page 38; Table 14, page 43; Table 27, page 66.** Disability: Patients with learning difficulties, those that are unable to communicate verbally and those with hearing/sensory impairment will need communication to be delivered in a way that is understandable to them. **See Appendix C, section 7, page 107.** Pregnancy and breastfeeding: Warfarin and DOACs cross the placenta and are contraindicated in pregnancy. **See section 4.1.2, page 17; section 4.2.3, page 28; section 4.2.7 page 48; section 6.0, page 62; section 9, page 88.** LMWH or UFH can be used in these circumstances however dosing needs adjusting in these patients. This is addressed in a separate guideline - Clinical Guideline for Thromboprophylaxis and Treatment of Venous Thromboembolism in Maternity. **See section 6, page 62.** Race: where language barriers are seen to be a factor which prevents comprehension of the information being provided, staff should be mindful of this and offer appropriate translation, interpreting and re-formatting of information as per Trust Policy. **See section 4.1.8, page 22; section 4.2.7, page 48; Appendix C, section 7, page 108.**
6.	**Please evidence how this work / policy will "Foster good relations between people sharing a protected**	Age: Older patients are at higher risk of bleeding when prescribed anticoagulants and doses used often need to be

	characteristic and those who do not" as per the Equality Act 2010?	reduced. This policy ensures that patients are treated with age-appropriate doses. **See Table 2, page 21; Table 5, page 28; Table 8, page 38; Table 14, page 43; Table 27, page 66.** Disability: Patients with learning difficulties, those that are unable to communicate verbally and those with hearing/sensory impairment will need communication to be delivered in a way that is understandable to them. **See Appendix C, section 7, page 107.** Pregnancy and breastfeeding: Warfarin and DOACs cross the placenta and are contraindicated in pregnancy. **See section 4.1.2, page 17; section 4.2.3, page 28; section 4.2.7 page 48; section 6.0, page 62; section 9, page 88.** LMWH or UFH can be used in these circumstances however dosing needs adjusting in these patients. This is addressed in a separate guideline - Clinical Guideline for Thromboprophylaxis and Treatment of Venous Thromboembolism in Maternity. **See section 6, page 62.** Race: where language barriers are seen to be a factor which prevents comprehension of the information being provided, staff should be mindful of this and offer appropriate translation, interpreting and re-formatting of information as per Trust Policy. **See section 4.1.8, page 22; section 4.2.7, page 48; Appendix C, section 7, page 108.**
7.	**Has the policy/guidance been assessed in terms of Human Rights to ensure service users, carers and staff are treated in line with the FREDA principles (fairness, respect, equality, dignity and autonomy)**	Information has been provided to allow provision of information to patients with protected characteristics.
8.	**Please evidence how have you engaged stakeholders with an interest in protected characteristics in gathering evidence or testing the evidence available?**	See Consultation table, page 3.
9.	**Have you have identified any negative impacts or inequalities on any protected characteristic and others? (Please attach evidence and plan of action ensure this negative impact / inequality is being monitored and addressed).**	None have been identified.

Appendix B - Drug information sheets

B1 Warfarin

For prophylaxis of systemic embolism in patients with rheumatic heart disease and AF; prophylaxis after insertion of prosthetic heart valves; prophylaxis and treatment of venous thrombosis and pulmonary embolism; TIAs.

To satisfy NICE in AF, document /complete the following:
Patient chose warfarin following a risk/benefit discussion of anticoagulation options (including no treatment)
CHA_2DS_2-VASc ≥2 or CHA_2DS_2-VASc ≥1 in men & ORBIT* score calculated
ABC - Alert Card, Yellow Book (Anticoagulation Information Pack) & Counselling have been completed/provided (for new patients complete Appendix E – VKA Discharge Advice Form & contact ward Pharmacist at earliest opportunity to arrange the above)

*** ORBIT** ORBIT Bleeding Risk Score for Atrial Fibrillation (mdcalc.com)

On discharge: Ensure warfarin discharge dose & date INR next due are written in both the Yellow Book and on the VKA Discharge Advice Form (Appendix E), & patient is clear on both. Request GP to arrange an URGENT INR by INR due date on the e-Discharge letter & complete the 'Anticoagulation' section of the e-Discharge letter.

Contraindications: hypersensitivity to warfarin or excipients; haemorrhagic stroke; clinically significant bleeding; ≤ 72 hours of major surgery with risk of severe bleeding; ≤ 48 hours postpartum; pregnancy; interacting drugs that ↑ risk of bleeding.

Caution: bacterial endocarditis; previous GI bleeding; active peptic ulcers; uncontrolled hypertension (systolic >200mmHg or diastolic >120mmHg); recent ischaemic stroke (hold for 14 days if large embolic stroke or uncontrolled HTN); recent surgery; concomitant NSAID; poor adherence; **lactose intolerance** (tablets).

Bleeding risk with Warfarin versus NOACs		
Major bleeding	**GI bleeding**	**Intracranial bleeding**
Warfarin ≡ dabigatran 150mg & rivaroxaban. Major bleeding less common with dabigatran 110mg, apixaban & edoxaban than warfarin.	**GI bleeding more common with dabigatran 150mg, rivaroxaban & edoxaban. Warfarin ≡ dabigatran 110mg & apixaban.**	**More common with warfarin.**

Dose: Dose is determined by INR. Target INR is 2.5 for most indications but higher (3.5) for recurrent VTE despite an INR ≥2. In mechanical prosthetic heart valves, target INR depends on prosthesis thrombogenicity and patient risk factors – refer to Table 1 in the Clinical Guideline for Anticoagulant Use for more information.

Warfarin initiation: Anticoagulant effect takes 48 – 72 hours to fully develop. See chart below for loading guidance. Prescribe concomitant enoxaparin or UFH for at least 5 days (unless INR >3) & until INR is ≥2 for at least 24 hours for patients with acute thrombosis (e.g. DVT or PE). Outpatients with AF can be slow loaded with 1-2mg to achieve their target INR in 3-4 weeks.

Dosing protocol for the initiation of warfarin to achieve a target INR of 2.5 – before starting read notes a) & b)

Day 1 Loading			**Day 2 Loading**			**Day 3 Loading**			**Day 4 Predicted maintenance**		
INR (i.e. pre-treatment)	Standard loading	*** Low dose loading**	INR	Standard loading	*** Low dose loading**	INR	Standard loading	***Low dose loading**	INR	Standard loading	***Low dose loading**
<1.4	10mg	**5mg**	<1.8	10mg	**5mg**	<2.0	10mg	**5mg**	<1.4	10mg	**5mg**
a) *Use low dose loading for high risk patients with likely increased sensitivity to warfarin/increased risk of bleeding: e.g. > 65 years old, body weight <50kg, poor nutritional status, low serum albumin (<30g/l), liver or kidney disease, heart failure, thyrotoxicosis &/or on interacting drugs			1.8	1mg	**1mg**	2.0 - 2.5	4mg	**2mg**	1.4	8mg	**4mg**
			>1.8	0.5mg	**0.5mg**	2.6 - 3.0	3mg	**2mg**	1.5 - 1.7	7mg	**4mg**
			b) Patients with **protein C deficiency** (& possibly protein S deficiency) are at risk of developing skin necrosis when starting warfarin – initiate without a loading dose even if heparin is given			3.1 - 3.4	2mg	**1mg**	1.8 - 2.0	6mg	**3mg**
						3.5 - 4.0	1mg	**1mg**	2.1 - 2.6	5mg	**3mg**
						>4.0	Nil	**Nil**	2.7 - 3.0	4mg	**2mg**
									3.1 - 3.5	3mg	**2mg**
									3.6 - 4.0	2mg	**1mg**
									>4.0	Omit & recheck following day	

Maintenance dose adjustments: ↑or ↓ dose by 15% expect ↑or ↓in INR by 1.0; ↑or ↓ dose by 10% expect ↑or ↓ in INR by 0.7-0.8.
Administration: Must be taken at the same time each day. **Tablets contain lactose**; 1mg/ml oral suspension is lactose free. Tablets can be crushed & mixed with water & administered via gastric tube or the suspension can be used. **Some enteral feeds contain vitamin K which will antagonise the effect of warfarin**. Tablets should NOT be put into monitored dosage systems (blister packs).
Reversal: Can be reversed with vitamin K or PCC (Beriplex®) depending on INR & degree of bleeding – refer to Over-anticoagulation and bleeding.

Warfarin interactions – those in bold have moderate effect, bold & underlined have moderate - severe effect			
Likely to ↑INR & ↑ risk of bleeding. May need to ↓ warfarin dose - monitor closely	**May ↓INR, ↓ efficacy & require ↑ warfarin dose**	**No change in INR but ↑risk of bleeding**	**Contain ++ vitamin K & likely to ↓ INR**
Alcohol (binge drinking); allopurinol; **amiodarone**; **antibiotics**: cephalosporins (NOT cephalexin), **co-trimoxazole**, **isoniazid**, **macrolides (e.g. azithromycin, clarithromycin)**, **metronidazole**, **quinolones** (e.g. ciprofloxacin, **ofloxacin)**, **tetracyclines (e.g. doxycycline)**; **azole antifungals (e.g. ketoconazole, fluconazole)**; **capecitabine**; **corticosteroids** (high dose); **cranberry juice**; **disulfiram**; **erlotinib**; **fibrates**; grapefruit juice; **lactulose**; **levothyroxine**; methylphenidate; **paracetamol** (prolonged regular use); PPIs e.g. omeprazole; **propafenone**; **quetiapine**; **ropinirole**; **statins** (NOT pravastatin or atorvastatin); stopping smoking; **tamoxifen**, **tramadol**; **zafirlukast** (NOT montelukast).	**Alcohol** (chronic); **azathioprine**; **bosentan**; **carbamazepine**; corticosteroids; griseofulvin; oral contraceptives; **phenobarbital**, **phenytoin** (initially transient ↑ in INR, then ↓in INR with long term use); **primidone**; **rifampicin**; **St John's Wort – avoid**.	**Thrombolytic agents - avoid concomitant use.** **Anticoagulants e.g. NOACs - avoid concomitant use (except switching).** Aspirin or other antiplatelet agents/NSAIDs - where possible avoid concomitant use. SSRI (e.g. citalopram) and SNRI antidepressants (e.g. duloxetine, venlafaxine) - use with caution.	Some enteral feeds. Liver, broccoli, Brussels sprouts, green leafy vegetables, chick peas, egg yolks, cereals containing wheat bran & oats, mature cheese, blue cheese, avocado, olive oil - *eat small portions if occasional intake, otherwise eat regularly to achieve steady INR levels.*

For full prescribing information see warfarin at www.medicines.org.uk

Iwona Ward & Dr Richard Grace East Sussex NHS Trust. October 2020 (Version 2). Revision date October 2023.

B2 Dabigatran

For treatment of DVT & PE and prevention of recurrent DVT & PE in adults – following at least 5 days of treatment with a parenteral anticoagulant

For prevention of stroke and systemic emboli in adults with non-valvular atrial fibrillation (NVAF) & ≥1 of: previous stroke, TIA or systemic embolism; LV ejection fraction <40%; symptomatic heart failure (NYHA Class ≥ II); ≥75 years; ≥ 65years & one of diabetes, coronary artery disease or HTN

To satisfy NICE in NVAF, document/complete the following:
Patient chose dabigatran following a risk/benefit discussion of anticoagulation options (including no treatment)
CHA_2DS_2-VASc ≥2 or CHA_2DS_2-VASc ≥ 1 in men & **HAS-BLED*** score calculated
ABC - Alert Card, dabigatran Book & Counselling have been completed /provided - **arrange with ward Pharmacist/Pharmacy technician**

* **ORBIT**– 1 point for each of **H**ypertension, **A**bnormal renal & liver function (1 point each), **S**troke, **B**leeding, **L**abile INR, **E**lderly (>65 years), **D**rugs or alcohol (1 point each). **Score ≥3 = high risk: caution regarding use & needs regular review**

On discharge: Complete the 'Anticoagulation' section of the e-Discharge letter.

Contraindications: CrCl <30mL/min; active clinically significant bleeding; lesion or condition considered a significant risk factor for bleeding; concomitant treatment with any other anticoagulant except when switching anticoagulant therapy or with UFH to maintain an open central venous or arterial catheter; hepatic impairment or liver disease expected to have an impact on survival; concomitant treatment with systemic ketoconazole, ciclosporin, itraconazole and **dronedarone**; prosthetic heart valves requiring anticoagulant treatment.
Avoid: In history of poor medication adherence; pregnancy & breastfeeding.

Bleeding risk with Dabigatran versus Warfarin		
Major bleeding	**GI bleeding**	**Intracranial bleeding**
Less common with dabigatran 110mg **Dabigatran 150mg ≡ warfarin**	**More common with dabigatran 150mg** **Dabigatran 110mg ≡ warfarin**	**More common with warfarin**

For VTE treatment (after 5 days parenteral anticoagulant treatment) & VTE prevention. For NVAF	Recommended dose	Comments
Adults 18-79 years	150mg bd	**Reduce dose to 110mg bd if on concomitant verapamil.** Consider 110mg bd after individual assessment of thromboembolic and bleeding risks if: 75-79 years; moderate renal impairment (CrCl 30-50mL/min); gastritis, oesophagitis or gastrointestinal reflux; high bleeding/ increased bleeding risk.
Adults ≥ 80 years	110mg bd	
In reduced renal function dose as below:		
CrCl > 50mL/minute	150mg bd	Consider 110mg bd if high bleeding/increased bleeding risk and/or gastritis, oesophagitis or gastro-intestinal reflux (particularly if CrCl <50mL/min and/or body weight <50kg)
CrCl 30-50mL/minute	150mg bd	
CrCl < 30mL/minute	**Do not use**	
Hepatic impairment	**Do not use**	If LFT> 2xULN : do not use

To calculate creatinine clearance (CrCl): $\frac{(140 - \text{age}) \times \text{weight (kg)} \times \text{Constant (C)}}{\text{Serum creatinine (micromol/L)}}$ **C = 1.23 men; 1.04 women**

Renal function: Check before starting treatment and at least annually. Check more frequently if suspect renal function could deteriorate acutely or chronically.
Administration: Capsules must be **swallowed whole**, with or without food. Opening capsules may increase bleeding risk. Dabigatran must be stored in the original container and **cannot** be put into monitored dosage systems (e.g. blister packs, etc.) **If concomitant verapamil or amiodarone is prescribed, dose at the same time.**
Reversal: A reversal agent - idarucizumab (Praxbind®) is available at the Trust. Refer to Dabigatran haemorrhage protocol & Idarucizumab protocol
Interactions: Refer to the tables below:
Table5: DOAC general drug interactions
Table6: DOAC interactions with antiepileptic drugs
Table7: DOAC drug interactions with anticancer drugs

For full prescribing information see dabigatran at www.medicines.org.uk

B3 Rivaroxaban

For treatment of DVT, treatment of PE and prevention of recurrent DVT and PE

For prevention of stroke and systemic emboli in adults with non-valvular atrial fibrillation (NVAF) & ≥ 1 of CHF; HTN; ≥75 years; diabetes mellitus; prior stroke or TIA

To satisfy NICE in NVAF, document/complete the following:
Patient chose rivaroxaban following a risk/benefit discussion of anticoagulation options (including no treatment)
CHA_2DS_2-VASc ≥2 or CHA_2DS_2-VASc ≥ 1 in men & **HAS-BLED*** score calculated
ABC - Alert Card, rivaroxaban Book & Counselling have been completed/provided **- arrange with ward Pharmacist/Pharmacy technician**

*** ORBIT** – 1 point for each of **H**ypertension, **A**bnormal renal & liver function (1 point each), **S**troke, **B**leeding, **L**abile INR, **E**lderly (>65 years), **D**rugs or alcohol (1 point each). **Score ≥3 = high risk: caution regarding use & needs regular review**

On discharge: Complete the 'Anticoagulation' section of the e-Discharge letter.

Contraindications: Hypersensitivity to active substance or excipients (including lactose); active clinically significant bleeding; lesion or condition considered a significant risk for major bleeding; other concomitant anticoagulants except when switching anticoagulant therapy or with UFH to maintain an open central venous or arterial catheter; hepatic disease associated with coagulopathy and clinically relevant bleeding risk including cirrhotic patients with Child Pugh B and C; pregnancy and breast feeding.
Avoid: In history of poor medication adherence; prosthetic heart valve; CrCl <15ml/min; **lactose intolerance**.

Bleeding risk with Rivaroxaban versus Warfarin		
Major bleeding	**GI bleeding**	**Intracranial bleeding**
Rivaroxaban ≡ warfarin	**More common with rivaroxaban**	**More common with warfarin**

For NVAF	Dose	Comments
CrCl **≥50ml/minute**	20mg od	With food
CrCl **30-49ml/minute**	15mg od	With food
CrCl **15-29ml/minute**	15mg od	Limited trial data: **caution** - increased blood levels and bleeding risk. With food
CrCl **<15ml/minute**	**Do not use**	
Hepatic impairment associated with coagulopathy	**Do not use**	

DVT & PE treatment & prevention	Recommended dose	Comments
Initial treatment of acute DVT or PE (Days 1-21)	15mg **bd** for **3 weeks** followed by 20mg od thereafter (see below)	With food. No dose reduction in renal impairment **If a dose is missed during initial 21-day phase**: take immediately to ensure dose = 30mg/day - in this case **2 x 15mg may be taken together**
Day 22 onwards (including patients switched from alternative anticoagulation >21 days after acute event)	20mg od	With food. Consider 15mg od if bleeding risk outweighs risk of recurrent DVT or PE. If dose is missed during once daily treatment phase **do not double up dose** to catch up dosing
Prevention of **recurrent** DVT and PE	Following completion of at least 6 months therapy of DVT or PE	10mg od – with or **without food**. Consider 20mg od (with food) where risk of recurrent VTE is high, e.g. complicated co-morbidities or DVT/PE with 10mg od.
CrCl <30ml/min CrCl <15ml/minute	Use with caution **Do not use**	Limited data; increased levels and bleeding risk. Consider 15mg od from day 22.
Hepatic impairment: associated with coagulopathy	Do not use	

No dose adjustment is required for age or body weight

To calculate creatinine clearance (CrCl): $\frac{(140 - \text{age}) \times \text{weight (kg)} \times \text{Constant (C)}}{\text{Serum creatinine (micromol/L)}}$ **C = 1.23 men; 1.04 women**

Administration: **Must be taken with food**. Can be put into a blister pack. Tablets may be crushed & mixed with water or apple puree immediately before administration. Can be administered via NG, followed by enteral feeding.
Interactions: Refer to the tables below:
Table5: DOAC general drug interactions
Table6: DOAC interactions with antiepileptic drugs
Table7: DOAC drug interactions with anticancer drugs

For full prescribing information see rivaroxaban at www.medicines.org.uk

B4 Apixaban

For treatment of DVT & PE and prevention of recurrent DVT & PE in adults

Prevention of stroke and systemic emboli in adults with non-valvular atrial fibrillation (NVAF) & ≥ 1 of: prior stroke or TIA; age ≥75 years; HTN; diabetes mellitus, symptomatic heart failure NYHA Class ≥ II

To satisfy NICE in NVAF, document/complete the following:
Patient chose apixaban following a risk/benefit discussion of anticoagulation options (including no treatment)
CHA_2DS_2-VASc ≥2 or CHA_2DS_2-VASc ≥ 1 in men & **HAS-BLED*** score calculated
ABC - Alert Card, apixaban Book & Counselling have been completed/provided - **arrange with ward Pharmacist/Pharmacy technician**

* **ORBIT** – 1 point for each of **H**ypertension, **A**bnormal renal & liver function (1 point each), **S**troke, **B**leeding, **L**abile INR, **E**lderly (>65 years), **D**rugs or alcohol (1 point each). **Score ≥3 = high risk: caution regarding use & needs regular review**

On discharge: Complete the 'Anticoagulation' section of the e-Discharge letter.

Contraindications: Hypersensitivity to active substance or excipients (including lactose); active clinically significant bleeding; hepatic disease associated with coagulopathy and clinically relevant bleeding risk; organic lesion or condition considered a significant risk factor for bleeding; concomitant treatment with other anticoagulants except when switching anticoagulant therapy or with UFH to maintain an open central venous or arterial catheter.
Avoid: In history of poor medication adherence; CrCl< 15mL/min; prosthetic heart valves; pregnancy & breastfeeding; **lactose intolerance**.

Bleeding risk with Apixaban versus Warfarin		
Major bleeding	**GI bleeding**	**Intracranial bleeding**
More common with warfarin	**Apixaban ≡ warfarin**	**More common with warfarin**

For NVAF	Recommended dose	Comments
CrCl≥ 30ml/minute	5mg bd	
CrCl 15-29ml/minute	2.5mg bd	Limited trial data: caution
CrCl < 15ml/minute	**Do not use**	
If 2 or more of: **Age ≥ 80 years, weight ≤ 60kg, creatinine ≥ 133umol/l**	2.5mg bd	Low body weight (<60kg) may increase haemorrhagic risk
Hepatic disease associated with coagulopathy **Severe hepatic impairment**	**Do not use**	Limited data in liver disease. AST/ALT > 2xULN or bilirubin >1.5x ULN excluded from trials. Check liver function prior to prescribing

Treatment and prevention of VTE	Recommended dose	Comments
Treatment of VTE	10mg bd for **7 days** followed by 5mg bd thereafter	**Avoid in patients on concomitant systemic treatment with strong inducers of both CYP3A4 & P-gp e.g. rifampicin, carbamazepine, phenytoin, phenobarbital, primidone or St John's Wort as likely to reduce apixaban levels and efficacy**
Prevention of recurrence of VTE following 6 months VTE treatment	**2.5mg bd**	Use with caution in patients on concomitant drugs as above
Renal impairment **CrCl 15-29 ml/min**	**No dose reduction recommended but manufacturer advises use with caution. Limited trial data shows apixaban concentrations are raised in severe renal impairment which may increase bleeding risk**	
CrCl <15ml/min or on dialysis	**Do not use**	No clinical experience - avoid

To calculate creatinine clearance (CrCl): $\frac{(140 - \text{age}) \times \text{weight (kg)} \times \text{Constant (C)}}{\text{Serum creatinine (micromol/L)}}$ **C = 1.23 men; 1.04 women**

Administration: With or without food. Can crush tablets and suspend in water or 5% dextrose in water, or apple juice or mix with apple puree and administer immediately orally. Can administer through a NG tube immediately after crushing and suspending tablet in 60 mL of water or 5% dextrose in water. Can be put in a blister pack.
Interactions: Refer to the tables below:
Table5: DOAC general drug interactions
Table6: DOAC interactions with antiepileptic drugs
Table7: DOAC drug interactions with anticancer drugs

For full prescribing information see apixaban at www.medicines.org.uk

B5 Edoxaban

For Treatment of DVT and Prevention of Recurrent DVT and PE - following initial use of parenteral anticoagulant for at least 5 days

For prevention of stroke and systemic emboli in adults with non-valvular atrial fibrillation & ≥ 1 of: congestive heart failure; hypertension; ≥ 75 years; diabetes mellitus; prior stroke or TIA

To satisfy NICE in NVAF, document/complete the following:
Patient chose edoxaban following a risk/benefit discussion of anticoagulation options (including no treatment)
CHA_2DS_2-VASc ≥2 or CHA_2DS_2-VASc ≥ 1 in men & **HAS-BLED** score calculated
ABC - Alert Card, edoxaban Book & Counselling have been completed/provided **- arrange with ward Pharmacist**/Pharmacy technician

*** ORBIT**– 1 point for each of **H**ypertension, **A**bnormal renal & liver function (1 point each), **S**troke, **B**leeding, **L**abile INR, **E**lderly (>65 years), **D**rugs or alcohol (1 point each). **Score ≥3 = high risk: caution regarding use & needs regular review**

On discharge: Complete the 'Anticoagulation' section of the e-Discharge letter.

Contraindications: Hypersensitivity to active substance or excipients; clinically significant active bleeding; hepatic disease associated with coagulopathy and clinically relevant bleeding risk; lesion or condition considered a significant risk for major bleeding; uncontrolled severe hypertension; concomitant treatment with any anticoagulants except when switching anticoagulant therapy or with UFH to maintain an open central venous or arterial catheter; pregnancy & breast-feeding.
Avoid: In history of poor medication adherence; prosthetic heart valves; moderate to severe mitral stenosis; severe hepatic impairment.
Caution: High CrCl (>95mL/min) – a trend towards decreasing efficacy seen with increasing CrCl.

Bleeding risk with Edoxaban versus Warfarin		
Major bleeding	**GI bleeding**	**Intracranial bleeding**
More common with warfarin	**More common with edoxaban**	**More common with warfarin**

For VTE treatment (after 5 days of parenteral anticoagulant treatment) & VTE prevention. For NVAF	Recommended dose	Comments
CrCl **> 50mL/min**	60mg od	Increased rate of ischemic stroke with edoxaban versus warfarin **in NVAF patients** with CrCl > 95mL/min. In the US edoxaban is not licensed in patients with CrCl>95mL/min
If one or more of: CrCl **15-50mL/min** **Weight ≤ 60 kg** **Concomitant ciclosporin, dronedarone, erythromycin, or ketoconazole**	30mg od	
CrCl **< 15mL/min**	**Do not use**	
Hepatic disease associated with coagulopathy **Severe hepatic impairment**	**Do not use**	Limited data in liver disease AST/ALT > 2xULN or bilirubin >1.5x ULN excluded from trials. **Check liver function prior to prescribing**

To calculate creatinine clearance (CrCl): $\frac{(140 - \text{age}) \times \text{weight (kg)} \times \text{Constant (C)}}{\text{Serum creatinine (micromol/L)}}$ **C = 1.23 men; 1.04 women**

Administration: With or without food. Can be put into a monitored dosage system, e.g. blister pack.
No dose reduction is required for concomitant use of amiodarone, quinidine or verapamil.
Interactions: Refer to the tables below:
Table5: DOAC general drug interactions
Table6: DOAC interactions with antiepileptic drugs
Table7: DOAC drug interactions with anticancer drugs

For full prescribing information see edoxaban at www.medicines.org.uk

Appendix C - The Provision of Patient Information for Patients Newly Initiated on Oral Anticoagulation Medication

1. Introduction
The aim of this document is to outline and clarify the process to follow when in-patients are newly initiated on oral anticoagulant medication, to ensure that they are provided with the relevant safety information prior to their discharge from East Sussex Healthcare NHS Trust.

2. Rationale
There is no in-house Anticoagulation Clinic service at ESHT. To ensure patient safety and adherence with NICE, all patients newly initiated on oral anticoagulants require **ABC** - **A**lert Card, **B**ook & **C**ounselling. The process detailed in this policy aims to ensure that these objectives are met.

3. Scope
This process applies to Pharmacy staff, Doctors and prescribers of oral anticoagulants and to Registered Nurses accountable for patient care**.**

4. Definitions
Vitamin K Antagonists (VKAs)
These are oral anticoagulants that antagonise the effects of vitamin K and include coumarins (warfarin and acenocoumarol) and phenindione.
Direct Oral Anticoagulants (DOACs)
These refer to the direct thrombin inhibitor, dabigatran, and the activated factor X inhibitors, rivaroxaban, apixaban and edoxaban.
International Normalised Ratio - INR (Therapeutic monitoring for VKAs)
This is the blood test used to monitor the effectiveness of vitamin K antagonist therapy. Patients will have a target INR range depending on their indication for anticoagulation.

5. Accountabilities
5.1. Doctors and Prescribers
The prescriber / doctor initiating this therapy is accountable for:

- Discussing relevant treatment options including risks and benefits with the patient and for involving the patient in any prescribing decisions.
- Following the appropriate process dependant on whether a VKA or DOAC is initiated.
- For patients initiated on warfarin or other VKA, the prescriber / doctor must ensure completion of Section 1 of Appendix E, VKA Discharge Advice form, as early in the patient's care episode as possible and filing it in the front of the patient's notes so that it can be easily accessed. This will need to be fully completed prior to discharge (by the prescriber, pharmacist or registered nurse (RN) caring for the patient) and should include the most recent INRs, therapeutic range and duration. The next INR due date should be marked as URGENT and should be three days post discharge (for patients newly initiated on VKAs).
- Contacting a member of the ward Clinical Pharmacy team to arrange **ABC** - **A**lert Card, **B**ook & **C**ounselling for patients newly initiated on an oral anticoagulant.
- Ensuring that the e-Discharge Summary is accurate, and the Anticoagulation section is fully completed.
    - For non-valvular atrial fibrillation (NVAF), the CHA_2DS_2-VASc, ORBIT, CrCl & weight values are mandatory requirements, as are confirmation of a risk/ benefit discussion, consent to treatment and provision of an Alert Card and written information.

In addition, when discharging patients newly initiated on an oral anticoagulant out of hours without having referred the patient to the Clinical Pharmacy Team, the prescriber / doctor is responsible for and accountable for:

- **ABC** - **A**lert Card, **B**ook & anticoagulation **C**ounselling

  - For patients initiated **on warfarin** or other VKA - the prescriber / doctor will be responsible for the provision of a **NPSA Oral Anticoagulation Therapy information pack* (Yellow Book) and completion of the Alert Card** (both sides).
  - For patients initiated **on a DOAC** - the prescriber / doctor will be responsible for the provision of an indication appropriate manufacturer issued **patient information booklet*** and a completed '**NOAC Alert Card'***.
- Ensuring the patient understands that any previous anticoagulant has been stopped and a new oral anticoagulant started.

* A supply of NPSA information packs, DOAC patient information leaflets and 'NOAC Alert Cards' are available from the **Emergency Drug Cupboards** on each site accessible via the Clinical Site Manager who will book out the appropriate information, completing the relevant paperwork for accessing medicines out of hours. This practice should only occur in exceptional circumstances.

N**o patient on a VKA should be discharged without having received their NPSA information pack and no patient on a DOAC should be discharged without a 'NOAC Alert Card' and written information**.

5.2. Ward Matrons

Ward Matrons are responsible for ensuring compliance with this process in their clinical areas and for ensuring that no patients are discharged from their area without receiving **ABC** - **A**lert Card, **B**ook & anticoagulation **C**ounselling. In the case of patients initiated on warfarin or other VKA, this will include provision of a completed NPSA Oral Anticoagulation Therapy information pack (**Yellow Book**) and **Alert Card** (both sides). For patients being discharged on a DOAC this will include an indication appropriate manufacturer issued **patient information booklet** and a completed **'NOAC Alert Card'**. Any failures to comply with this process should be reported on [redacted] following the Trust's Incident Reporting and Management Policy http://nww.esht.nhs.uk/wp-content/uploads/2018/08/00184_P.pdf.

5.3. Heads of Nursing

Heads of Nursing will have oversight of the implementation of the policy within their Clinical Units and will report any risks or non-compliance issues through their Governance structure.

5.4. Registered Nurses

The Registered Nurse caring for the patient is responsible for:

- Liaising with the Clinical Pharmacy team to provide patient information outlined above (5.2 Ward Matrons) as early in the care episode as possible to ensure that the provision of patient information occurs in a timely fashion, rather than at the point of discharge from hospital.
- Ensuring that the referral process is followed.
- Ensuring the patient understands that any previous anticoagulant has been stopped and a new oral anticoagulant started.
- Ensuring that the VKA Discharge Advice form is:
  - Completed for ALL patients on continuing VKA therapy Appendix E
  - Explained to the patient. This includes confirming that the patient understands the discharge dose, when their INR blood test is due, what to expect regarding follow up and the importance of attending.
  - Sent home with the patient on discharge.
- Ensuring that carers / relatives / care home staff or District Nurses (where appropriate) are informed of the need to arrange follow up and INR monitoring appointments as soon as possible when patients with mental capacity problems are discharged from hospital. For patients being discharged to residential care facilities,

this should be incorporated into the clinical handover and recorded in the patient's notes prior to discharge.

The VKA Discharge Advice form Appendix E will be found in the NPSA information pack (Yellow Book) in the patient's POD locker following counselling by a member of the Clinical Pharmacy Team.

For patient's being discharged out of hours, who have not received Clinical Pharmacy input, a VKA Discharge Advice form Appendix E may be completed by the prescriber or Registered Nurse caring for the patient.

5.5. The Clinical Pharmacy Team

The Clinical Pharmacy team (comprising of the Pharmacy Technician and Ward Pharmacist) are responsible for providing anticoagulation safety information to patients in the clinical areas they cover and completing an appropriate Alert Card. VKA counselling will be based on the information provided on the drug chart and in Section 1 of the VKA Discharge Advice form, Appendix E, which will be located in the front of the patient's notes. DOAC counselling will be based on the indication on the drug chart.

The Technician / Pharmacist providing the patient information is responsible for ensuring that Appendix D1 Warfarin checklist or Appendix D2 DOAC checklist is completed and filed in the patient's notes. After VKA counselling, VKA Discharge Advice form, Appendix E should be put into the patient's NPSA information pack (Yellow Book) and kept in the patient's POD locker.

The Technician / Pharmacist is responsible for ensuring the patient understands that any previous anticoagulant has been stopped and a new oral anticoagulant has been started.

5.6. The Clinical Site Management Team or Site Manager

It is recognised that occasionally patients will be discharged out of hours without having been referred to the Clinical Pharmacy team for **ABC** - **A**lert Card, **B**ook & anticoagulant **C**ounselling. In these exceptional circumstances the Clinical Site Manager should be contacted who can access a supply of NPSA Yellow Oral Anticoagulant Therapy patient information packs; apixaban, dabigatran, edoxaban or rivaroxaban patient information books; or NOAC Alert Cards from the Emergency Drug Cupboards on each site. These packs should be booked out in the same way as medicines which are accessed for out of hours supply.

6. Process

6.1 Summary of process guiding patient counselling and discharge process – warfarin

Refer to Figure 4.

6.2 **Summary of process guiding patient counselling and discharge process** – apixaban dabigatran, edoxaban and rivaroxaban

Refer to Figure 5.

7. Special Considerations

Where mental capacity issues are identified or where patients may require additional support in complying with their medication regimens, the medical or nursing team will liaise with the Clinical Pharmacy team to identify solutions and arrange for the information to be provided to relevant family members, the patient's carer or residential / community care staff as appropriate. A record should be made in the patient's notes.

For patients with mental capacity issues / learning difficulties who are already known to Adult Social Care / community support services and who are being discharged to residential care facilities, or with ongoing support from the District Nursing service, the relevant patient information will be transferred with the patient and communicated in the clinical handover procedure / discharge process by the Registered Nurse responsible for the patient's discharge.

For patients who are new to community support services, who require post discharge support with their medicines and who will be discharged on warfarin or other VKA, a formal referral highlighting the need for support in ongoing monitoring of their INR levels should be made. This should be recorded in the patient's notes.

Staff should refer to the Trust Guidance for Staff on the Implementation of the Mental Capacity Act (MCA)
http://nww.esht.nhs.uk/wp-content/uploads/2018/08/00933_P.pdf
and MCA 2005 Code of Practice
https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/497253/Mental-capacity-act-code-of-practice.pdf for guidance when necessary.

Where language difficulties are identified, the ward or medical team, in conjunction with Pharmacy should arrange for translation services appropriate to the individual following the Trust process. This should be addressed as early in the care episode as is practical.

8. Evidence Base / References

National Institute of Health and Clinical Excellence (2009) Medicines Adherence: Involving patients in decisions about prescribed medicines and supporting adherence (Clinical Guideline 76)
National Patient Safety Agency (2007) Oral Anticoagulation Therapy: patient information pack (Ref: 0417).
NICE Venous Thromboembolic diseases: diagnosis, management and thrombophilia testing, 26 March 2020 NG1581 https://www.nice.org.uk/guidance/ng158.
National Institute for Health and Clinical Excellence (2014): Atrial fibrillation: management. Clinical Guideline180. London: NICE.

9. Competencies and Training Requirements

Pharmacy Technicians with Medicines Management responsibilities are accountable for following the appropriate process to ensure competence in providing VKA / DOAC patient counselling.

Pharmacists and Pharmacy Technicians will attend annual refresher Anticoagulant Counselling training sessions run by the Anticoagulation Pharmacist.

Training records will be maintained on the Trust's Electronic Staff Record (ESR) in line with the Learning and Development policy.

Further training will be made available on an ad hoc basis depending on local need.

Element to be monitored	Lead	Tool for Monitoring	Frequency	Responsible individual / group / committee for review of results / report	Responsible individual / group / committee for acting on recommendations / action plan	Responsible individual / group / committee for ensuring action plan / lessons

						learnt are Implemented
The provision of patient information for patients newly initiated on oral anti-coagulation document	Pharmacy Leadership Group	Document review	Every 3 years	Medicines Optimisation Development and Delivery Sub-Group	Medicines Optimisation Group	Medicines Optimisation Group / Divisional Management Teams
Patient Safety Incidents	Medication Safety Officer	[redacted]	Ongoing / monthly	Medicines Quality Group Sub-Group	Medicines Optimisation Group	Medicines Optimisation Group / Divisional Management Teams

11. Equality and Human Rights Statement

Equality, human rights issues, dignity and respect need to be considered in the provision of information about medicines. These considerations include the need for awareness of the patient's ability to understand the information provided.

This policy considers that all the interventions which meet the standards of care in relation to the provision of patient information for oral anticoagulants in acute areas, for staff, patients, relatives or carers (if appropriate) have been met. That it takes steps to ensure they have understood the process even if English is not their first language.

A full Equality Impact Assessment has been undertaken on this policy Appendix A. The assessment document ensures that this policy satisfies the Trust's responsibilities in respect of the Equality Legislation and that all parties' staff and or patients' rights are considered.

Appendix D - Patient Counselling Checklists: VKAs & DOACs
D1 - Patient information safety checklist for in-patients newly initiated onto Warfarin / Acenocoumarol / Phenindione

Patient ID label

East Sussex Healthcare NHS Trust

Introduction	Has the patient got mental capacity issues? Check with the nurse looking after them and obtain advice. Introduce yourself and explain the purpose of your visit -explain that the GP / Practice Nurse will provide further information at next INR appointment. Is the patient already aware of the treatment (if so may require less information)?	**Tick**
Prescription	Provide the patient with the NPSA Yellow Information Pack 'Oral Anticoagulant Therapy'.	
	Complete the patient details section in both the information book and the Oral Anticoagulant Therapy Record book. Ensure that the patient's latest INR is recorded in the Anticoagulant Record book, together with the date and current dose - sign in the appropriate section.	
	Explain the importance of the Alert Card and the need to carry it at all times.	
Treatment Information	Mode of action: Making your blood take longer to clot to treat or prevent clots from forming.	
	Explain reason for use.	
	Current dose and tablet strength identification (use book to explain (mg and colours). 'Test' the patient to ensure they understand.	
	Frequency and timing (preferably with a full glass of water) - take at approximately 6PM daily.	
	Ensure you do not run out of tablets.	
Missed / exceeded dose	What to do if a dose is missed or wrong dose is taken: make a note in Record book and take normal dose the next day and advise your Clinic.	
Monitoring information	Reason for monitoring - to tailor the dose to the individual patient.	
	Individual current INR target range.	
	Importance of regular INR monitoring and attendance at INR Clinic appointments.	
	Explain INR - International Normalised Ratio blood test - the results indicate the time taken for blood to clot compared to a person not on warfarin (VKA). INR 2 means they will take twice as long to clot, INR 3 – 3 times longer to clot, etc.	
	Frequency of blood tests - depends on stability of treatment, introduction or stopping of interacting drugs, planned surgery, and will be covered in more detail by GP - initially at least weekly then interval extended over time up to 12 wkly.	

Patient Name:

Hospital Number:

	Effects of taking too high or too low a dose.	
	Bleeding, unexplained bruising or unusual headaches may require medical attention - seek advice from your GP. **Refer to FULL list in Yellow book.**	
	Head injury or prolonged bleeding will require urgent medical attention, **go to A&E.**	
	Reduce risks of bleeding where possible e.g. use an electric razor, gardening gloves, take care when handling sharp objects.	
	Inform your GP if you take part in high-risk activities such as skiing or contact sports.	
	Inform your dentist that you are currently on anticoagulant therapy. He/ she may want to see your latest INR result, so bring this with you to your dental appointment.	
Other medicines	Seek advice from your GP or community pharmacist BEFORE you take any medicines purchased over the counter (including herbal remedies). For pain relief stick to paracetamol – avoid ibuprofen or diclofenac.	
	Warfarin interacts with a lot of other medicines so seek advice on this from your GP / community pharmacist. If your GP starts or stops a medication (especially antibiotics) it would be advisable to arrange an extra INR appointment.	
	Avoid taking Aspirin unless your GP has advised this.	
Diet and alcohol	Maintain a balanced diet where possible.	
	Be aware of the effects of (but do not avoid) vitamin K rich foods / garlic - refer to Diet section in book - avoid binging on these foods.	
	Avoid cranberries and grapefruit (including cranberry and grapefruit juice as this is concentrated), and 'crash diets'.	
	Try not to exceed the national guidelines for alcohol intake, avoid binge drinking. Discuss this with your GP if you are worried.	
Pregnancy & menstruation	Warfarin is not recommended in pregnancy-discuss with your GP if you are trying to get pregnant or if your menstrual cycle becomes heavier and you are worried.	
Annotate on chart / Yellow Book	Endorse the Prescription Chart to record that you have provided the Yellow Book and counselled the patient, ensure the INR due date is documented in the Yellow Book.	
Sign and date	**Name:** **Signature:**	**Date**

Refer the patient to their GP for further information and show them the VKA Discharge Advice form with dose information and date when they need to be seen by their GP for an INR blood test. Place the form in the front of the Yellow Book and return to patient's locker or put in the green bag with discharge medication, if discharge is imminent.

D2 - Patient information safety checklist for in-patients newly initiated onto direct oral anticoagulants (DOACs) - apixaban, dabigatran, edoxaban & rivaroxaban

Patient ID label

East Sussex Healthcare NHS Trust

Introduction	Has the patient got mental capacity issues? Check with the nurse looking after them and obtain advice. Introduce yourself and explain the purpose of your visit. Is the patient already aware of the treatment (if so may require less information)?	**Tick**
Prescription	Provide the patient with a NOAC Alert Card and with the appropriate manufacturer provided, written information specific to their indication.	
	Complete the patient details on the NOAC Alert Card.	
	Explain the importance of the Alert Card and the need to carry it at all times.	
Treatment Information	Mode of action: Making your blood take longer to clot to treat or prevent clots from forming.	
	Explain reason for use: AF, DVT, PE or post knee or hip replacement.	
	Frequency, timing & administration: All NOACs MUST be taken on time. No dose means **no** protection.	
Apixaban	All indications – take twice a day (12 hours apart). DVT/PE treatment dose is higher for initial 7 days then reduced.	
Dabigatran	AF, DVT, PE – take twice a day (12 hours apart). Knee or hip replacement – take once a day. Swallow whole (must not open the capsule as this will increase risk of bleeding); must be kept in original foil packaging – cannot go in blister pack or pill box as will become ineffective.	
Edoxaban	All indications – take once a day at the same time each day.	
Rivaroxaban	AF, knee or hip replacement – take once a day at the same time each day. For DVT / PE Rivaroxaban is taken 15mg TWICE daily for initial 21 days, thereafter 20mg once daily (though occasionally may be reduced to 15mg daily). **Must be taken with FOOD (except 10mg dose)** or won't absorb full dose.	
	Ensure you do not run out of tablets. Do not stop taking your NOAC without talking to your doctor.	
Missed / exceeded dose	What to do if a dose is missed: **Apixaban** – take as soon as remembered but don't take two tablets at the same time; then continue as before. **Dabigatran** – take as soon as remembered but do not take within 6 hours of when next dose is due. **Edoxaban** – take as soon as remembered but do not take two tablets in the same day; then continue with intake as before. **Rivaroxaban** – take as soon as remembered but do not	

	take two tablets in the same day; then continue with intake as before. EXCEPT in DVT/PE, if dose is missed during initial 21 day phase must ensure 30mg / day so can take 2 x 15mg together. If dose is doubled: **Apixaban**: miss the next scheduled dose (12 hours) and then continue treatment in 24 hours as normal. **Dabigatran:** miss the next scheduled dose (12 hours) and then continue treatment in 24 hours as normal. **Rivaroxaban:** if twice daily dosing, miss the next scheduled dose (12 hours) and then continue treatment in 24 hours as normal. For once daily dosing, take the next dose as normal the following day. **Edoxaban:** no info available	
	Effects of taking too high or too low a dose.	
	Bleeding, unexplained bruising or unusual headaches may require medical attention - seek advice from your GP. **Refer to FULL list on NOAC Alert Card.**	
	Head injury or prolonged bleeding will require urgent medical attention, **go to A&E**.	
	Reduce risks of bleeding where possible e.g. use an electric razor, gardening gloves, take care when handling sharp objects.	
	Inform your GP if you take part in high-risk activities such as skiing or contact sports.	
	Inform your dentist that you are currently on anticoagulant therapy & show him / her your NOAC Alert Card.	
Other medicines	Seek advice from your GP or community pharmacist BEFORE you take any medicines purchased over the counter (including herbal remedies). For pain relief stick to paracetamol – avoid ibuprofen or diclofenac.	
	Inform your surgeon or doctor that you are on an anticoagulant and show your Alert Card before any procedure or new drug prescription.	
	Avoid taking aspirin unless your GP has advised this.	
Diet and alcohol	There are no dietary or alcohol restrictions with NOACs.	
Monitoring	No regular monitoring is necessary. Your GP will check your kidney function at least annually.	
Pregnancy & menstruation	NOACs are not recommended in pregnancy - discuss with your GP if you are trying to get pregnant or if your menstrual cycle becomes heavier and you are worried.	
Annotate on chart	Endorse the Prescription Chart to record that you have provided the NOAC Alert Card, written information and counselled the patient.	
Sign and date	**Name:** **Signature:**	**Date**

Appendix E - VKA Discharge Advice Form

Section 1 to be completed by the Doctor as early as possible in the patient's care episode.
Section 2 to be completed by the Doctor or Ward Nurse prior to discharge for all patients on Warfarin or other VKAs.

Section 2

Patient ID label

East Sussex Healthcare NHS Trust

Dear ……

You have been discharged on the **anticoagulant** ……..

From __/__/__

take _____ mg of ……..EACH EVENING

until __/__/__ when another INR blood test is needed.

Your GP will contact you to let you know when and where your INR blood test appointment has been arranged.

Contact your GP directly if they do not contact you by the above date, to confirm the dose of warfarin to take and the arrangements for your INR blood test.
Please refer to your YELLOW book for more information.

NEXT BLOOD TEST must be within 3 days of discharge. Please show this to the person managing your warfarin at your next blood test appointment

Section 1

The patient has been issued with an interim supply of Warfarin tablets / other VKA / Low Molecular Weight Heparin injections (circle as appropriate).

Indication for anticoagulation: …… INR Target range: ……

Duration of therapy: …… Date commenced: ……..

Most recent INR results: -

Date				
INR				
Dose (mg)				

Concomitant antiplatelet drugs: ……

Are these to continue? Yes☐ No☐ Stop when INR in range☐ Stop in…… (duration) ☐

Anticoagulation to be discontinued:
After stated period ☐ After consultant review ☐ N/A (long-term) ☐

Hospital /Ward: …… Consultant ……

Discharging Doctor's name (sign)……(print)…….. ……BLEEP……
Date……Discharging Nurse: (print name)……

Appendix F - Heparin Intravenous Infusion Pump Protocol

A full blood count and renal function should be taken prior to starting any infusion.

Affix Identity Label. NHS number/hospital number: Patient's name: DOB:	**Allergies** **Weight (Kg)**

1) Prescribe Loading Dose as per the patient's baseline APTT

GIVE ONE LOADING DOSE ONLY. If APTT ratio > 1.9 then discuss with Haematology Consultant. If patient admitted with acute stroke, discuss with Stroke Consultant as to whether a loading dose is appropriate.

2) Prescribe the Initial Heparin Infusion

Use the below table to calculate the initial infusion rate.

Patients weight in kg	Initial infusion rate in ml/hr
40	0.6
45	0.7
50	0.8
55	0.9
60	1.0
65	1.0

Patients weight in kg	Initial infusion rate in ml/hr
70	1.1
75	1.2
80	1.3
85	1.4
90	1.4
95	1.5

Patients weight in kg	Initial infusion rate in ml/hr
100	1.6
105	1.7
110	1.8
115	1.8
120	1.9
≥125	2.0

Alternatively, the following calculation can be used to determine the initial infusion rate: Initial infusion rate (mL/hour) = (16 units x body weight (Kg))/1000 (units/mL)

3) Check APTT and change the infusion rate as required

- Check APTT ratio 6 hours after staring an infusion, or after any change in dose, and adjust infusion rate according to table below.
- Check APTT ratio 24 hourly once patient established within therapeutic range.
- If total dose > 40 000 units discuss with Haematology Consultant to consider monitoring and anti-Xa levels (aiming for 0.35-0.7) instead of APTT ratio.
- Check platelets at 24 hours and on alternate days thereafter.

APTT ratio	≤ 1.59	1.6 - 1.99	**2.0 - 2.59**	2.6 - 3.09	3.1 - 4.09	4.1 - 5.09	≥ 5.1
Administer bolus IV	5000 units	2500 units	**Therapeutic range**	No	No	No	NO
Stop infusion	No	No	No	No	For 30 mins	For 60 mins	For 60 mins
Change dose	Increase rate by 0.4mL/hr	Increase rate by 0.2mL/hr	Do not adjust rate	Decrease rate by 0.1mL/hr	Decrease rate by 0.2mL/hr	Decrease rate by 0.3mL/hr	Decrease rate by 0.5mL/hr
Repeat APTT ratio	6 hours. Contact Haematology if APTT ratio remains < 1.6 despite this action	6 hours	Repeat APTT ratio after 24 hours	6 hours	6 hours	6 hours	6 hours

Heparin Intravenous Infusion Pump Protocol- Prescription Page

Draw 30mL of 1000 units/mL heparin into a 50ml syringe, give via syringe driver. Purge the line with solution prior to staring the infusion. DO NOT DILUTE FURTHER.
Change heparin syringe and giving set every 24 hours.

1) Loading dose - **GIVE ONE LOADING DOSE ONLY** determined by APTT ratio. Cross out other prescription to avoid error.

Baseline APTT ratio	Drug	Dose	Route	Duration	Signature	Date	Administration	
≤ 1.5	**Heparin** (5000 units in 5mL)-ready diluted	5000 units	IV	5 minutes			Given by:	
							Checked by:	
1.6 - 1.9	**Heparin** (5000 units in 5mL)-ready diluted	2500 units	IV	5 minutes			Given by:	
							Checked by:	

2) Heparin infusion

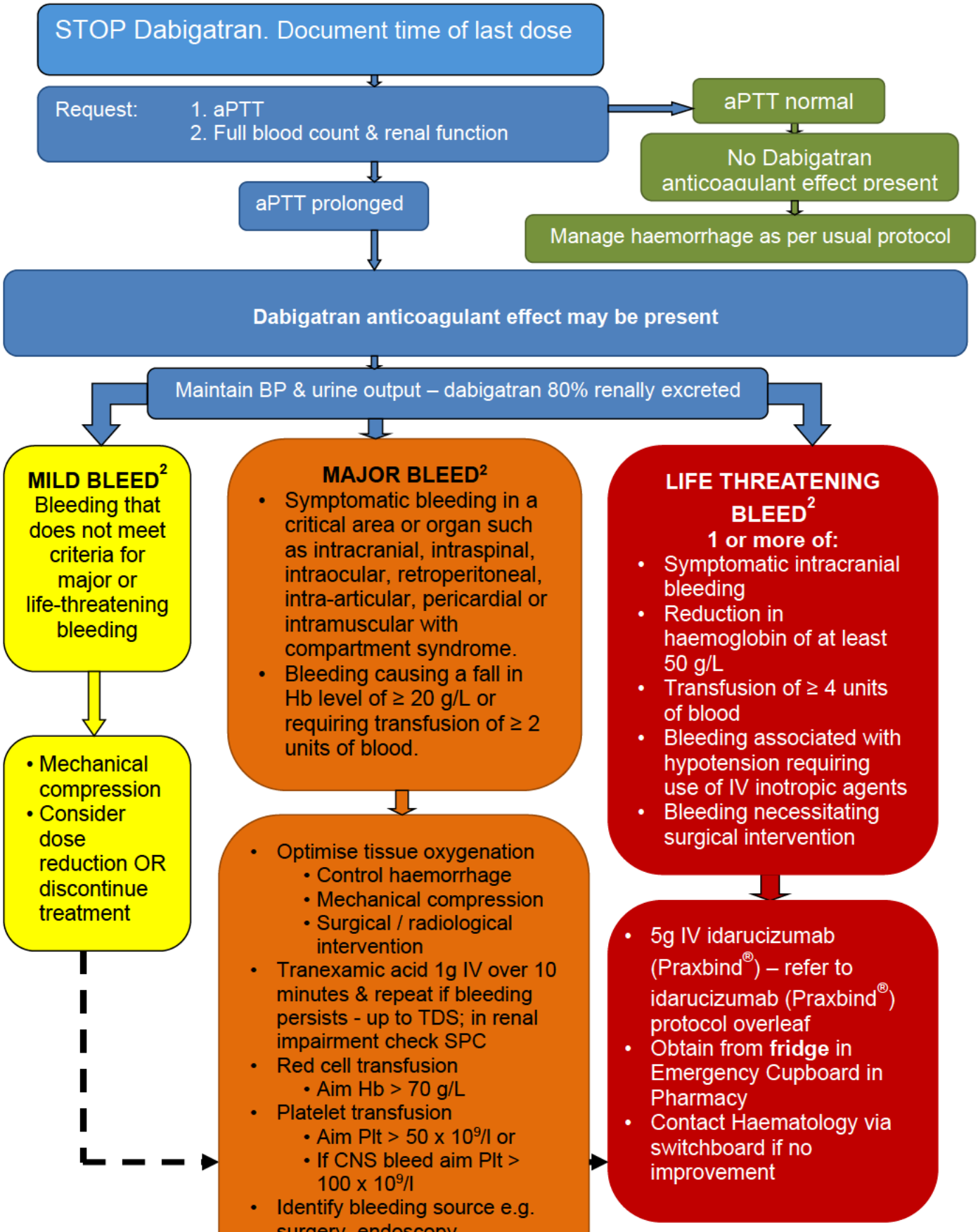
Drug	Route	Date	Time	APTT ratio	Change in infusion rate (mL/hr)	Infusion rate (mL/hr)	Doctor signature	Given by	Checked by	Date/ time given
Heparin (1000 units/mL)	IV									
Heparin (1000 units/mL)	IV									
Heparin (1000 units/mL)	IV									
Heparin (1000 units/mL)	IV									
Heparin (1000 units/mL)	IV									
Heparin (1000 units/mL)	IV									
Heparin (1000 units/mL)	IV									
Heparin (1000 units/mL)	IV									
Heparin (1000 units/mL)	IV									
Heparin (1000 units/mL)	IV									

Drug	Route	Date	Time	APTT ratio	Change in infusion rate (mL/hr)	Infusion rate (mL/hr)	Doctor signature	Given by	Checked by	Date/ time given
Heparin (1000 units/mL)	IV									
Heparin (1000 units/mL)	IV									
Heparin (1000 units/mL)	IV									
Heparin (1000 units/mL)	IV									

3). Bolus doses

APPT ratio	Drug	Dose (units)	Route	Duration	Signature	Date	Administration	
	Heparin (5000 units in 5mL)-ready diluted		IV	5 minutes			Given by:	
							Checked by:	
	Heparin (5000 units in 5mL)-ready diluted		IV	5 minutes			Given by:	
							Checked by:	
	Heparin (5000 units in 5mL)-ready diluted		IV	5 minutes			Given by:	
							Checked by:	
	Heparin (5000 units in 5mL)-ready diluted		IV	5 minutes			Given by:	
							Checked by:	
	Heparin (5000 units in 5mL)-ready diluted		IV	5 minutes			Given by:	
							Checked by:	

Appendix G - Adult Patient Receiving Dabigatran Therapy: Haemorrhage Protocol



Appendix H - Idarucizumab (Praxbind®) Protocol

Indications

Idarucizumab (Praxbind®) is a specific reversal agent for **adult patients treated with dabigatran**[1]. It is a humanized monoclonal antibody fragment that has a very high binding affinity for dabigatran. **Idarucizumab will not reverse the effects of other anticoagulants.** It is used for the **emergency reversal of dabigatran** in the following circumstances:

1. **Life –threatening bleed** defined as one or more of: symptomatic intracranial bleeding, reduction in haemoglobin of at least 50 g/L, transfusion of ≥ 4 units of blood, bleeding associated with hypotension requiring use of IV inotropic agents and/or bleeding necessitating surgical intervention.[2]
2. **Emergency surgery or other invasive procedure that cannot be delayed for at least 8 hours**[3], requiring urgent reduction of dabigatran anticoagulation effect.

Precautions to use

- Known hypersensitivity to Idarucizumab.
- Hereditary fructose intolerance or allergy to sorbitol.[5]

Procedure

1. Stop dabigatran.
2. Note time of last dabigatran dose.
3. Request:
   a. Coagulation screen to include aPTT
   b. Full blood count & renal function.
4. If aPTT is prolonged this suggests the presence of dabigatran[4].
   Collect idarucizumab from the **fridge in the Emergency Drug cupboard in Pharmacy**.
5. Administer idarucizumab as per 'Administration' section below, in conjunction with other supportive measures as appropriate.
6. Repeat aPTT at 12 hours and 24 hours after idarucizumab administration.
7. In the event of a **recurrence of clinically relevant bleeding** or a need for a **second emergency/urgent procedure**, contact **Haematology** via switchboard to discuss administration of a second 5g dose of idarucizumab.

Dose

The dose of idarucizumab is 5g. No dose adjustment is required in renal or hepatic impairment, or in the elderly[5]. It comes as 2 x 2.5g/50ml vials of **ready to use solution**.

Administration[5]

- Idarucizumab is stored in the **fridge** but can be used for up to 48 hours if stored unopened in its original container at room temperature, and for up to 6 hours if taken out of its original container and exposed to light (unopened).
- Idarucizumab should be **administered immediately after the vial has been opened**; although it can be used up to one hour after the vial has been opened if kept at room temperature.
- Inspect visually for particulate matter and discolouration prior to administration.
- Do not mix with other medicinal products.
- If using an existing IV line for intravenous infusion of idarucizumab, no other infusion should be administered in parallel via the same intravenous access.
- If using an existing IV line, flush the line with 0.9% sodium chloride for injection prior to and at the end of the infusion.

Administer 2 x 2.5g/50ml intravenously (IV) as either:

- **two consecutive 50ml infusions over 5 – 10 minutes each**

OR

- **two consecutive 50ml bolus injections** – no rate is specified but the aim should be to administer idarucizumab as fast as possible

There is no preferred method of administration. The aim is to administer idarucizumab into the patient in the fastest method deemed clinically appropriate on an individual patient basis.[6]

Duration of effect

- Reversal of dabigatran occurs within minutes of administration of idarucizumab.[5,6]
- The majority of patients show sustained reversal of dabigatran plasma concentrations up to 12 hours.[5]
- In trials some patients had a subsequent increase in dabigatran levels and an associated increase in clotting time at 12 hours and 24 hours after the administration of idarucizumab.[3]
- In trials the median time between first administration of idarucizumab and surgery was 1.7 hours (range 1.2 -26.4 hours).[6]
- Antithrombotic therapies (e.g. LMWH) can be started at any time after the administration of idarucizumab if clinically appropriate.[5]
- Dabigatran can be restarted after 24 hours if the patient is clinically stable and adequate haemostasis has been achieved.[5,7]

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4. https://pro.boehringer-ingelheim.com/us/products/pradaxa/dosing-administration [accessed 8/3/24]
5. Boehringer Ingelheim Limited. Summary of Product Characteristics Praxbind 2.5 g/50 mL solution for injection/infusion [internet]. 2015 November 20 [cited 2016 April 29]. Available from: http://www.medicines.org.uk/emc/medicine/31243.
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7. https://pro.boehringer-ingelheim.com/us/products/praxbind/bipdf/prescribing-information [accessed 8/3/24]

Iwona Ward & Dr Richard Grace. East Sussex Healthcare NHS Trust. November 2024 (Version 3). Review Date November 2027.

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Appendix I - Andexanet Alfa Administration Procedure

To calculate dose of andexanet alfa required			
Fxa inhibitor	What was the last dose?	When was last dose taken? <8 hours or unknown?	When was last dose taken? ≥ 8 hours
Apixaban	≤ 5 mg	Low dose	Low dose
	> 5 mg/ unknown	High dose	
Rivaroxaban	≤ 10mg	Low dose	Low dose
	> 10mg / unknown	High dose	

Each vial contains 200mg dry powder of andexanet alfa
Each vial is reconstituted with 20 mL water for injections

Low dose = 5 vials x 200mg dry powder
High dose = 9 vials x 200mg dry powder

Administration requires a 0.2 or 0.22 micron in-line polyethersulfone (PES) or equivalent low protein-binding filter.

Administration rate					
Dose	**Initial** IV dose	**Syringe pump setting for INITIAL dose (use 50 mL syringe)**	**Followed by** continuous IV infusion	**Syringe pump setting for FOLLOW ON infusion (use 50 mL syringe)**	No. of 200mg vials
Low	400mg **over 15 mins** (rate 30mg/min)	40 mL over 15 mins Set at 160 mL/hr for 15 mins **Summary:** Vials reconstituted = 2 Total volume = 40mL Total time = 15 mins	4 mg/min for 120 mins (480mg)	48 mL over 120 min Set at 24 mL/hr for 2 hours **Summary**: Vials reconstituted= 3 Total volume = 48mL Total time = 2 hours	5
High	800mg **over 30 mins** (rate 30mg/min)	40 mL over 15 mins Set at 160 mL/hr for 15 mins AND then repeat ONCE more **Summary**: Vials reconstituted = 4 Total volume = 80 mL Total time = 30 mins	8 mg/min for 120 mins (960mg)	48 mL over 60 min Set at 48 mL/hr for 1 hour AND then repeat ONCE more **Summary**: Vials reconstituted = 5 Total volume = 96 mL Total time = 2 hours	9

Reconstitution

The following are needed before starting reconstitution:

- Calculated number of vials.
- Same number of 20 mL (or larger) solvent syringes equipped with a 20 gauge (or larger) needle.
- Alcohol swabs.
- Large (50 mL or larger) sterile syringe. If a syringe pump is used for administration, multiple syringes should be used to contain the final volume of reconstituted product.
- Water for injections.
- 0.2 or 0.22 micron in-line polyethersulfone (PES) or equivalent low protein-binding filter.

Andexanet alfa **does not need to be brought to room temperature** before reconstitution or administration to the patient. Aseptic technique during the reconstitution procedure should be used.

Each vial is reconstituted according to the following instructions:

1. Remove the flip-top from each vial.

2. Wipe the rubber stopper of each vial with an alcohol swab.

3. Using a 20 mL (or larger) syringe and a 20 gauge (or larger) needle, withdraw 20 mL of water for injections.

4. Insert the syringe needle through the centre of the rubber stopper.

5. Push the plunger down to slowly inject the 20 mL of water for injections into the vial, directing the stream toward the inside wall of the vial to minimise foaming.

6. Gently swirl each vial, until all of the powder is completely dissolved. DO NOT SHAKE the vials, as this can lead to foaming. The dissolution time for each vial is approximately three to five minutes.

7. The reconstituted solution should be inspected for particulate matter and/or discolouration prior to administration. Do not use if opaque particles or discolouration are present.

8. For the most efficient reconstitution of the needed dose, and to minimise errors, inject each vial needed with 20 mL of water for injections before proceeding to the next step.

9. **Use within eight hours after reconstitution when stored at room temperature**.

Administration using a syringe pump

1. Once all required vials are reconstituted, the reconstituted solution is withdrawn from each vial, using the large volume (50 mL or larger) syringe equipped with a 20 gauge (or larger) needle.

2. The bolus and infusion are prepared in separate large volume syringes.

3. Due to the additional volume, the high dose bolus and infusion have to be further separated into additional syringes (two syringes apiece for bolus and infusion).

4. To prevent the inadvertent transfer of air, be careful to hold the syringe needle up, and do not set the syringe down between multiple withdrawals from vials.

5. Attach ancillary equipment (i.e., extension tubing, 0.2 or 0.22 micron in-line polyethersulfone (PES) or equivalent low protein-binding filter, syringe pump) in preparation for administration.

6. Administer the reconstituted solution at the appropriate rate.

7. Discard all used syringes, needles, and vials, including any unused portion of reconstituted solution.

Disposal

All used syringes, needles, and vials, including any unused portion of reconstituted solution, should be disposed of in accordance with local requirements.

References:

1. Ondexxya 200 mg powder for solution for infusion - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk) [accessed December 2021].

Iwona Ward & Dr Richard Grace. East Sussex Healthcare NHS Trust. January 2022 (Version 1). Review Date January 2025.

Appendix J - Enoxaparin syringes: doses, volumes, concentrations and graduations

Enoxaparin syringes:

- Enoxaparin may be supplied by Pharmacy as Inhixa® or Clexane® brand.
- ePMA will specify the brand currently available.
- The concentration of syringes differs depending on dose, so be mindful that high strength syringes (120mg and 150mg) will deliver a higher dose per graduation than the lower strength syringes (60mg, 80mg and 100mg).
- Each brand is available in the following prefilled syringes for subcutaneous injection:

Inhixa® brand

Table J1 - Inhixa® enoxaparin doses, volumes, concentrations and graduations

Dose	Volume	Concentration	Additional information
20mg			
40mg			
60mg	0.6mL	100mg/mL	imprinted with graduated markings: 0.025ml = 2.5mg 0.1ml =10mg
80mg	0.8mL	100mg/mL	imprinted with graduated markings: 0.025ml = 2.5mg 0.1ml =10mg
100mg	1.0mL	100mg/mL	imprinted with graduated markings: 0.025ml = 2.5mg 0.1ml =10mg
120mg	0.8mL	150mg/mL	imprinted with graduated markings: 0.025ml = 3.75mg 0.1ml =15mg
150mg	1.0mL	150mg/mL	imprinted with graduated markings: 0.025ml = **3.75mg** 0.1ml =15mg

Clexane® brand

Table J2 - Clexane® enoxaparin doses, volumes, concentrations and graduations

Dose	Volume	Concentration	Additional information
20mg	0.2ml	100mg/mL	
40mg	0.4ml	100mg/mL	
60mg	0.6ml	100mg/mL	imprinted with graduated markings: 0.1ml =10mg
80mg	0.8ml	100mg/mL	imprinted with graduated markings: 0.1ml =10mg
100mg	1.0ml	100mg/mL	
120mg	0.8ml	150mg/mL	imprinted with graduated markings: 0.1ml =15mg
150mg	1.0ml	150mg/mL	imprinted with graduated markings: 0.1ml =15mg

Appendix K - Argatroban Infusion Protocol for the management of HIT
(Heparin-Induced Thrombocytopenia) – HOSPITAL USE ONLY- Non-Formulary

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Patient's weight (kg) ……. Ward…….. Consultant……

- **Discuss with Haematology Consultant before initiating argatroban.**
- **Ensure heparin therapy has been discontinued before starting treatment.**
- **This protocol is not for HIT patients undergoing PCI – please see SPC for specific information.**
- Argatroban is contra-indicated in patients with severe liver impairment/Childs Pugh class C.
- Allergy status to heparin must be recorded on the drug chart.
- Prior to administration perform baseline clotting screen and platelet count. Monitor FBC daily.
- Dilute argatroban 250mg/2.5ml amp in either:
  250mL **sodium chloride 0.9%** or 250mL **glucose 5%**
  to give final concentration of 1mg/ml (1000mcg/ml). For dilution instructions refer to Injectable Medicines Guide - Display - Argatroban monohydrate - Intravenous - Version 7 - IVGuideDisplayMain.asp
- Preferably administer via central venous access to avoid potential venous irritation due to low ph. If given peripherally, choose a large vein and monitor site closely for phlebitis.
- Check aPTT ratio 2 hours after starting infusion, then adjust rate to achieve optimal therapeutic range of 1.5 – 3.0 using the dose adjustment table. Check aPTT ratio 2 hours after dose changes (range may differ from product literature).
- For critically ill patients or patients with hepatic impairment check aPTT ratio 4 hours after starting infusion and 4 hours after a dose change.
- After 2 consecutive aPTT ratios are within target range, check DAILY.
- Maximum dose 10mcg/kg/min.

Conversion to oral VKA anticoagulant, e.g. warfarin:

- **Argatroban interferes with the INR assay**; stopping this drug too early could result in a lapse in therapeutic anticoagulation. Please seek haematology advice if necessary.
- Argatroban should be continued as bridging therapy with oral VKA anticoagulation for a minimum of 5 days and until the **INR is 4 or above** for 2 days (this INR value takes into account the effect of argatroban on the INR assay to give a false high reading).
- Warfarin should not be started until platelets are above 100 x 10^9d/l.
- **Do not use loading dose of warfarin – please start on predicted maintenance dose.**
- Measure INR 4-6 hrs after stopping argatroban and restart infusion if INR is below target range.

Conversion to a DOAC, i.e. apixaban, dabigatran, edoxaban or rivaroxaban:

- A DOAC should not be started until platelets are above 100 x 10^9d/l.
- Initiate the DOAC 2 hours after discontinuation of the argatroban infusion.

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Argatroban Infusion Protocol

To calculate standard initial infusion rate (ml/hr): $\frac{\text{1mcg/kg/min x weight (kg) x 60mins}}{\text{1000mcg/ml Body weight (kg)}}$

	Initial Infusion Rate of Argatroban (1000mcg/ml) ml/hr	
Body Weight (kg)	**Standard dosing*** **1 microgram/kg/min**	**For critically ill or hepatically impaired (Child-Pugh Class B) patients, and post cardiac surgery** **0.5 microgram/kg/min**
50	3.0 ml/hr	**1.5 ml/hr**
60	3.6 ml/hr	**1.8 ml/hr**
70	4.2 ml/hr	**2.1 ml/hr**
80	4.8 ml/hr	**2.4 ml/hr**
90	5.4 ml/hr	**2.7 ml/hr**
100	6.0 ml/hr	**3.0 ml/hr**
110	6.6 ml/hr	**3.3 ml/hr**
120	7.2 ml/hr	**3.6 ml/hr**
130	7.8 ml/hr	**3.9 ml/hr**
140	8.4 ml/hr	**4.2 ml/hr**

***Standard initial infusion rate differs from the SPC which states 2mcg/kg/min and is based on specialist centre UK data and specific recommendation from the manufacturer. The ESHT lower standard dose regime is reflective of the population and the high risk of co-morbidities.**

Doctor's Signature…… Print Name…….. Bleep Number…… Date ……

Treatment Discontinued: ☐ Date: Doctor's signature:

Record of infusion preparation

Date	Time (24 hour clock)	Batch number of argatroban	Signature of nurse making infusion	Signature of second check	Line primed with new syringe?	
					Yes	No

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Argatroban Infusion Protocol

Infusion rate adjustment of argatroban according to aPTT ratio

	Standard dosing schedule **Initial Infusion Rate 1 mcg/kg/min**		Critically ill / hepatically impaired (Child-Pugh Class B) patients /post cardiac surgery **Initial infusion rate 0.5 mcg/kg/min**	
aPTT ratio	**Infusion Rate change**	**Next aPTT ratio**	**Infusion Rate change**	**Next aPTT ratio**
< 1.5	Increase by 0.5 mcg/kg/min.	2 hours	Increase by 0.1 mcg/kg/min.	4 hours
1.5-2.5	No change	2 hours After 2 consecutive aPTTs within target range check at least once per day	No Change	4 hours After 2 consecutive aPTTs within target range check at least once per day
2.5-3.0	Reduce by 0.2 mcg/kg/min	2 hours	Reduce by 0.1 mcg/kg/min	4 hours
> 3.0	Stop infusion until aPTT 1.5-3.0. Resume at half of the previous infusion rate.	2 hours	Stop infusion until aPTT 1.5-3.0. Resume at half of the previous infusion rate.	4 hours

Maximum dose: 10mcg/kg/min

To calculate adjusted infusion rate (ml/hr):

$$\frac{A \text{ mcg/kg/min} \times \text{weight (kg)} \times 60\text{mins}}{1000\text{mcg/ml}} + \text{Current Infusion Rate (ml/hr)}$$

Where A is the infusion rate change

For Example:
A 60kg man with a current infusion rate of 3.6ml/hr has an aPTT of 1.2. The infusion rate needs to be increased by **0.5mcg/kg/min.**

To calculate the rate increase:

$$\frac{\mathbf{0.5}\text{mcg/kg/min} \times \mathbf{60}\text{kg} \times \mathbf{60}\text{min}}{\mathbf{1000\ mcg/ml}} = 1.8\text{ml/hr}$$

The new infusion rate (ml/hr) is 1.8ml/hr + 3.6ml/hr = 5.4ml/hr

See Medusa the injectable medicines guide for further information.
Injectable Medicines Guide - Display - Argatroban monohydrate - Intravenous - Version 7 - IVGuideDisplayMain.asp

Please contact ward pharmacist, medicines information or the on-call pharmacist via switchboard for further advice on this calculation if necessary.

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Argatroban Infusion Protocol

Administration Details

Date	Time (24 hour clock)	APTT Ratio	Infusion rate (ml/hr)	Volume remaining in syringe	IV trained nurse signature	Doctor signature*

*Doctor signature only required if doctor is contacted in cases of clinical need (e.g. aPTT ratio >5, patient bleeding).

References:

1. Argatroban Protocol Brighton and Sussex University Hospitals NHS Trust , review date April 2023.
2. Exembol 1 mg/ml Solution for Infusion - Summary of Product Characteristics (SmPC) - (emc) Accessed 12/4/24
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Appendix L - Anticoagulation in Patients with Valvular Heart Disease and Prosthetic Valves

Anticoagulation for atrial fibrillation (AF) in valvular heart disease

- **Valvular AF**
  Moderate to severe mitral stenosis or prosthetic heart valves (and valve repair in North American guidelines) with atrial fibrillation should be treated with Vitamin K antagonists (VKA), usually warfarin.

- **Non-valvular AF**
  All other patients with valvular heart lesions and AF may be treated with VKA or direct oral anticoagulants (DOACS)

- **Patients who have AF associated with a surgical or transcatheter aortic valve bioprosthesis**
  May be treated with a DOAC or VKA after the third month of implantation.

Anticoagulation for prosthetic valves

The level of anticoagulation (target INR) is defined by the cardiac surgeon at the time of the operation, and this information must be passed onto primary and secondary care.

- **Biological (Tissue) prosthetic heart valves or Valve repair**
  - **Aortic position**: No anticoagulation needed. Current recommendation is for an anti-platelet agent, e.g. aspirin, for 3 months post-surgery provided patient is in normal sinus rhythm and there is no other indication for anticoagulation.

  - **Mitral and Tricuspid position**: Post-operative anticoagulation with warfarin is recommended for **3 months** only (target INR 2.5), provided in normal sinus rhythm and there is no other indication for continued anticoagulation.

- **Mechanical prosthetic heart valves**
  - All patients with mechanical heart valves require life-long anticoagulation with a Vitamin K antagonist, i.e. Warfarin guided by regular monitoring of the INR to inform dosing.
  - DOACs (i.e. Dabigatran, Rivaroxaban, Apixaban and Edoxaban) are **NOT licensed and are CONTRAINDICATED** for use in patients with mechanical prosthetic heart valves.

Managing anticoagulation treatment

The optimal target INR with mechanical heart valves depends on the varying thrombotic risk associated with different valve types, and patient related risk factors. It is recommended to target a median INR value rather than a range to avoid considering extreme values in the target range as a valid target INR. For more information see Table1- Indications for VKA-Oral Anticoagulant Therapy and target INR (including mechanical heart valve targets).

- **Managing sub-therapeutic anticoagulation - INR falls more than 0.5 below target INR**
  - These patients require bridging cover with intravenous unfractionated heparin (UFH) infusion or off label subcutaneous low molecular weight heparin (LMWH) until the INR is within 0.5 of target INR.
  - Intravenous unfractionated heparin (UFH) is suitable even in severe renal impairment (CrCl <15mL/min).
  - Where bridging with off-label subcutaneous LMWH is required, enoxaparin 1mg/kg bd dosing should be used at CrCl ≥ 30mlL/min or 1mg/kg od at CrCl

15-30mL/min. Enoxaparin is contraindicated at CrCl <15mL/min as it accumulates.
    - The INR needs to be rechecked in 2-3 days, to guide warfarin dosage. After adjusting warfarin dose, it takes around 48 hours for the INR to respond.

- **Managing a high INR**
    - Refer to the table below.
    - In the presence of mechanical valves, **reversal of anticoagulation with Vitamin K must be carefully assessed against perceived bleeding risk**. If vitamin K is given, INR should be rechecked as specified in the table below or within 12-24 hours as heparin may be required if INR subsequently becomes sub-therapeutic.

Indication	Action	Vitamin K	Additional treatment	Monitoring	Resuming VKA
Major and /or life-threatening bleeding	Discontinue VKA	10mg by slow IV. Repeat 12 hrly if necessary	Beriplex® as per weight and INR Table 22	INR at 30 mins and every 4-6 hrs	Resume VKA once INR in therapeutic range or slightly elevated
Urgent surgery required	Discontinue VKA	10mg by slow IV. Repeat 12 hrly if necessary	Beriplex® as per weight and INR Table 22	INR at 30 mins and every 4-6 hrs	
INR >10 no bleeding	Discontinue VKA	2.5 – 5mg using the IV preparation orally (unlicensed use).	N/A	INR daily until stable	
INR 4.5 – 10 minor bleeding	Discontinue VKA	**Consider on an individual basis** 1 – 2mg using the IV preparation orally. Use Konakion MM Paediatric 2mg/0.2ml solution for injection for 1 - 2mg doses.	N/A	More frequently until stable	
INR <4.5 asymptomatic	Down titrate VKA. Miss 1-2 doses depending on target	N/A	N/A	More frequently until stable	

VKA = vitamin K antagonist (e.g. warfarin)

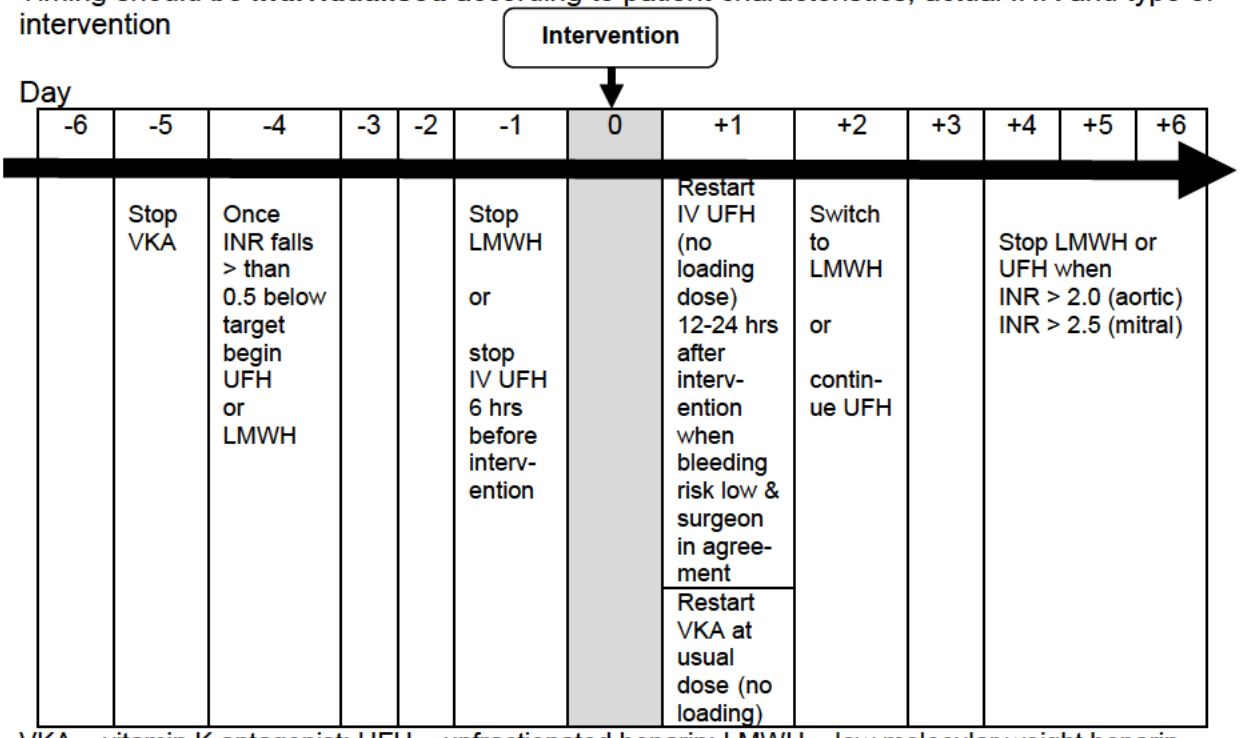
Beriplex® is a blood product and is available from blood bank - consider religious preferences or other beliefs

Managing patients in need of peri-procedure temporary discontinuation of anti-coagulation

- Warfarin **should not** be stopped for most minor surgical, superficial, dental and ophthalmic procedures. Appropriate techniques of haemostasis should be used, the INR measured on the day of the procedure; this should not be >0.5 above target INR.
- **Major surgical procedures require an INR of less than 1.5 depending upon bleeding risk.** Warfarin should be stopped 3-5 days before surgery (depending on current INR) and bridging using heparin is recommended once the INR falls > 0.5 below the target INR.
- Therapeutic bridging can be carried out with intravenous unfractionated heparin (UFH) or off label use of low molecular weight heparin (LMWH). Similar safety and efficacy outcomes have been reported following bridging with either UFH or LMWH in patients with mechanical prostheses. Fondaparinux should not be used.

Figure 1. Bridging plan

Timing should be **individualised** according to patient characteristics, actual INR and type of intervention



VKA = vitamin K antagonist; UFH = unfractionated heparin; LMWH = low molecular weight heparin

Pregnancy and mechanical valves

- These patients should be managed jointly between Cardiology, Obstetrics and Haematology.
- Therapeutic anticoagulation is extremely important to avoid complications.
- In patients requiring ≤5mg of warfarin, continue with oral anticoagulation during pregnancy and change to unfractionated heparin prior to delivery.
- In patients requiring ≥ 5mg of warfarin, switch to LMWH during the first trimester with strict anti-Xa monitoring (therapeutic range 0.8-1.2IU/ml). The use of oral anticoagulants thereafter is favoured.

References:

1. Guidelines on the management of valvular heart disease (2017) The Task Force of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

2. 2021 ESC/EACTS Guidelines for the management of valvular heart disease. European Journal of Cardio-Thoracic Surgery 60 (2021) 727–800
3. 2021 ESC/EACTS Guidelines for the management of valvular heart disease Supplementary data European Heart Journal (2021) 00, 1_12

Appendix M - Management of Superficial Vein Thrombosis of the Lower Limb

Background[1]

- Superficial venous thrombosis of the lower limb, involving long or short saphenous veins or their branches, is possibly more common than DVT of the leg[2,3].
- Two thirds of cases are seen in females and three quarters occur in an existing varicose vein[4].
- Risk factors for SVT are essentially the same as for DVT[3,5] and superficial venous thrombosis itself contributes 5.4% (95% CI 3.0–7.7) of the adjusted population attributable risk for first DVT or PE event[6].
- Pregnancy is associated with an increased risk of superficial venous thrombosis, similar to that of DVT, most commonly post-partum[7,8].
- Heritable thrombophilia is an aetiological factor; superficial venous thrombosis has been reported as the first manifestation of venous thrombosis in 11–15% of patients with protein C or S deficiency and around 40% of those with factor V Leiden[9, 10, 11, 12]. However, there are no data to suggest that the presence of a thrombophilia should alter management or influence rates of superficial venous thrombosis recurrence or progression.

Management[1]

Patients with lower limb superficial venous thrombosis should have ultrasound assessment to exclude DVT, particularly if affecting the proximal long saphenous vein[1].

- Patients with **confirmed superficial venous thrombosis within 3 cm of the saphenofemoral junction[1] or extension[13] should be considered for therapeutic anticoagulation[1, 13]** for a **duration of at least 3 months**[13].
- Refer to Table 35 for suggestions for choice of anticoagulant for acute VTE treatment.
    - First line, as do not require initial parenteral treatment:
        - **Apixaban** - 10mg bd for 7 days thereafter 5mg bd or
        - **Rivaroxaban** - 15mg bd for 21 days thereafter 20 mg od; consider 15mg od if bleeding risk outweighs risk of recurrent superficial venous thrombosis.
    - Alternatively:
        - **Edoxaban** or **dabigatran** – click links for dosing - require an initial 5 days of parenteral anticoagulant treatment with enoxaparin (LMWH) **before commencing DOAC**. Refer to Table 25 to select the correct enoxaparin regime and Table 26 for enoxaparin dosing according to weight and dosage regime.
        - **Warfarin** (target INR 2.5; range 2.0 to 3.0) with at least 5 days of **concomitant** treatment-dose, weight-adjusted enoxaparin (LMWH) or heparin infusion until INR is ≥ 2.0 in 2 consecutive readings followed by warfarin alone. Refer to Table 25 to select the correct enoxaparin regime and Table 26 for enoxaparin dosing according to weight and dosage regime.
- Patients with superficial venous thrombosis and risk factors for extension, recurrence or progression should be offered treatment with heparin thromboprophylaxis for 30 days (currently an unlicensed indication) or prophylactic fondaparinux for 30–45 days[1].
- Other patients with superficial venous thrombosis should be offered 8–12 days NSAIDs unless contraindicated[1].
- Investigation of patients with superficial venous thrombosis for underlying thrombophilia is not routinely indicated and should follow existing guideline criteria[1].

References

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Appendix N - Protocol for the Management of Pulmonary Embolism (PE) requiring Thrombolysis using Alteplase (or Urokinase ONLY if Alteplase SHORTAGE)

Thrombolysis is NOT first line treatment for non-massive/stable PE (SBP>90mmHg)

Patient Assessment - clinical scenario, investigations & when to thrombolyse

- Refer to Table N1 for management of PE as per clinical scenario.
- Consider referral to Critical Care and/or Cardiology.

If Alteplase is unavailable for PE thrombolysis urokinase should be used.

Table N1 - Management of PE as per clinical scenario using alteplase (or urokinase in the event of alteplase shortage)

CLINICAL SCENARIO	INVESTIGA-TIONS	THROMBOLYSE IF EVIDENCE OF:	ALTEPLASE (rt-PA) REGIMEN	UROKINASE REGIMEN– use ONLY in event of alteplase SHORTAGE
Peri-arrest/PEA arrest due to PE	ECHO (bedside ECHO acceptable) NOT FOR CT	RV enlargement (with basal RV/LV ratio >1.0) RV impairment (especially with 60/60 sign, McConnell sign, or right heart thrombi) Pulmonary hypertension (if possible to measure) **DO NOT DELAY** decision making if timely investigations are not possible	**Regimen 1** Refer to Table N3 for dosing	Refer to: Table N4 for dosing Table N4a for urokinase **bolus loading dose** according to weight Table N4b for urokinase **infusion dosing** and rate according to weight
PE with obstructive shock[a] or persistent hypotension[b]	ECHO CTPA[c]	RV enlargement (with basal RV/LV ratio >1.0) RV impairment (especially with 60/60 sign, McConnell sign, or right heart thrombi) PE confirmed/likely Discuss with cardiothoracic surgeons	**Regimen 2** Refer to Table N3 for dosing	

[a]Obstructive shock:

Systolic BP < 90 mmHg or vasopressors required to achieve a BP ≥ 90 mmHg despite adequate filling status AND end-organ hypo-perfusion (altered mental status; cold, clammy skin; oliguria/anuria; increased serum lactate).

[b]Persistent hypotension:

Systolic BP < 90 mmHg or systolic BP drop ≥ 40mmHg, lasting longer than 15 min and not caused by new-onset arrhythmia, hypovolaemia, or sepsis.

Selected normotensive patients but with clinical evidence of instability (see indicators below) and a low bleeding risk may derive benefit from thrombolysis:

- Clinical evidence of poor tissue perfusion or right ventricular compromise
- Severe hypoxaemia
- Failure to improve on anticoagulant therapy
- Elevated troponin
- Right ventricular dysfunction on echocardiogram

- Right ventricular enlargement/dysfunction on chest CT

CTPA = Computed tomographic pulmonary angiography; ECHO = Echocardiography; PE = Pulmonary embolism; PEA = pulseless electrical activity; RV= right ventricular; SBP = systolic blood pressure; 60/60 sign = coexistence of acceleration time of pulmonary ejection <60 ms and midsystolic "notch" with mildy elevated (<60 mmHg) peak systolic gradient at the tricuspic valve.
[c]CTPA is considered diagnostic of PE if it shows PE at the segmental or more proximal level.

Contraindications to thrombolysis

ASSESS FOR POSSIBLE CONTRA-INDICATIONS before administering (refer to Table N2).

In an immediately life-threatening PE, 'absolute' contraindications may become 'relative'.

Table N2 - Contraindications to PE thrombolysis, relative and absolute

ABSOLUTE CONTRAINDICATIONS	RELATIVE CONTRAINDICATIONS
• Hypersensitivity to the active substance or to any of the excipients • Active clinically relevant bleeding • Recent severe gastrointestinal bleeding • Recent major surgery • Recent cerebrovascular accident (e.g., within 2 months) • Recent trauma including cardiopulmonary resuscitation, thoracic or neurosurgery (e.g., within 2 months) • Severe hypertension • Severe hepatic or renal insufficiency unless the patient is receiving renal replacement therapy • Blood coagulation defects and severe thrombocytopenia • Aneurysm and arteriovenous malformation • Intracranial neoplasm or other neoplasm with risk of haemorrhage • Acute pancreatitis or pericarditis or bacterial endocarditis or sepsis • Recent obstetric delivery	• Recent surgery • Severe cerebrovascular disease • Moderate coagulation defects including those due to severe renal or hepatic disease • High likelihood of a left heart thrombus (e.g., mitral stenosis with atrial fibrillation) with possible risk of cerebral embolism • Cavernous pulmonary diseases • Genitourinary tract diseases with existing or potential sources of bleeding (e.g., implanted bladder catheter) • Known septic thrombotic disease • Elderly patients, especially those over 75 years of age • Concomitant administration with other thrombolytics, anticoagulants or anti-platelet agents may increase the risk of bleeding • Concomitant administration of urokinase with angiotensin converting enzyme (ACE) inhibitors, may increase the risk of angioedema

Thrombolysis Treatment

Thrombolysis for PE should be delivered in an appropriate clinical setting with adequate clinical monitoring facilities. These include:

- Emergency Department (ED)
- Coronary Care Unit (CCU)
- Intensive Care Unit (ICU)

The patient should be attached to a cardiac monitor throughout the administration of the thrombolysis.

Therapeutic Monitoring

Before thrombolytic therapy the following laboratory tests are indicated:

- Activated partial thromboplastin time ratio (APTR),
- Prothrombin time (PT),
- Full blood count (FBC).

If heparin has been given it should be discontinued (unless the patient is receiving haemodialysis) and the APTR should be < 2.0 before thrombolytic therapy is started.

Therapeutic monitoring should consist of circulating fibrinogen levels and fibrinogen degradation products. However, these tests do not reliably predict efficacy and bleeding complications.

Table N3 - Alteplase dosing information for PE thrombolysis

ALTEPLASE (rt-PA) DOSAGE REGIMENS[1,2,3]	
Regimen 1 Massive PE with imminent cardiac arrest	**Alteplase** 1) Reconstitute **50mg vial** with **50mls water for injection** provided, using transfer cannula to produce a 1mg/ml solution. 2) Give alteplase **50mg** (50ml) **IV bolus over 1-2 minutes.** 3) In cardiac arrest continue **CPR for 60-90 minutes** post administration of thrombolysis. 4) Repeat dose after 30 minutes if patient still critical. **In patients <65kg actual body weight, total dose must NOT exceed 1.5mg/kg.** In all patients **do NOT exceed total dose 100 mg alteplase** (associated with an additional increase in intracranial bleeding).
Regimen 2 For all other PE patients who meet criteria for thrombolysis	**Alteplase** 1) Reconstitute each **50mg vial** with **50mls water for injection** provided using transfer cannula to produce a 1mg/ml solution. 2) Give alteplase **10mg** (10ml) **IV bolus over 1-2 minutes** then immediately **3)** Give alteplase **90mg** (90ml) as an **IV infusion over 2 hours,** using a syringe driver. **In patients <65kg, total dose must NOT exceed 1.5mg/kg.**

Table N4 - Urokinase dosing information - ONLY for use in event of alteplase shortage

UROKINASE DOSAGE – Use 250,000-unit vials

1) **4,400 units/kg as a loading dose** in 15 ml 0.9% sodium chloride, infused in a peripheral vein over 10 mins.[2,6] **Refer to Table N4a.**
2) Followed by **4,400 units/kg/hr infusion over 12 hrs.**[2,6] **Refer to Table N4b.**
   Dilute each 1,000,000 units (1 million units) to 50mL with 0.9% sodium chloride (20,000 units in 1mL).[5].
3) In cardiac arrest continue **CPR for 60-90 minutes** post initiation of thrombolysis.[7,8]

Urokinase PE Thrombolysis Protocol

Urokinase bolus dosing according to weight

Table N4a – Urokinase **bolus loading dose** according to weight

Bolus dose – using 250,000-unit vials

Weight kg	Dose (weight x 4400 units)	Vial 1 Reconstitute with 5ml 0.9% NaCl Withdraw (mls)	Vial 2 Reconstitute with 5ml 0.9% NaCl Withdraw (mls)	Column 5 Total (mls)	
50	220,000	4.4	N/A	4.4	**Administration advice: Dilute total mls (column 5) to 15mls with 0.9% NaCl and give over 10 mins**
55	242,000	4.8	N/A	4.8	
60	264,000	5	0.3	5.3	
65	286,000	5	0.7	5.7	
70	308,000	5	1.2	6.2	
75	330,000	5	1.6	6.6	
80	352,000	5	2	7	
85	374,000	5	2.5	7.5	
90	396,000	5	2.9	7.9	
95	418,000	5	3.4	8.4	
100	440,000	5	3.8	8.8	
105	462,000	5	4.2	9.2	
110	484,000	5	4.7	9.7	
>110		5	5	10	

Urokinase infusion dosing and rate according to weight

Table N4b - Urokinase **infusion** dosing and rate according to weight

12-hour infusion - administered after bolus

Weight (kg)	Total dose (units) over 12 hours calculated as 4,400 units/kg/hr	Total number of vials required for 12-hour infusion		Rate: Administer diluted volume in mls/hour	Total volume for 12 hr infusion (mls)
50	2,640,000	11	**Administration advice: Dilute each 1 million units (4 x 250,000-unit vials) to 50mL with 0.9% sodium chloride (20,000 units/mL) and give at rate as per next column**	11	132
55	2,904,000	12		12.1	145.2
60	3,168,000	13		13.2	158.4
65	3,432,000	14		14.3	171.6
70	3,696,000	15		15.4	184.8
75	3,960,000	16		16.5	198
80	4,224,000	17		17.6	211.2
85	4,488,000	18		18.7	224.4
90	4,752,000	19		19.8	237.6
95	5,016,000	21		20.9	250.8
100	5,280,000	22		22	264
105	5,544,000	23		23.1	277.2
110	5,808,000	24		24.2	290.4
115	6,072,000	25		25.3	303.6
120	6,336,000	26		26.4	316.8

Post thrombolysis care

- After fibrinolytic therapy has been completed, suitable anticoagulant therapy should be considered provided that APTR is < 2.0.
- APTR < 2.0 – start an unfractionated heparin (UFH) infusion as per Anticoagulation Guidelines Title of Procedural Document (esht.nhs.uk), p.112 , Appendix F, Heparin Intravenous Infusion Pump Protocol.
- If an UFH infusion has previously been started and suspended during thrombolysis, restart the infusion **without the bolus dose**.

When patient is clinically stable:

- If CrCl >30ml/min switch to enoxaparin 1mg/kg twice daily as per Anticoagulation Guidelines Title of Procedural Document (esht.nhs.uk), p.61, Table 26: Enoxaparin dose bandings according to weight and dosing regimen.
- If CrCl 15-30ml/min continue UFH or switch to enoxaparin 1mg/kg ONCE daily with anti-Xa monitoring.

- If CrCl <15ml/min continue UFH infusion.

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East Sussex Healthcare NHS Trust

Venous Thromboembolism Diagnosis, Treatment and Prevention Policy and Procedure

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Version Control Table

Version number and issue number	Date	Author	Reason for Change	Description of Changes Made
V2.2	May 2019	Emma Jones-Davies	Update	Updated to include change in NICE NG89 requirements
V2.3	January 2022	Emma Jones-Davies	Review date moved to allow time to review	Review date changed from May 2021 to May 2022
V2.4	March 2022	Dr Clarke	Addition of appendix and narrative	Appendix I and narrative under section 5.6
V3.0 20230703	July 2023	James Wilkinson	Update	Updated to include changes in NICE guidance and PE pathway
V3.1	August 2024	James Wilkinson	Flowchart added as an appendix	Appendix I added – Flowchart VTE Data imputing process

Consultation Table

This document has been developed in consultation with the groups and/or individuals in this table:

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1. Introduction

The Department of Health (DH) has stated that Venous Thromboembolism (VTE) is responsible for approximately 25,000 preventable deaths per year. Patients who are admitted with a VTE and who have had a previous admission to hospital within a ninety-day period or who are diagnosed with a VTE during an inpatient episode when the reason for admission was not suspected VTE are classified as having a Hospital Acquired Thrombosis (HAT). The Trust aims to implement a robust VTE prevention strategy to reduce the incidence of HAT and improve patient safety.

This document describes the Trust wide multi-disciplinary processes relating to VTE prevention and risk management for all adult patient admissions in accordance with Department of Health (DH) and the NHS Standard Contract (Service Condition 22).

Current DH requirements focus on acute care areas though the Trust is committed to VTE prevention across the organisation and this document should be referenced across all inpatient areas, in which VTE prevention strategies are being implemented.

2. Purpose

2.1. Rationale

This document outlines the roles, responsibilities and actions required to drive and implement effective VTE prevention across the organisation. For in depth clinical guidance please refer to Anticoagulant Guidance.

2.2. Principles

All acute care providers are required to demonstrate compliance with the NICE recommendations for Venous Thromboembolism (VTE) prevention (2010, 2012, 2018, 2019, 2020).

The Trust is committed to the implementation of effective VTE prevention, diagnosis and treatment processes in order to reduce the incidence, mortality and subsequent co-morbidities relating to VTE. Current recommendations to manage the risk of VTE are described in NICE guidance NG158 (2020) and QS201(2019)

2.3. Scope

All adult in patients (16 years and above) will be risk assessed on admission and re-assessed ‘as the clinical situation changes’ in line with trust requirements.

Patients assessed to be at risk of VTE will be offered appropriate thromboprophylaxis in accordance with NICE recommendations.

This document also outlines the diagnosis and treatment pathways for VTE together with guidance in the use of mechanical thromboprophylaxis. **For detailed clinical direction in relation to the management of VTE and the use of anti-coagulants, the Trust Clinical Guideline for Anticoagulant Use in Adults, (available on the Extranet)**

This document applies to Divisional leads, Associate Directors of Nursing, General Managers, Heads of Service and Service Managers, Heads of Nursing, Deputy Heads of Nursing, Ward Matrons, Consultants and other Doctors, Registered Nurses and Registered Midwives, Doctors Assistants, Physician’s Associates, Pharmacists,

Operating Department Practitioners, Ward Clerks and Health Care Assistants working in in-patient care environments.
The document applies to all adult patients of sixteen years and above, including day case patients and pregnant women admitted to in patient areas across the Trust, in adherence with the NICE Quality Standard for VTE Prevention. This policy does not apply to patients below sixteen years of age. For specific guidance in relation to VTE prevention in pregnancy, refer to Thromboprophylaxis and Treatment of Venous Thromboembolism in Maternity Policy.

3. Definitions

Anti-embolic Stockings (AES)
Anti-embolic Stockings (AES) are compression stockings used to aid in the prevention of VTE.

CTPA
CTPA stands for Computed Tomographic Pulmonary Angiogram and is used in the diagnosis of Pulmonary Embolism.

Duplex Doppler Ultra sound scan
Duplex Doppler Ultra sound scan is used in the diagnosis of Deep Vein Thrombosis.

D Dimer
D Dimer is a blood test used to aid in the diagnosis of VTE, it is useful in ruling out VTE.

Direct-acting Oral Anticoagulants (DOACs)
The term refers to a group of oral anticoagulant medicines (such as Rivaroxaban, Apixaban) which act directly on the coagulation cascade. They provide an alternative to traditional Vitamin K Antagonists, such as Warfarin. They do not require regular therapeutic monitoring and may be used to treat as well as prevent VTE.

Graduated Compression Stockings (GCS)
Graduated Compression Stockings (GCS) are no longer stockings recommended in the prevention and management of Post Thrombotic Syndrome on diagnosis of DVT. They differ from AES as they have a higher compression profile.

Hospital Associated Thrombosis (HAT)
Hospital Associated Thrombosis (HAT) is used to describe VTE which has arisen following a previous hospital admission (within a preceding ninety day period of diagnosis with VTE) or during the patient's hospital care episode, when the reason for admission was not suspected VTE.

Intermittent Pneumatic Compression Devices (IPCD)
Intermittent Pneumatic Compression Devices (IPCD) aim to reduce venous stasis and enhance fibrinolytic activity to reduce the risk of early clot (DVT) formation.

Thromboprophylaxis (TP)
Thromboprophylaxis (TP) is the term used to describe various measures to prevent VTE and are often described as chemical (pharmacological) and mechanical (the use of Anti-embolic Stockings and Intermittent Pneumatic Compression Devices / Foot Impulse Devices).

Venous Thromboembolism (VTE)
Venous Thromboembolism (VTE) is the term used to describe blood clots which form in the veins, and which can lead to chronic co-morbidities and death. These blood clots are

usually described as Deep Vein Thrombosis (DVT) and Pulmonary Embolism (PE). A PE is a blood clot which has travelled to the lungs and can be fatal.

Vitamin K Antagonist (VKA)
Vitamin K Antagonist (VKA) is used to describe certain anti-coagulants used to treat or prevent VTE; for example, Warfarin.

4. Accountabilities and Responsibilities

4.1. Divisional and Clinical Unit Responsibilities

Divisional leads, General Managers, Service Managers and Heads of Nursing are responsible for the implementation of this policy and for driving the national VTE prevention programme within their areas of responsibility.

Divisional Chiefs, Assistant Directors of Nursing and Midwifery (ADN), Assistant Directors of Operations (ADO) General Managers (GM), Service Managers and Heads of Nursing (HoN) are responsible for ensuring that clinical practice for VTE prevention is compliant with NICE NG89 and trust policy within their specialties.

Divisional Chiefs, GMs, Service Managers and HoNs are responsible for ensuring compliance with the VTE Root Cause Analysis process in line with national requirements (Service Condition 22, NHS Standard Contract). They are also responsible for the dissemination of learning from RCAs within their Divisions and for investigating incidents on [redacted] including Serious Incidents, when fatal preventable Hospital Associated Thrombosis cases are identified for review.

The Divisional teams are responsible for the implementation of regular audit within their departments / specialties to comply with the NHS Standard Contract for Acute Services, with oversight and monitoring by the appropriate leads.

4.2. Consultants

The consultant in charge of the patient is responsible for ensuring that VTE Risk Assessment is undertaken and appropriate thromboprophylaxis is offered. They are also responsible for compliance with the Hospital Associated Thrombosis (HAT) Root Cause Analysis process and any Duty of Candour issues arising as a result of the reporting of preventable HAT Serious Incidents. Please refer to section 8.3 Hospital Associated Thrombosis Root Cause Analysis process in section 8.3, page 26.

4.3. Doctors

Doctors are responsible for carrying out VTE risk assessments as part of the clerking/admission process. They are also responsible for re-assessment of VTE and bleeding risk ‘as the clinical situation changes. Risk Assessment should be recorded using the ratified VTE Risk Assessment tool.

Doctors are responsible for the diagnosis and treatment of patients with VTE in line with this policy and NICE CG158 (2020)

Doctors are responsible for prescribing both chemical and mechanical thromboprophylaxis on the patient’s prescription chart and TTA letter / Electronic Discharge Summary if required post discharge. They are also responsible for specifying the duration of use.
Doctors are also responsible for discussing VTE and bleeding risks with patients, appropriate thromboprophylaxis measures and signs and symptoms of VTE.

4.4. Medical Staff working in Community and Rehabilitation Settings

Patients admitted to Community and Rehabilitation settings direct from Primary Care do not currently require a VTE and bleeding risk assessment on admission. However, it is recommended that the GP / Trust doctor should carry out a VTE Risk Re-assessment on transfer from acute areas to inpatient community areas or where there are concerns about the individual patient's condition raised by nursing staff. The GP / Trust doctor should ensure that appropriate risk management interventions are instigated and communicated to the nursing team. Mechanical thromboprophylaxis should be available as first line prevention intervention in community bedded units.

East Sussex Healthcare Trust staff working in all care settings may raise any VTE risk concerns using the incident reporting process.

4.5. Ward Matrons (W/Ms), Heads of Nursing and Deputy Heads of Nursing (HoNs)

Ward Matrons, Heads of Nursing and Deputy HoNs are responsible and accountable for ensuring compliance with the national and trust VTE requirements including Risk Assessment in their clinical areas.

Ward Matrons and Heads of Nursing (HoNs) are responsible and accountable for ensuring that all nurses and Health Care Assistants (HCAs) in their clinical areas adhere to this policy and have attended relevant training. They are also responsible for providing and storing evidence of attendance and training records to comply with governance requirements.

Ward Matrons, HoNs and ADNs are accountable for ensuring patient safety in their clinical areas, they are accountable for ensuring Ward Clerks accurately enter the VTE Risk Assessment data and for managing arrangements for Ward Clerk cover during periods of absence. They are also responsible managing and reporting compliance with the VTE Risk Assessment process as part of their Integrated Performance Reviews.

4.6. Registered Nurses (RNs), Operating Department Practitioners (ODPs),Registered Midwives (RMs), Physician Associates (PAs) and Doctors Assistants (DAs)

Registered Nurses are responsible for prompting VTE and bleeding risk assessment and reassessment of patients as the clinical situation changes.

RNs are also responsible for ensuring that VTE patient information is provided to patients and recorded in line with the NICE Quality Standard QS201 (2020). Registered Nurses, Operating Department Practitioners and Registered Midwives are accountable for the safe use of mechanical thromboprophylaxis. Health Care Assistants, Student Nurses and Allied Health Professionals may use these devices under the supervision and accountability of the Registered Practitioners above.

RNs and RMs are accountable for ensuring that anti-coagulant medicines are administered safely and for avoiding delays or omissions unless clinically justified. Any delays or omissions should be recorded with appropriate action taken.

RNs/ RMs/ODPS are responsible for recording all mechanical thromboprophylaxis interventions and for fitting and monitoring the safe use of this equipment in their care areas. RNs are also responsible for ensuring that patients are assessed as competent to self-administer Low Molecular Weight Heparin post-discharge where necessary and for ensuring that written and verbal patient information and sharps boxes are provided prior to discharge. Refer to Extended Thromboprophylaxis process (Section 5.3) on page 13.

Both PAs and DAs should prompt VTE assessment.

4.7. Clinical Quality Improvement Lead

The DH require all acute providers to perform individual Root Cause Analysis where patients have developed a VTE following a previous hospital admission (within a 90-day period) or where patients have developed a VTE whilst in hospital for another reason and for women who develop a VTE during pregnancy or six weeks post-partum. At ESHT, the Root Cause Analysis process applies to patients who have died with VTE in part 1a, 1b or 1c of the death certificate and to patients identified by CHKS as having developed a PE within six weeks of a surgical procedure.

The Improvement Lead will monitor in hospital patient deaths from VTE and will instigate the Root Cause Analysis process, reporting cases identified as clinical incidents where patients meet the DH criteria.

4.8. Pharmacists

Pharmacists will also contribute to the on-going monitoring and evaluation of thromboprophylaxis practices Trust wide including prescribing, training, clinical effectiveness, procurement, and regular audit.

4.9. Ward Clerks

Ward Clerks and Administration staff are responsible for inputting VTE Risk Assessment data accurately onto [redacted] / PAS / [redacted] once the patient has been admitted. This data should be entered on to the system as early in the patient's care episode as feasible. Ward Clerks should enter whether the VTE Risk Assessment has been recorded within the 24-hour timeframe by the doctor. Planned surgical patients will generally have their VTE and bleeding Risk Assessment carried out at Pre-operative Assessment Clinic. The data can then be entered as recorded within 24 hours onto [redacted] / PAS. Ward Matrons should monitor and manage the data recording process in their clinical areas.

If Ward Clerks are absent, arrangements should be made by their manager to ensure that the VTE data is entered either retrospectively as a priority, or temporary cover put in place.

4.10 Virtual Wards

VTE assessment should be undertaken on patients referred to the Virtual Wards. From acute assessment areas (including AMU, AAU, SAU, SDEC) or from inpatient wards. Many of these patients will have acute medical conditions, such as infections requiring intravenous antibiotics, and may have relatively restricted mobility compared to their usual state. Patients admitted to virtual wards should be VTE assessed at referral.

4.11. All Staff

All staff (including non-accountable staff) required to measure and fit AES and Intermittent Pneumatic Compression Devices (IPCD) are responsible for ensuring that they have attended training and are competent to use these medical devices. AES training is available via the Extranet (on video) and training for IPCD is provided by the Medical Device Educators.

5. Procedures and Actions to Follow

5.1 Individual Risk Assessment

To comply with DH requirements, all adult patients (over 16 years of age) will, on admission to acute care areas, receive an assessment of their individual VTE and bleeding risk using the ratified, national tool. The standard Adult VTE Risk Assessment tool is included in the Integrated Patient Documentation and relevant care pathway documents. The tools currently approved for use at ESHT are included in Appendices A, B, C and D.

Doctors are responsible for carrying out VTE risk assessments as part of the clerking / admission process, however it is recognised that due to operational pressures responsibility for VTE risk assessment cannot rest solely with the gateway (assessment) areas. Therefore, a proportion of assessments will be carried out on transfer from the assessment areas. The VTE and bleeding risk assessment must be carried out within 24 hours of admission. Any risk assessments undertaken outside this timeframe will not be included in the trust's compliance reporting data.

Doctors are also responsible for re-assessment of VTE and bleeding risk 'as the clinical situation changes', this should be recorded clearly in the patient's notes / on the paper risk assessment tool.

Doctors are responsible for ensuring that ALL individual VTE and bleeding risk factors are considered and recorded on the risk assessment tool including previous history of VTE and first-degree family history which may not be recorded elsewhere in the notes.

Planned admission patients admitted for day case procedures that require an overnight stay should be re-assessed for VTE and bleeding risk on transfer to the inpatient area.

Patients who are transferred from Critical Care to ward areas will be re-assessed by the doctor responsible for taking over the individual patient's on-going management at the point of transfer.

In certain areas, including Pre-operative Assessment Clinics, Radiology and Day Surgery, Registered Nurses undertake VTE and bleeding risk assessments. Nurse led assessments should be checked with the patient on the day of admission for any changes. VTE risk assessment concerns should be recorded and raised with the relevant doctor on admission. Appropriate thromboprophylaxis interventions should be implemented and recorded in the patient documentation. See Appendix C for Nurse Led VTE Assessment Tool.

Patients transferred to in-patient Rehabilitation and Community care settings within the Trust, will have been risk-assessed as part of their acute care admission. Where patients are prescribed post discharge thromboprophylaxis, the receiving unit / facility will continue with the VTE risk management interventions as prescribed. Where advice is required, all East Sussex Healthcare settings will be supported by the Clinical Improvement Lead.

5.2. Cohort Groups (Appendix G)

Cohorting has previously been agreed, at regional NHS level, for certain patient groups deemed as presenting a similar risk profile, Cohort groups should be entered on to [redacted] / PAS as 'cohorted' for monitoring purposes.
The current list of cohort groups includes:

- All day case patients with local/regional/topical anaesthetic with or without sedation and have NO previous diagnosis of cancer
- non-cancer ENT surgery lasting less than 90 minutes
- non-cancer plastic surgery lasting less than 90 minutes
- non-cancer dental and maxillofacial surgery lasting less than 90 minutes.
- minor ophthalmological procedures (eg. eyelid surgery, cataract extraction)
- bone marrow aspirate and trephine
- renal biopsy
- colposcopy
- dermatological procedures

Refer to **Appendix G** for agreed more detailed, locally agreed VTE cohort group information.

Where patients are risk-assessed, the identification of one or more thrombosis risk factor in the relevant section indicates that the patient is at risk of VTE and thromboprophylaxis should be considered. Where patients are identified as at risk of VTE and at risk of bleeding, mechanical thromboprophylaxis may be indicated. If the patient's bleeding risk outweighs the risk of VTE, chemical thromboprophylaxis will be contra-indicated.

5.3. Risk Assessment for VTE and recommended interventions summary (from Kings Thrombosis Centre)

VTE Risk	SURGICAL PATIENTS* - Recommended T/P	MEDICAL PATIENTS*-
HIGH with low risk of bleeding	Anticoagulant + AES ± IPCD + Encourage early mobilisation and hydration	Anticoagulant + Encourage early mobilisation and adequate hydration
HIGH with significant risk of bleeding	AES ± IPCD + Encourage early mobilisation and hydration	AES +/- IPCD + Encourage early mobilisation and hydration
LOW	Encourage early mobilisation and hydration	Encourage early mobilisation and hydration

* Dosages will vary depending on patient's condition.

Refer to specific pathways for orthopaedic and obstetric patients.

5.4. Chemical Thromboprophylaxis Guidance

Please refer to Anticoagulant Guidance for in depth clinical and prescribing information.

All prescribers should adhere to the Summary of Product Characteristics (SPC) for each drug and consult advice from the British National Formulary (BNF) or Medicines Information where appropriate.

Doctors are responsible for ensuring that patients are offered appropriate thromboprophylaxis including post discharge thromboprophylaxis where indicated in line with NICE NG191). All prophylaxis interventions (mechanical and chemical) should be prescribed on the patient's prescription chart and Discharge Summary (where appropriate) with a specified duration of therapy.

All patients receiving chemical thromboprophylaxis should have baseline platelet, renal and liver function tests to ensure appropriate therapy.

For Medical patients assessed as requiring thromboprophylaxis NICE recommend that Enoxaparin (LMWH) should be administered till the patient's risk is reduced and mobility increases, usually for a period of 5-7 days or for the duration of the in-patient episode, depending on re-assessment of bleeding and clotting risk.

For Surgical patients assessed as requiring thromboprophylaxis, NICE recommend that mechanical TP is used till mobility increases and chemical TP should continue till the patient's risk is reduced. Specific guidance applies to patients undergoing high risk procedures.

For patients with active cancer undergoing major bowel / pelvic surgery, extended thromboprophylaxis for 28 days is recommended (NG191).

Orthopaedic patients undergoing Total Hip Replacement (28-35 days), and Total Knee Replacement (10-14 days) will be offered extended thromboprophylaxis (post discharge) in line with NICE recommendations-please refer to Specialty specific guidelines.

Patients admitted with hip fracture will also require extended thromboprophylaxis (LMWH) for 28 days in line with NICE NG191.

Patients receiving chemical thromboprophylaxis with UFH will be monitored for Heparin Induced Thrombocytopenia (HIT) in line with Anticoagulant Guidance. For patients receiving LMWH, a baseline Full Blood Count -Platelet count, must be performed and unless there are clinical concerns, no further monitoring is routinely required. HIT incidence is generally thought to be low (<0.1%) particularly with LMWH. Where HIT is suspected, advice should be sought from the senior clinician or consultant haematologist in line with Anticoagulation Guidance.

5.5 Thromboprophylaxis and treatment of VTE in Stroke patients

Deep vein thrombosis (DVT) and pulmonary embolism (PE) are common complications of hemiplegic stroke with up to 50% of patients having thrombus in either the calf or thigh of the paretic limb (Kelly et al, 2004). **RCP National Clinical Guideline for Stroke (2016)**

5.6 Evidence underpinning recommendations in stroke patients

The risk of symptomatic intracerebral haemorrhage (ICH) outweighs the benefit from the prevention of venous thromboembolism (VTE) with routine anticoagulation with low dose heparin (including low molecular weight heparin) following acute ischaemic stroke (Geeganage et al, 2013). It is also not possible to predict which patients with acute stroke may be at sufficiently high risk of VTE compared to haemorrhagic complications to inform the targeted use of heparin treatment in selected patients (Whiteley et al, 2013).

The CLOTS 3 trial showed that intermittent pneumatic compression (IPC) using sequential compression with venous refill technology in immobile patients in the first 30 days after stroke is an effective treatment for reducing proximal DVT and improves survival but not functional outcomes (CLOTS Trials Collaboration, 2014). In evaluating the cost-effectiveness of IPC in stroke, NICE recommended that healthcare professionals explain to the patient or their family members or carers that IPC reduces the risk of DVT and may provide an increase in survival, but it will not help them recover from their stroke, and there may be an associated increased risk of surviving with severe disability (NICE, 2015c).

If proximal DVT does occur in a patient with ischaemic stroke, the risk of PE is high and such patients should receive treatment-dose anticoagulation.

If DVT occurs in a patient with ICH there are no randomised trial data to support any particular treatment, but single-centre case series have reported that in such cases a vena caval filter is probably safe and effective for the prevention of PE (Somarouthu et al, 2011). There is no evidence to guide the management of patients with ICH and PE, and the decision to use or to avoid the use of anticoagulant treatment can only be made on the physician's individualised assessment of the balance of risk and benefit.

Recommendations for prevention and treatment of VTE in acute stroke patients

Patients with immobility after acute stroke should be offered intermittent pneumatic compression within 3 days of admission to hospital for the prevention of deep vein thrombosis. Treatment should be continuous for 30 days or until the patient is mobile or discharged, whichever is sooner.

Patients with immobility after acute stroke should *not* be routinely given low molecular weight heparin or graduated compression stockings (either full-length or below-knee) for the prevention of deep vein thrombosis.

Patients with ischaemic stroke and symptomatic deep vein thrombosis or pulmonary embolism should receive anticoagulant treatment provided there are no contraindications.

Patients with intracerebral haemorrhage and symptomatic deep vein thrombosis or pulmonary embolism should receive treatment with a vena caval filter.

5.7. Contraindications and Cautions to Heparins

Doctors and Registered Nurses should be aware of the contraindications to chemical thromboprophylaxis including bleeding risks which should be clearly documented on the risk Assessment tool.

Cautions include use in the elderly, hypersensitivity to heparins, hepatic and renal impairment.

Contraindications include

- Active bleeding
- Platelet count <75 ($x10^9/l$)
- Untreated inherited bleeding disorder
- Previous HIT or allergy to Enoxaparin
- Recent cerebral haemorrhage / head injury
- On therapeutic anticoagulation
- Acquired bleeding disorder
- Severe uncontrolled hypertension
- Recent neurosurgery or eye surgery
- Peptic ulcers
- Severe liver disease
- Oesophageal varices
- Acute bacterial endocarditis
- Patient objection to porcine products

For detailed clinical guidance related to the use thromboprophylaxis /anti-coagulants including managing adverse events, refer to Anticoagulant Guidance.

5.8. VTE Prevention Patient Information

Patients and carers will be offered both verbal and written VTE prevention information as part of the admission and discharge processes. Planned surgical admission patients will be offered information at Pre-Operative Assessment Clinics as appropriate.

Emergency admission patients will be offered information during the inpatient episode. Patients being discharged with extended thromboprophylaxis will be offered Anti-embolic Stockings information where indicated and medicines (including self-injection and sharps management guidance) information. Nurses should record information provision in the patient's notes.

5.9. Extended (Post Discharge) Thromboprophylaxis Process (Chemical and Mechanical)

Where indicated, in line with NICE NG89, patients will be offered extended thromboprophylaxis. If there are concerns regarding post discharge patient compliance and anti-embolic stockings (AES) use, this will be recorded in the notes by the RN and AES will not be supplied.

Prior to discharge the patient (or carer) should have their medicine checked and correlated with the Prescription Chart and Discharge Summary and explained to them (as per joint RPS & RCN Professional Guidance on the Administration of Medicines in
Healthcare Settings (2019) and Trust policy) including duration of treatment, possible side effects (bleeding risks), signs and symptoms of VTE, where appropriate. Verbal consent to administer should be obtained from the patient or carer. Where patients are being discharged with extended chemical thromboprophylaxis, the discharging nurse will ensure that the patient is provided with the appropriate 'Clexane at Home' Patient Information Leaflet, together with the Trust's ratified 'Preventing blood clots' Patient Information Leaflet prior to discharge.

Where patients are being discharged with Low Molecular Weight Heparin, the RN will ensure that the patient or carer consents to self-administer and is assessed as competent in self-injection technique.

Where patients require additional support for post discharge administration of chemical thromboprophylaxis, a district nurse referral may be indicated

The RN should also ensure that the patient / carer is provided with the appropriate Patient Information Leaflet and sharps box and is made aware of the sharps collection arrangements for their locality.

A Waste Transfer / Duty of Care Form for the relevant local council (depending on which area the patient is being discharged to) should be completed and signed by the Discharging Nurse / Health Care Professional, then faxed or scanned (with the HCP signature) or emailed. There are separate Waste Transfer Forms for each local council; these are available by contacting the Anti-coagulation Pharmacist.

The patient should be provided with the appropriate local council's telephone number and advised to contact the council to arrange sharps collection when the course of treatment has been completed.

All extended thromboprophylaxis interventions should be recorded in the patient's notes prior to discharge.

5.10 Post Discharge use of Mechanical Thromboprophylaxis

The NICE Quality Standard for VTE prevention includes the prescribing of extended thromboprophylaxis where indicated. Very occasionally immobile patients may be discharged whilst continuing to use AES as part of their continuing VTE prevention plan.

Checks should be made to ensure suitability and patient compliance post discharge. If patients are unable to apply, remove or wash AES in line with the manufacturer's instructions and do not have adequate support to do this, they should not be supplied. Where AES are indicated but not supplied, the rationale should be documented. Where patients are identified as at high risk of VTE, a District Nurse referral may be indicated in order to support the patient's use of AES at home.

Where patients are discharged with AES and are expected to wear them for longer than 72 hours post discharge, the GP should be informed via the Discharge Summary and responsibility for post discharge monitoring should be transferred to the patient's GP. If patients are discharged with AES and are expected to wear them for more than 72 hours, two pairs should be provided to facilitate washing.

Patients discharged with AES must be provided with verbal and written instructions related to their safe use and prescribed duration of wear and this should be documented in the patient's notes and GP correspondence.

There are currently no processes in place to facilitate post discharge continuation of IPCD therapy. For patients transferred to community and rehabilitation settings, the Equipment Library should be contacted where continuing IPCD use is indicated.

5.11. Clinical Guidelines for the use of Mechanical Thromboprophylaxis

5.11.1. Introduction

Mechanical Thromboprophylaxis incorporating the safe use of Anti-embolic Stockings (AES) and Intermittent Pneumatic Compression Devices (IPCD) are important tools in the prevention of Venous Thromboembolism. The main advantages of mechanical thromboprophylaxis measures are that they do not carry any risk of bleeding and are non-invasive.

This section of the document aims to support Registered Nurses (RNs), Midwives (RMs) and Operating Department Practitioners (ODPs) who are responsible for the safe use of these devices.
Health Care Assistants and other Allied Health Professionals may use these devices under the accountability of the Registered Nurse / Midwife / ODP.

5.11.2. Procedures / Course of Action required

Patients provided with Anti-embolic Stockings (AES) and Intermittent Pneumatic Compression Devices (IPCD) will be measured, fitted, and monitored appropriately in line with the NICE Quality Standard for VTE Prevention. Registered Nurses (RNs and RMs) and Midwives will carry out twice daily skin checks in line with Mechanical Thromboprophylaxis Guidelines.

5.11.3. Risk assessment for VTE and recommended interventions

All VTE risk management interventions should be based on individual risk assessment in accordance with DH requirements. Changes in thromboprophylaxis

intervention should be based on individual re-assessment of risk and documented clearly in the patient's notes and in the Thromboprophylaxis section of the Medicines Order and Administration Chart ('Prescription chart').

For guidance in the use of compression devices to manage other conditions including Post Thrombotic Syndrome, please consult the Vascular Nurse Specialist.

The Trust has standardised on knee length AES for VTE prevention. Thigh length AES are available from the Equipment Libraries on both acute sites for use where patients are undergoing vascular procedures such as Varicose Veins surgery. Where the patient is deemed to be at risk of VTE, appropriate thromboprophylaxis (T/P) should be administered in line with NICE guidance (NG158, 191). Mechanical T/P may be used where there is a risk of VTE together with an identified risk of bleeding. It may be used in combination with chemical T/P, other mechanical T/P or alone.

Refer to specific pathways for Orthopaedic patients and Obstetric patients. * Dosages will vary depending on patient's condition.

Where indicated, Mechanical Thromboprophylaxis should be used till the patient's mobility is restored relative to the patients 'normal' state.

NICE (2010) define reduced mobility as 'Bed bound, unable to walk unaided or likely to spend a proportion of the day in bed or chair' (NICE 2010 Venous Thromboembolism: reducing the risk of venous thromboembolism (deep vein thrombosis and pulmonary embolism) in patients admitted to hospital (Clinical GuidelineNG89, NG158, QS201).

Mechanical Thromboprophylaxis modalities in use at East Sussex Healthcare Trust include Fitlegs Anti-embolic Stockings (AES) and Huntleigh Flowtron Universal Intermittent Pneumatic Compression devices (IPCDs). This policy applies specifically to these makes and models of equipment.

This guideline will describe the correct use of Anti-Embolism Stockings (AES). AES aid in the prevention of VTE in the immobile patient by reducing venous stasis (pooling) and passive venous distension, both of which can trigger the formation of blood clots.

Fitlegs AES comply with the Sigel profile to exert approximately 18mmHg compression at the ankle, 14mmHg at the mid-calf point and 8mmHg at the upper thigh in accordance with NICE recommendations.

Correct measuring, application, and monitoring of the use of AES in accordance with NICE is essential and is the responsibility of RNs, RMs, ODPs across the Trust. Health Care Assistants and Students may undertake application of AES and IPCD under supervision by a registered practitioner. Incorrect application can result in tissue damage, heel ulceration and permanent circulatory impairment.

Daily monitoring including correct fitting and twice daily skin checks should be carried out to ensure patient safety in line with the NICE Quality Standard for VTE and recorded in the patient's notes.

Where AES are prescribed, they should be used until the patient's mobility has returned to their 'normal' level. Patients should be re-measured every 72 hours whilst they are in hospital to monitor for changes in their size requirements.

AES are single patient use items and can be washed up to sixteen times. They should be changed every 72 hours (or sooner if soiled) both in hospital and at home. They can be washed by hand or machine at a maximum of 75 degrees. They must not be bleached or tumble dried, and patients should be issued with washing instructions where appropriate.

AES should be worn for 23.5 hours per day and removed for up to 30 minutes to check skin integrity and facilitate personal hygiene.

Oily substances may damage the material and should be avoided, aqueous solutions should be used to moisturise the patient's legs.

5.11.4. Contra-indications

AES and IPCDs are contra-indicated in the following conditions:

- Known or suspected acute DVT / PE*
- Suspected or confirmed Peripheral Arterial Disease-intermittent claudication, rest pain, aneurysmal disease, vasospastic disease
- Peripheral neuropathy Cellulitis
- Previous skin grafts, gangrene, dermatitis, gout, skin lesions Absent foot pulses / Doppler Pressure Index <0.8
- Femoral popliteal bypass grafts and lower limb arterial bypass Extensive swelling or pitting oedema
- Pulmonary oedema
- Acute Stroke (AES ONLY-use full leg IPCD)
- Allergies to fabric components (NB Fitlegs AES are Latex Free)
- Where compliance problems are identified

Mechanical Thromboprophylaxis should be used with caution in the following conditions, consult medical, TVN or Vascular Nurse advice as appropriate:

- Diabetes
- Extreme leg deformity
- Confirmed or suspected Ischaemic Heart Disease
- Current or previous history of leg, foot and heel ulceration
- Fragile skin and trophic skin changes (cold, pale, shiny, hairless limb)
- Congestive Cardiac Failure (do not use IPCD)
- Patients on Noradrenaline

Staff should ensure that the arterial status of the patient is sufficient to allow safe compression. In certain circumstances a Doppler ultra-sound will be indicated to confirm the Ankle Brachial Pressure Index (ABPI) where there are doubts about arterial status. In these circumstances, the relevant medical team should be contacted for further assessment. The Vascular Nurse Specialist may also be contacted for advice before applying AES.

All VTE prevention interventions should be recorded in the patient's notes. When providing AES to patients, the Fitlegs AES packaging which contains comprehensive user instructions should be issued to the patient / carer and recorded as above.

5.11.5. Process for the application of knee length AES

Action	Rationale
Discuss the procedure with the patient ascertaining if there are contra-indications, explaining the rationale for use and gain consent where possible.	To assess the patient for suitability, involve the patient in decisions around care and ensure compliance.
Locate the measuring point two fingers above the ankle bone	To ensure that the stockings fit correctly.
Measure both ankles in Centre Metres (CM) using the colour zoned measure tape supplied	The measure tape colour zone indicates the size required.
Note the size (s) indicated and ankle circumference. Observe the shape and size of both legs for any difference or abnormality.	Occasionally patients may require two different sized garments where there is a difference in limb proportion.
Select the correct colour coded size(s) for the patient.	Measurement tape and packs of stockings are colour coded to aid in correct measuring and fitting.
Ensure the garment is not inside out and insert your hand in as far as the heel pocket.	To fit the stocking correctly in accordance with the manufacturer's instructions.
Grasp the centre of the heel pocket and keeping hold of it, turn the stocking inside out. Turn back to the heel area only.	As above.
Ease the stocking over the foot ensuring the heel patch is aligned under the heel.	To ensure correct fitting.
Gently ease the stocking over the ankle and up the leg ensuring that the fabric is not dragged against the skin.	To avoid tissue damage.
Smooth out any creases on the foot ensuring that the top of the toes are covered and the open section is located under the toes area. Do not push the toes through the open section.	To avoid tissue damage.
Stretch the stocking over the calf, up to two fingers below the back of the knee joint, smoothing out any wrinkles. Ensure that the band at the top is flat against the skin and not rolled over.	To prevent tourniquet effect and ensure blood flow is not compromised
Check the patient 30 minutes after initial application to ensure that there are no adverse effects.	Monitoring to ensure patient safety.
Document the size, date issued, date due to be changed, and recommended duration of wear.	To comply with NICE Quality Standard and to ensure that all team members are aware of the date to change and date to discontinue use.

Ensure the patient is comfortable. Explain the need to report any changes of sensation, swelling or discolouration in the toes and feet to a member of the care team.	Compliance may be affected if the patient is uncomfortable. In some patients it may be necessary to try a smaller or larger size. Changes in sensation etc. could indicate circulatory impairment and AES should be removed without delay.
Monitor use and document daily. Remove the stockings for up to 30 minutes each day to check the patient's skin condition and clean and dry the patient's legs and feet.	AES should be worn for 23.5 hours per day for maximum effectiveness. Personal hygiene and skin checks are essential to basic care. Documentation provides evidence of care.
To remove, grasp the top of the stocking and pull down gently over the calf, heel, and foot, taking care not to damage the skin.	Care in removing stockings is essential in preventing damage to the patient's skin.
Observe for any damage to the skin and remove the stockings as necessary. Contact the Tissue Viability Nurse as soon as possible and document.	To prevent further complications and to gain advice as to future management.
Where tissue damage has been identified, alert the relevant medical team so that the patient's VTE prevention plan may be re-evaluated.	To ensure that the individual patients VTE risk is managed using appropriate interventions.
Re-measure the patient's legs and document every 72 hours and as the clinical situation changes	Re-measuring is an essential part of monitoring use to ensure that stockings fit properly as the patient may lose or gain weight whilst in hospital. Swelling and oedema may also alter leg dimensions.
Ensure that stockings are changed every three days whilst the patient is in hospital. AES are single patient use-do not dispose if patient is to be discharged with AES as these can be laundered by the patient / carer on discharge.	In line with the manufacturer's instructions and to ensure effective management of resources.
Document that you have issued the patient with the AES packaging which contains user instructions and care advice where appropriate.	To comply with the NICE Quality Standard for VTE and trust policy.
Avoid using oil-based creams and emollients where possible, use aqueous solutions.	These substances can damage the fabric of the stockings.

5.11.6. Process for the application of thigh length AES

Action	Rationale
Refer to section 5.11.5. Measure the ankle as for knee length stockings, then measure the widest part of the thigh and ensure that it does not exceed the maximum thigh measurements set out by the manufacturer.	To aid in correct fitting- refer to the packaging which contains the maximum thigh measurement range. If in doubt advise the Equipment Library of the patient's thigh measurements in CM so the correct size can be provided.
Follow the procedure as above pulling the stocking up over the knee ensuring that the darker colour section ends below the knee. Ease the top band up the thigh to rest below the buttocks.	The darker zone exerts a different (higher) level of compression in order to be effective.
If the patient's thigh is long, stretch the upper part of the stocking till it is at the desired length, smoothing out any wrinkles and ensuring the top does not roll over.	The stockings are designed to stretch to the required length. The band should lie flat against the patient's skin to avoid tourniquet effect.
Ensure the patient is comfortable. Explain the need to report any changes of sensation, swelling or discolouration in the toes and feet to a member of the care team.	Compliance may be affected if the patient is uncomfortable. In some patients it may be necessary to try a smaller or larger size. Changes in sensation etc. could indicate circulatory impairment and AES should be removed without delay.
For removal, refer to below knee stockings guidance as above.	

If the patient has a large ankle compared to calf, or small calf, the next smaller size stocking may be indicated.

If the patient has a large calf compared to ankle or smaller ankles, or long large feet, the next larger size may be indicated.

Patients who are undergoing decolonisation for MRSA should have their AES changed every day to ensure effective decolonisation.

5.11.7. Intermittent Pneumatic Compression Devices (IPCD) use

IPC devices work by augmenting venous blood flow velocity, thus reducing venous stasis and by enhancing early fibrinolytic activity to reduce the risk of clot formation. Contra-indications and cautions reflect those relating to AES use and are listed on page 16 (Section 5.5.4)

IPC devices are useful in VTE prevention for both medical and surgical patients where there is an identified risk of VTE together with a risk of bleeding.

Patients should be consulted, and consent obtained prior to use wherever possible. This should be documented including the date on which therapy started.

IPC devices are used widely within the Operating Theatre setting where patients are immobilised. For intra and immediate post-operative guidance refer to Local Protocol for the Use of Compression Devices to Prevent Deep Vein Thrombosis in the Operating Department.

IPCD should be applied on admission or prior to induction of anaesthesia where possible and continued in the recovery phase until anaesthetic effects have worn off. Ideally therapy will continue with minimal interruption (garments only should be removed to perform skin checks and hygiene) till the patient's mobility level has increased and they are no longer confined to bed or chair.

The manufacturer recommends that the device is used for a minimum period of 72 hours or until the patient's mobility has increased.

IPCD can be applied to one limb if necessary intra-operatively, however both limbs should be connected to the device as soon as practicable.

IPCD garments are deemed as Single Patient Use, however the Trust has accepted re-use in certain controlled situations, please refer to the Local Protocol for the Use of Compression Devices to Prevent Deep Vein Thrombosis in the Operating Department.

IPCD should be used to manage the risks of VTE in Stroke patients deemed at high risk with reduced mobility provided there are no contraindications as described in 5.1.5.

Where IPCD is indicated in general care areas, garments and devices are accessible from the Equipment Libraries. The garments should be labelled with the patient's name to avoid multiple patient use and to reduce the risk of cross infection.

AES should not be used purely as a skin barrier in conjunction with IPCD.

Stockinettes should be made available where a non-sterile skin barrier is required though neither AES nor stockinettes offer any protection against infection risk.

IPCD can be used in certain cases where AES are not suitable for example where the patient objects to AES or is allergic to the AES fabric. They should not be used for patients who are mobile as their use necessitates movement restriction.

As a minimum, twice daily safety checks should be made to monitor and prevent any damage to the patient's skin, all checks should be recorded in accordance with NICE Quality Standards.

IPCD use should be discontinued immediately if the patient reports tingling, numbness or discomfort associated with the device. Discontinuation and the rationale should be recorded in the patient's documentation.

Any damage to the patient's skin should be incident reported and the TVN or Vascular Nurse should be contacted as soon as possible for advice.

IPC devices should not be used in known or suspected acute Deep Vein Thrombosis (DVT), phlebitis, severe Congestive Cardiac Failure, or acute Pulmonary Embolism.

If the patient has a large ankle compared to calf, or small calf, the next smaller size stocking may be indicated.

If the patient has a large calf compared to ankle or smaller ankles, or long large feet, the next larger size may be indicated.

Patients who are undergoing decolonisation for MRSA should have their AES changed every day to ensure effective decolonisation.

6. Diagnosis and Management of VTE

Where patients present with suspected VTE (unless haemodynamically unstable), they will be referred via the GP or A&E to the Medical Assessment Units or Same Day Emergency Care (SDEC). Patients will be investigated and managed following the VTE pathways.

GPs may also opt to manage their own patients presenting with suspected VTE. GPs will carry out investigations including D dimer and Pre-test Probability assessment to aid diagnosis in line with the joint Clinical Commissioning Groups DVT Assessment and Treatment Scheme. GPs may access the Trust's Ultrasound service. Where possible a same or next day appointment will be arranged. Where indicated, treatment with anticoagulation should be commenced. A written USS request should accompany the patient. Ultrasound results will be verbally reported to the practice on the day of the examination or the following morning. A written report will follow. GPs will be responsible and accountable for ongoing management, initial and longer-term monitoring of anti-coagulation.

Where DVT or PE is suspected the doctor responsible for patient assessment should undertake a Pre-Test Probability assessment (PTP), using the Two-Level Wells Score or equivalent in line with NICE NG158 Venous thromboembolic diseases: diagnosis, management, and thrombophilia testing (2020).

If PTP is positive (2 level Wells >2), a proximal ultrasound scan (USS) should be offered within 4 hours and if 2 level Wells score is negative, a D-dimer test should be considered. A Full Blood Count (FBC) and Urea and Electrolytes (U&E) should also be initiated. If the USS is unavailable within 4 hours, consider a D-dimer and interim treatment dose of anticoagulant. If the D-dimer is positive but the USS is negative, re-scan in 6-8 days.

If PTP is low, proceed to a D-dimer test and if D-dimer is positive, arrange an USS in 4 hours, or offer an interim treatment dose of anticoagulant and scan within 24 hours.

Doctors may also consider the use of NICE approved Direct Oral Anticoagulants (DOACs) where deemed clinically appropriate, in line with the trust's Anticoagulation Guidance.
If the Doppler Ultrasound confirms the presence of DVT, a senior medical review is required, and a follow up appointment should be arranged with GP.
All patients under investigation for acute VTE (PE or DVT) should be screened for possible manifestation of occult cancer. Consultation should aim to uncover any symptoms of common solid tumours (abdomen, chest, back pain, cough, weight loss etc.). A rectal examination should also be performed on all patients with a breast examination recommended for females.

Further investigation or imaging is not recommended by NICE unless specific symptoms or signs indicate. (NG12 2015,2021, and NG158, 2020)

A chest X-ray is indicated for all patients and blood tests including Full Blood Count (FBC), Liver Function Tests (LFTs). A PSA test should also be considered for male patients. Any abnormal finding should prompt a senior medical review.

Doctors may also select from the other Direct Oral Anticoagulants (DOACs) according to the risks and benefits based on individual assessment and patient preference.

Please refer to Anti-coagulant Guidance for in depth advice including management of patients with renal failure.

Patients discharged on anti-coagulant therapy will be provided with an alert card and relevant patient information including information on side effects.

Unfractionated Heparin should also be considered for patients with an increased risk of bleeding and patients with PE and haemodynamic instability-see Anticoagulant Guidance.

Patients with active cancer may be managed with a DOAC (eg Rivaroxaban), or with Low Molecular Weight Heparin for 3-6months, unless contraindicated. Consideration should be given to lifelong anticoagulation.

Fondaparinux may be considered for patients who object to porcine products, providing renal function is normal.

Vitamin K Antagonists (VKA), where indicated, should be instigated within 24 hours of diagnosis to patients with a confirmed proximal DVT or PE with no underlying cancer. Regular INR monitoring arrangements should be made via the patient's GP.

Treatment with VKA should be reviewed at three months by the GP. The duration of treatment with VKA may be extended beyond three months for patients with an unprovoked proximal DVT or unprovoked PE, depending on review of the risks and benefits to the individual patient.

For detailed clinical guidelines relating to the use of VKA Anticoagulants including cautions and contraindications and the management of bleeding / adverse events please refer to Anticoagulant Guidance.

All patients who are newly initiated on to VKA therapy in acute care areas will be provided with a NPSA Oral Anticoagulation Therapy patient information pack and alert card prior to discharge from hospital. Refer to Policy and Process for the provision of patient information for newly initiated Oral Anticoagulation.

Patients with unstable PE (syncopal, hypotensive, or hypoxic) should be considered for further tests including measurement of Right Ventricle (RV) and Left Ventricle (LV) transverse diameter on CTPA. Where RV > 90% of LV a same day ECHO should be arranged. A Troponin test should also be considered.

The indications for pharmacological systemic thrombolysis for treatment of acute PE include Patients presenting with systolic BP <90 mm Hg, without a high bleeding risk and patients with a low bleeding risk who are deemed at risk of developing hypotension following commencement of treatment, particularly where there is significant RV dysfunction and raised Troponin level or BNP. The decision to administer systemic thrombolysis must be made by a senior clinician.

At ESHT the first line fibrinolytic drug for systemic thrombolysis is Alteplase. Refer to Anticoagulant Guidance and the Summary of Product Characteristics (SPC) of the drug for further guidance.

Detailed clinical guidance aimed at doctors in the use of Inferior Vena Cava Filters (IVCFs), anti-coagulant use (including monitoring) is available via Quick Links on the extranet home page. IVCFs should be considered only in patients who are unable to receive anticoagulant therapy for example stroke patients with a confirmed VTE.

Inferior Vena Cava Filters (IVCF) may be considered for use by senior doctors where pharmacological anticoagulants are contraindicated or for patients diagnosed with a recurrent proximal DVT / PE despite appropriate anticoagulation therapy. The decision to insert an IVCF should be made by a consultant, following discussion with a Consultant Haematologist where possible. A plan for removal of the IVCF, including intended duration, should be clearly documented in the notes with appropriate referral to Radiology.

Catheter directed thrombolytic therapy (CDTT) may be considered for patients diagnosed with ilio-femoral deep vein thrombosis (DVT) where bleeding risk is low, and the onset of symptoms is less than 14 days duration. The decision to use CDTT will be made by the consultant radiologist liaising with the senior clinician in line with NICE CG144.

Graduated Compression Stockings are no longer recommended to manage the risks of long-term Post Thrombotic Syndrome (PTS), following diagnosis with DVT. Occasionally they may be used for patient comfort purposes.

7. Equality and Human Rights Statement

This policy endeavours to support the delivery of care which is fair and respectful to patients regardless of age, gender, race, ethnicity, religion / belief, sexual orientation and or disability. The policy has been reviewed against the Trust's core values of promoting Equality and Human Rights.

8. Training

Doctors are required to complete the E-learning VTE Module as part of the Induction process, compliance will be monitored, and records held by Post Graduate Medical Education (PGME).

Basic VTE prevention training is provided for clinical staff including nurses and Healthcare Assistants within the Clinical Induction programme and recorded on the Electronic Staff Record.

Bespoke specialty specific training programmes are available for nurses upon request and are currently delivered by the Clinical Improvement Lead.

All relevant training records of attendance for permanent staff should be held on the Trust’s Electronic Staff Record (ESR) system. Records are input on to ESR by Learning and Development.

Training programmes are in place to support the correct use of both Anti-embolic Stockings and Intermittent Pneumatic Compression Devices facilitated by the Medical Devices Educators in line with Trust policy for Medical Devices Training.

An Anti-embolic Stockings training video is available on the Extranet for staff.

RNs, RMs, ODPs are required to attend VTE training relevant to their role. In areas where nurse led risk assessment has been introduced, bespoke training programmes incorporating mechanical thromboprophylaxis are in place.

9. Monitoring Compliance with the Document

9.1. Process for Monitoring Compliance

Compliance with DH and national requirements to risk assess adult patients on admission will be monitored by the Divisional Leads, General Managers, Heads of Service and Service Managers, Heads of Nursing, Deputy HoNs and Ward Matrons. Currently daily operational monitoring can be done using the trust's Executive Information System (EIS).

Weekly electronic VTE Risk Assessment monitoring information is generated by Knowledge Management using EIS and distributed to the trust's senior management team for oversight and assurance.

Compliance with the implementation of this policy will be monitored and reported on at Clinical Outcomes Group meetings.

Where doctors are failing to comply with trust requirements for VTE prevention and management, this will be addressed by the relevant Divisional leads, Service Managers and Senior Medical Advisors or Chief of Service.

If junior doctors persistently fail to undertake their responsibilities in relation to VTE prevention, this will be escalated via the Clinical Outcomes Group and disciplinary action may be taken in accordance with Trust policy.

Where there is a failure to comply by nursing, midwifery and administration staff, the Assistant Director of Nursing, Head of Nursing or relevant Ward Matron will be contacted to take further action as necessary.

Clinical incidents arising from the use of chemical and mechanical thromboprophylaxis will be reported and investigated following the trust's incident reporting procedures.

Monitoring of prescribing practices of anti-coagulant medicines is undertaken by Pharmacists who address prescribing and safety issues direct with the prescriber as part of the prescription chart safety screening process and through training for prescribers.

The Trust is currently not required to assess neonate or paediatric patients for VTE risk, however if mechanical thromboprophylaxis is requested for any individual deemed at risk, every effort will be made to meet this clinical need.

9.2. Monitoring this Policy: Standards/Key Performance Indicators

The Department of Health national VTE goal compliance data (95% of adult patients admitted receive a risk assessment for VTE and bleeding risk on admission to acute care areas) is submitted on a quarterly basis via UNIFY in line with NHS England and Commissioner requirements - the results are disseminated to the Divisional managers to facilitate continuous monitoring at ward /department level and within each Specialty.

The NHS Standard Contract for Acute Services (Service Condition 22) requires acute care providers to perform regular audits of 'appropriate thromboprophylaxis', in line with NICE CG92, currently the Trust has not been asked to provide reports to Commissioners. Regular audits will be planned at Divisional / Speciality level to meet this requirement.

The individual divisional management teams are responsible for ensuring that audits are conducted periodically within each area, with support from the Clinical Effectiveness team.

9.3 Root Cause Analysis process for Hospital Associated Thrombosis (HAT)

The NHS Standard Contract, May 2018 (Service Condition 22) requires acute care providers to perform Root Cause Analysis (RCA) where patients are diagnosed with a VTE having been previously admitted to hospital within a ninety-day period.

RCA is also indicated when a patient develops a VTE during an inpatient episode when the reason for admission was not VTE.

Women who develop a VTE during pregnancy are also required to have a Root Cause Analysis investigation. Patients who meet the DH criteria are described as Hospital Associated Thrombosis cases.

The trust has agreed to focus on RCAs for patients who have died from Pulmonary Embolism (PE) in part 1a, 1b or c of the death certificate and RCAs for patients who have developed a PE within six weeks of a surgical procedure as identified by CHKS.

These are identified and reported using [redacted] by the Clinical Improvement Lead who assigns severity of 3 to ensure escalation to Weekly Patient Safety Summit (WPSS).
WPSS will then assign the investigation to the appropriate division(s) and they will complete the Hospital Associated Thrombosis Root Cause Analysis template as required.

If the investigation findings indicate that the HAT was unavoidable and that all relevant actions to prevent a Hospital Associated Thrombosis were undertaken in line with trust policy and NICE NG158, the investigation will be closed pending any actions for improvement or confirmation that any identified learning has been shared.

The relevant consultant will then be required to record the findings on the mortality database.

If the initial investigation findings indicate that the HAT was potentially avoidable, WPSS will determine who will investigate and complete a comprehensive Serious Investigation (SI) report following the trust's Incident Reporting and Management Policy.

Avoidable Hospital Associated Thrombosis cases will be reported at Clinical Outcomes Group and a sample of avoidable HAT deaths will be included for review at the quarterly mortality review audit to ensure the integrity of the process.

Document Monitoring Table

Element to be Monitored	Lead	Tool for Monitoring	Frequency	Responsible Individual/Group / Committee for review of results/report	Responsible individual/ group/ committee for acting on recommendations/action plan	Responsible individual/group/ committee for ensuring action plan/lessons learnt are Implemented
95% of patients admitted will be risk assessed for VTE and bleeding on admission	Chief Medical Officer	EIS & UNIFY	Monthly via COG / quarterly reporting via UNIFY to	Clinical Outcomes Group	Divisional Leads / Chief of Service / ADoN / HoNs / W/Ms	Divisional Leads
Appropriate Thromboprophylaxis in line with NICE NG89	Chief Medical Officer	Excellence In Care Audits / ad hoc divisional / specialty audits	Quarterly	Clinical Outcomes Group	Divisional Leads / Chief of Service / Consultants / ADoN / HoNs W/Ms	Divisional Leads
Root Cause Analysis for Hospital Acquired Thrombosis	Chief Medical Officer	RCA records	As required	Weekly Patient Safety Summit & Clinical Outcomes Group	Divisional Leads / Chief of Service / Consultants / ADoN / HoNs / W/Ms	Divisional Leads
Training for staff (VTE)	Chief Medical Officer	ESR Report & Training Records from PGME	Annual	Learning and Development / PGME	Learning and Development & PGME	Divisional Leads
VTE Policy document	Chief Medical Officer	Documentation Steering Group & Audit	As required	Clinical Outcomes Group (COG) & Medicines Optimalisation Group (MOG)	Divisional Leads / Chief of Service / Consultants / ADoN / HoNs / W/Ms	Divisional Leads

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Appendix A: Risk assessment for Venous Thromboembolism (VTE)

RISK ASSESSMENT FOR VENOUS THROMBOEMBOLISM (VTE)

All patients should be assessed on admission to hospital or within a maximum of 24 hours.
Patients should be reassessed whenever their clinical situation changes.

1: ASSESS MOBILITY

Assess all patients admitted to hospital for level of mobility (tick one box). All surgical patients, and all medical patients with significantly reduced mobility, should be considered for further risk assessment.

(Tick one box)	Tick		Tick		Tick
Surgical patient		Medical patient expected to have ongoing reduced mobility relative to normal state		Medical patient **NOT** expected to have ongoing reduced mobility relative to normal state	
Assess for thrombosis and bleeding risk below				**Assessment complete** (Sign where indicated)	

2: ASSESS THROMBOSIS RISK

Review the patient-related factors shown on the assessment sheet against **thrombosis** risk, ticking each box that applies (more than one box can be ticked).
Any tick for thrombosis risk should prompt thromboprophylaxis according to NICE guidance.
The risk factors identified are not exhaustive. Clinicians may consider additional risks in individual patients and offer thromboprophylaxis as appropriate.

Patient related	Tick	Admission related	Tick
Active cancer or cancer treatment		Significantly reduced mobility for 3 days or more	
Age >60		Hip or knee replacement	
Dehydration		Hip fracture	
Known thrombophilias		Total anaesthetic + surgery time >90 minutes	
Obesity (BMI >30kg/m^2)		Critical care admission	
One or more significant medical comorbidities (e.g. heart disease; metabolic; endocrine or respiratory pathologies; acute infectious diseases; inflammatory conditions)		Surgery involving pelvis or lower limb with a total anaesthetic + surgery time >60 minutes	
Personal history or first-degree relative with a history of VTE		Surgery with a significant reduction in mobility	
Use of hormone replacement therapy		Acute surgical admission with inflammatory or intra-abdominal condition	
Use of oestrogen-containing contraceptive therapy			
Varicose veins with phlebitis		Information provided to patient – verbally or written	
Pregnancy or <6 weeks post partum (see NICE guidance for specific risk factors)			

3: ASSESS BLEEDING RISK

Review the patient-related factors shown against **bleeding risk** and tick each box that applies (more than one box can be ticked).
Any tick should prompt clinical staff to consider if bleeding risk is sufficient to preclude pharmacological intervention.

Patient related	Tick	Admission related	Tick
Active bleeding		Neurosurgery, spinal or eye surgery	
Acquired bleeding (such as acute liver failure)		Other procedure with high bleeding risk	
Concurrent use of anticoagulants known to increase the risk of bleeding (such as warfarin with INR>2)		Lumbar puncture/epidural/spinal anaesthesia expected within the next 12 hours	
Acute stroke		Lumbar puncture/epidural/spinal anaesthesia **within previous** 4 hours	
Thrombocytopaenia (platelets <75x10^9/l)			
Uncontrolled hypertension (230/120 mmHg or higher)			
Untreated inherited bleeding disorders (eg haemophilia and von Willebrand's disease)			

Physician must review recommended prophylaxis and check for contra-indications before prescribing appropriate thromboprophylaxis on drug chart – document decision below:

Prophylaxis indicated: YES NO (Circle as appropriate)

Chemical / Mechanical Prophylaxis contra-indicated: YES NO (Circle as appropriate)

Document any reason for deviation from recommended guideline: .....

VTE risk discussed: YES NO

Written VTE information given: YES NO DECLINED

Prescriber's name: BLOCK CAPITALS	**Prescriber's signature:**	**Date:** **Time:**
Reassessment Changes:		
Re-assessed by: BLOCK CAPITALS	**Signature:**	**Date:**

All heparins are porcine-derived. Inform patient and if an alternative is required consider Fondaparinux which is artificially manufactured. However, Fondaparinux is contra-indicated if creatinine clearance is <20ml/min. If advice is needed contact the Haematology service or Medicines Information service.
Monitoring: Perform baseline FBC (Platelets) / U & E / LFT before prescribing thromboprophylaxis. Platelet monitoring for HIT is not routinely required for LMWH use.
Detailed guidance on thromboprophylaxis options for patients at risk of VTE is available within the Trust policy "Anticoagulant Guidance" on the intranet. Summary details are available within the Junior Doctors' Handbook.

Appendix B

Obstetrics Risk Assessment Tool Risk Assessment Profile for Thromboprophylaxis during Pregnancy, Labour and Post-partum

PAS Label

Step One: Assess Mobility
Step Two: Assess Thrombosis Risk
Step Three: Assess Bleeding Risk
Step Four: Action If Required

Assess **ALL** Women On Admission To Hospital:

Antenatal /Postnatal ward (admissions and readmissions)
Date of Admission:
Delivery Suite (in labour)
Date of Admission:

To be signed when Risk Assessment completed

Signature:

Print:

Designation:

Step Two

Pre-existing risk factors	**Tick**	**Score**	**Obstetric risk factors**	**Tick**	**Score**
Step one: Assess Mobility – ALL Women (tick one box)		**Normal Mobility**		**Reduced Mobility**	
Antenatal Admission					
Postnatal Admission/Readmission					
Admitted in Labour					
Previous recurrent VTE		3	Pre-eclampsia		1
Previous VTE – associated with contraceptive or pregnancy		3	Dehydration/hyperemesis		1
Previous VTE – by transient major risk factor no longer present		2	Multiple Pregnancy or Assisted Reproductive Therapy		1
Family History of VTE (Parent or Siblings)		1	Caesarean Section in labour		2
Known thrombophilia		2	Elective caesarean section		1
Medical Co-morbidities		2	Mid-cavity or rotational forceps		1
Age over 35years		1	Prolonged Labour (more than 24hours)		1
BMI 30-39 (based on booking weight)		1	PPH more than 1 litre or transfusion)		1
BMI 40 or above (based on booking weight)		2	**Transient Risk Factors**		
Parity more than or equal to 3		1	Current systemic infection		1
Smoker		1	Immobility		1
Gross Varicose Veins		1	Surgical procedure in pregnancy or up to 6 weeks postpartum		2
Add total from both columns (Score of 2 or more = High Risk)					

Decision		
Middle Grade Obstetrician must review recommended prophylaxis and check for contra-indications before prescribing appropriate thromboprophylaxis on drug chart – document decision below: Prophylaxis indicated: F Yes F No Prophylaxis contra-indicated: F Yes F No Document any reason for deviation from recommended guideline:		
Prescriber's name: (BLOCK CAPITALS)	**Prescriber's signature:**	**Date:**

Reassess risks of VTE and bleeding within 24 hours of admission and whenever clinical situation changes – document below:

All heparins are porcine derived – inform women and if an alternative is required consider Fondaparinux only if intolerant to heparin which is artificially manufactured. However,

Changes:		
Reassessed by – name: (BLOCK CAPITALS)	**Signature:**	**Date:**

Fondaparinux is contraindicated if creatinine clearance <20ml/min. If advice is needed contact the Haematology service.

Rationale:

The aim of this risk assessment is to assess all women using the maternity service, based on clinical evidence where available, regarding the prevention of VTE during pregnancy, birth and following delivery.

The National Institute for Health and Clinical Excellence (NICE) guideline on venous thromboembolism (November 2009) includes pregnancy and the puerperium as risk factors and the present guideline aims to be consistent with the clinical practice recommendations included in the NICE guideline.

ROCOG *Green-top Guideline No. 37 November 2009 REDUCING THE RISK OF THROMBOSIS AND EMBOLISM DURING PREGNANCY AND THE PUERPERIUM* states that: 'All women should undergo a documented assessment of risk factors for venous thromboembolism (VTE) in early pregnancy or before pregnancy. This assessment should be repeated if the woman is admitted to hospital for any reason including labour or develops any other problems.'

Appendix C

Preoperative Assessment Nurse Led Risk Assessment Tool

ASSESSMENT FOR VENOUS THROMBOEMBOLISM (VTE)

All patients should be risk assessed on admission to hospital. Patients should be reassessed within 24 hours of admission and whenever the clinical situation changes.

Patient Details – Please attach addressograph

Pre-assessment nurse's pre-assessment of VTE risk: Thrombosis risk

Active cancer or cancer treatment	**Y / N**
Age > 60	**Y / N**
Dehydration	**Y / N**
Known thrombophilias	**Y / N**
Obesity (BMI > 30kg/m2)	**Y / N**
One or more significant medical comorbidities: - heart disease - metabolic - endocrine - respiratory pathologies - acute infectious diseases - inflammatory conditions	**Y / N**
Personal history of VTE (Deep Venous Thrombosis or Pulmonary Embolism)	**Y / N**
First-degree relative with a history of VTE (Deep Venous Thrombosis or Pulmonary Embolism)	**Y / N**
Varicose veins with phlebitis	**Y / N**

Women patients only

Use of hormone replacement therapy	**Y / N**
Use of oestrogen-containing contraceptive therapy	**Y / N**
Pregnancy or <6 weeks post partum	**Y / N**

Bleeding risk

Acquired bleeding (such as acute liver failure)	**Y / N**
Concurrent use of anticoagulants known to increase the risk of bleeding (such as warfarin with INR>2)	**Y / N**
Thrombocytopaenia (platelets<75x10⁹/l)	**Y / N**
Uncontrolled hypertension (230/120 mmHg or higher)	**Y / N**
Untreated inherited bleeding disorders (such as haemophilia and von Willebrand's disease)	**Y / N**

Also, be aware: OTHER ACTION NEEDED FROM PRE-ASSESSMENT:	**Present?**	**Action?**
Is the patient on Warfarin, which might need to be stopped?	**Y / N**	
Is the patient on Clopidogrel and does this need to be stopped?	**Y / N**	
Is the patient on oestrogen-containing contraceptive therapy and having a lower leg procedure, and should the OCP be stopped 4 weeks before surgery, with alternative methods discussed?	**Y / N**	
Is patient a smoker (increased clotting risk) East Sussex Stop Smoking Service 0800 9178896	**Y / N**	
Renal failure or dehydration **MAY NEED A REDUCED DOSE OF PROPHYLAXIS**	**Y / N**	

Pre-assessment nurse's name: (BLOCK CAPITALS)	**Signature:**	**Date:**
Comments:		

VTE RISK DISCUSSED and VTE PATIENT INFORMATION SUPPLIED YES / NO / REFUSED

STEP ONE: ASSESS MOBILITY

Assess all patients admitted to hospital for level of mobility (tick one box).

All surgical patients, and all medical patients with significantly reduced mobility, should be considered for further risk assessment.

STEP TWO: ASSESS THROMBOSIS RISK

Review the patient-related factors shown on the assessment sheet against **thrombosis** risk, ticking each box that applies (more than one box can be ticked).

STEP THREE: ASSESS BLEEDING RISK

Review the patient-related factors shown against **bleeding risk** and tick each box that applies (more than one box can be ticked). Any tick should prompt clinical staff to consider if bleeding risk is sufficient to preclude pharmacological intervention.

Continued…….

Preoperative Assessment Nurse Led Risk Assessment Tool

ASSESSMENT FOR VENOUS THROMBOEMBOLISM (VTE)

Any tick for thrombosis risk should prompt thromboprophylaxis according to NICE guidance. Detailed guidance on thromboprophylaxis options for patients identified as being at risk of VTE is available within the Trust Policy "Anticoagulant Guidance" on the intranet. Summary details are available within the junior doctors' handbook and on posters around the hospital. If advice is required please contact the haematology or medicines information services.

Mobility – all patients (tick one box)	**Tick**		**Tick**		**Tick**
Surgical patient		Medical patient expected to have ongoing reduced mobility relative to normal state		Medical patient NOT expected to have significantly reduced mobility relative to normal state	
Assess for thrombosis and bleeding risk below				**Risk assessment now complete**	

Thrombosis risk

Patient related	**tick**	**Admission related**	**tick**
Active cancer or cancer treatment		Significantly reduced mobility for 3 days or	
Age > 60		Hip or knee replacement	
Dehydration		Hip fracture	
Known thrombophilias		Total anaesthetic + surgical time > 90 minutes	
Obesity (BMI > 30kg/m_2)		Surgery involving pelvis or lower limb with a total anaesthetic + surgical time >	
One or more significant medical comorbidities (e.g. heart disease; metabolic; endocrine or respiratory pathologies; acute infectious diseases; inflammatory conditions)		Acute surgical admission with inflammatory or intra-abdominal condition	
Personal history or first-degree relative with a history of VTE		Critical care admission	
Use of hormone replacement therapy		Surgery with significant reduction in mobility	
Use of oestrogen-containing contraceptive therapy			
Varicose veins with phlebitis			
Pregnancy or <6 weeks post partum (see NICE guidance for specific risk factors)			

Bleeding risk

Patient related	**tick**	**Admission related**	**tick**
Active bleeding		Neurosurgery, spinal surgery or eye surgery	
Acquired bleeding (such as acute liver failure)		Other procedure with high bleeding risk	
Concurrent use of anticoagulants known to increase the risk of bleeding (such as warfarin with INR>2)		Lumbar puncture/epidural/spinal anaesthesia expected within the next 12 hours	
Acute stroke		Lumbar puncture/epidural/spinal anaesthesia within the previous 4 hours	
Thrombocytopaenia (platelets<75x10_9/l)			
Uncontrolled hypertension (230/120 mmHg or higher)			
Untreated inherited bleeding disorders (such as haemophilia and von Willebrand's disease)			

Decision

Physician must review recommended prophylaxis and check for contra-indications before prescribing appropriate thromboprophylaxis on drug chart – document decision below:

Prophylaxis indicated: F Yes F No

Prophylaxis contra-indicated: F Yes F No

Document any reason for deviation from recommended guideline: ……

Prescriber's name: (BLOCK CAPITALS)	**Prescriber's signature:**	**Date:**

Reassess risks of VTE and bleeding within 24 hours of admission + whenever clinical situation changes – document below:

Changes:

Reassessed by – name: (BLOCK CAPITALS)	**Signature:**	**Date:**

All heparins are porcine derived – inform patients and if an alternative is required consider Fondaparinux which is artificially manufactured. However, Fondaparinux is contraindicated if creatinine clearance <20ml/min. If advice is needed contact the Haematology service.

Monitoring: Monitor FBC – check platelets on day 5 of treatment due to risk of thrombocytopenia. Re-check every2-4 days. For specific sub-speciality, check guidance.

Appendix D

Risk Assessment for Venous Thromboembolism (VTE) in Lower Limb Trauma Patients / Trauma Patients who are immobilised in a boot or cast

Name: **Hospital No:**

DOB: **Diagnosis:**

Patients who are non-weight bearing or are expected to have reduced mobility relative to normal state and have either one major or two minor risk factors should be considered for Enoxaparin 40mg daily until mobility increases provided they are not at increased risk of bleeding.

Thrombosis risk

	Yes	No
Weight bearing		
Major risk factors		
Personal history of VTE		
BMI > 30 kg/m^2		
Active cancer or cancer treatment		
Pregnancy or < 6 weeks post partum		
Age > 80 years		
Plaster with ankle in equinus due to Achilles tendon rupture		
Minor risk factors		
Age > 60 years		
Significant medical comorbidities (e.g. heart disease, metabolic, endocrine, or respiratory pathologies; acute infectious disease; inflammatory conditions)		
First degree relative with history of VTE		
On hormone replacement therapy		
On Oestrogen containing contraceptive		
Varicose veins with phlebitis		

Contra-indications/Bleeding Risk

	Yes	No
Active bleeding		
Acquired bleeding (such as liver failure)		
Concurrent use of anticoagulants known to increase the risk of bleeding (such as Warfarin with INR > 2)		
Thrombocytopenia (platelets < 75x10^9/l)		
Uncontrolled systolic hypertension (230/120 mmHg or higher)		
Untreated inherited bleeding disorder (such as haemophilia and Von Willebrand's disease)		

Prophylaxis indicated: Yes [ ] No [ ]

Prophylaxis Contra-indicated: Yes [ ] No [ ]

Patient Information Leaflet provided: Yes [ ] No [ ]

Patient consents and competent to self-inject: Yes [ ] No [ ]

Prescriber's name: Prescriber's signature: Date:

Comments

All heparins are porcine derived- inform patients and if an alternative is required consider Fondaparinux which is artificially manufactured. Fondaparinux is contraindicated if creatinine clearance < 20ml/min

Appendix E

Current List of Agreed Cohort Groups who do not require full VTE Risk Assessment – Guidance for Clinical staff and Ward Co-ordinators

Critical Care Unit admissions (VTE prevention and bleeding risk management is part of the care bundle)-Re-assessment of risk should be undertaken on transfer to general care area in line with NICE CG92 and Trust Policy.

The rationale for cohort decisions is based on patient groups accepted as low risk or where the risk of bleeding outweighs the risk of clotting.
All agreed cohort groups have been agreed by the Medical Director and based on nationally accepted guidance from East of England Strategic Health Authority (2010).

In exceptional circumstances where a patient reverts to an overnight stay due to clinical complications, the receiving ward is responsible for ensuring that a VTE Risk Assessment is carried out on transfer.

Where patients are admitted for planned surgery, having attended Pre-operative Assessment Clinic, the W/C may enter the 'Nurse led VTE Risk Assessment' as done on [redacted] / PAS, however the doctor will be required to re-assess the patient on transfer from theatre to the ward using the Risk Assessment tool in the relevant pathway documentation.

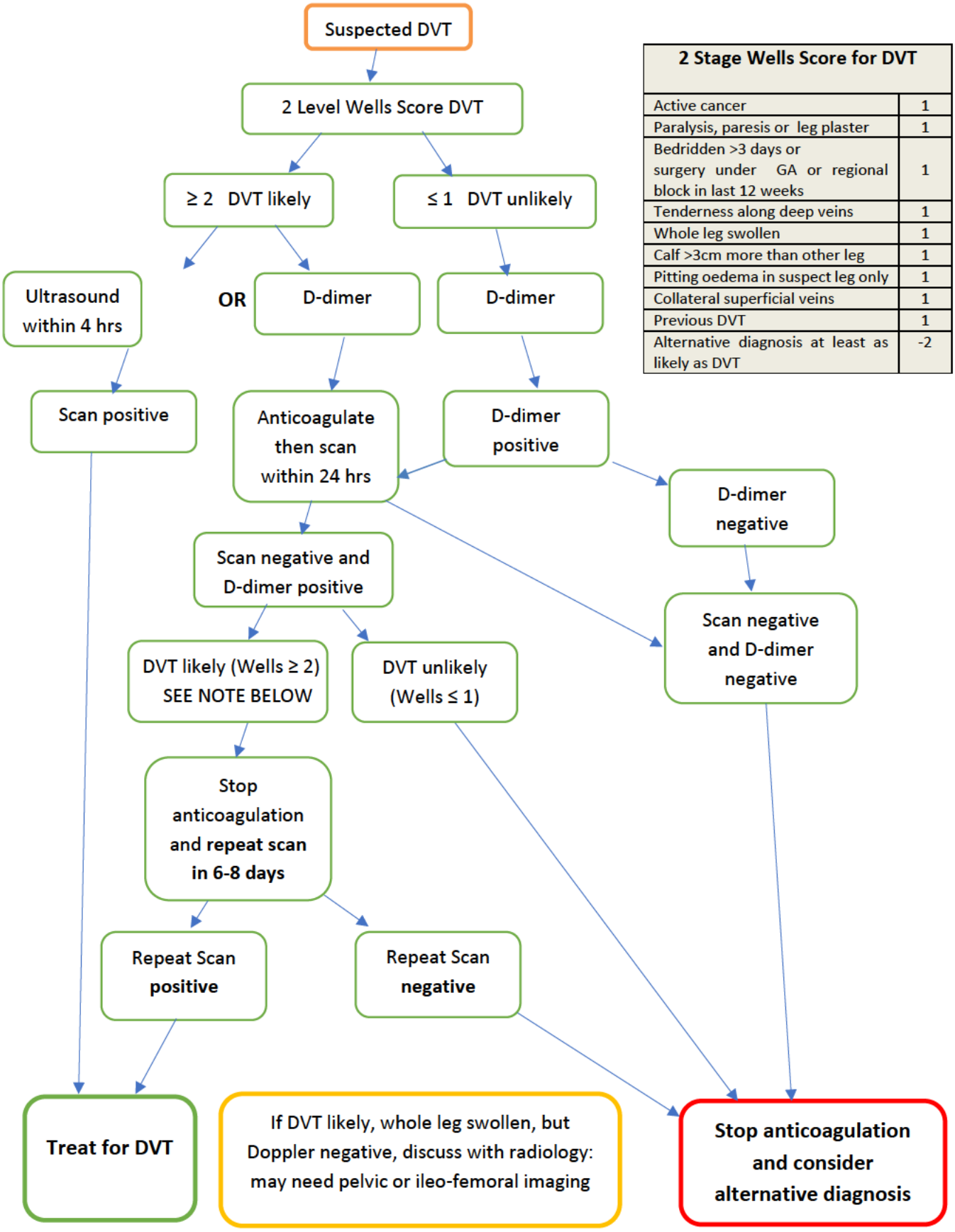
Day Case Medical Procedures	**Day Case Surgery procedures**
Allergy challenges /allergy desensitisation	Dupytrens contracture (Local Anaesthetic-LA)
Blood Transfusions	Carpel Tunnel Decompression (LA)
DVT follow up (Ambulatory Care)	Zadeks / toenail excisions (LA)
PE attendance for CTPA / VQ (Ambulatory Care)	Vasectomy (LA)
Cellulitis Day Attenders (Ambulatory Care)	Excision of lipomas / sebaceous cysts / superficial lesions / moles (LA)
Lumbar puncture	Trigger finger release (LA)
Lung biopsy	Partial fasciectomy (LA)
Pleural Taps (Pleural Effusion drainage / Pleural Biopsies)	Inguinal Hernia Repairs (LA)
Thoracoscopies (+/- pleurodesis)	Spinal probes
Tunnelled chest drain (eg Pleur-X) insertions	All Ophthalmic procedures NOT under General Anaesthetic
Endoscopy patients staying overnight post procedure	Non-cancer ENT surgery lasting < 90 minutes NOT under GA
Cont'd overleaf	Circumcisions (LA)

Day Case Medical	Day Case Surgery procedures
Liver biopsy	Epydidimal cysts
Drainage of ascites	Hydrocele Repairs
PEG changes	Orchidectomy
GI Endoscopy (OGD, Sigmoidoscopy, colonoscopy)	Non cancer Maxillo-Facial surgery lasting < 90 minutes NOT under GA
ERCP	ESWL
Apomorphine Tests	Banding of Haemorrhoids
Tensilon Test	
Botulinium toxin injections	
Chemotherapy (Ward Attenders)	
Platelet Transfusions	
Immunoglobulin Infusions	
Iron Infusions	
Illoprost Infusions	
Monoclonal Antibody Infusions (e.g Infliximab,	
Bone Marrow sampling (Trephine / Aspirate)	
Portacath / Groshong Line	
Once Daily IV Antibiotic infusions	
Pamidronate Infusions	
Short Synacthen Tests	
Glucose Tolerance and fasting	
Dynamic Endocrine Tests	
Haemodialysis day cases	
Planned Angiograms	
Bronchoscopy, thoracoscopy, pleurodesis and tunnelled chest drain patients *staying*	

Should you have any queries or concerns, please contact Emma Jones-Davies, Clinical Improvement Lead on 13 4755 / 07825 99578

Appendix F

Deep Vein Thrombosis Pathway



2 Stage Wells Score for DVT	
Active cancer	1
Paralysis, paresis or leg plaster	1
Bedridden >3 days or surgery under GA or regional block in last 12 weeks	1
Tenderness along deep veins	1
Whole leg swollen	1
Calf >3cm more than other leg	1
Pitting oedema in suspect leg only	1
Collateral superficial veins	1
Previous DVT	1
Alternative diagnosis at least as likely as DVT	-2

Appendix G: Pulmonary Embolism Pathways

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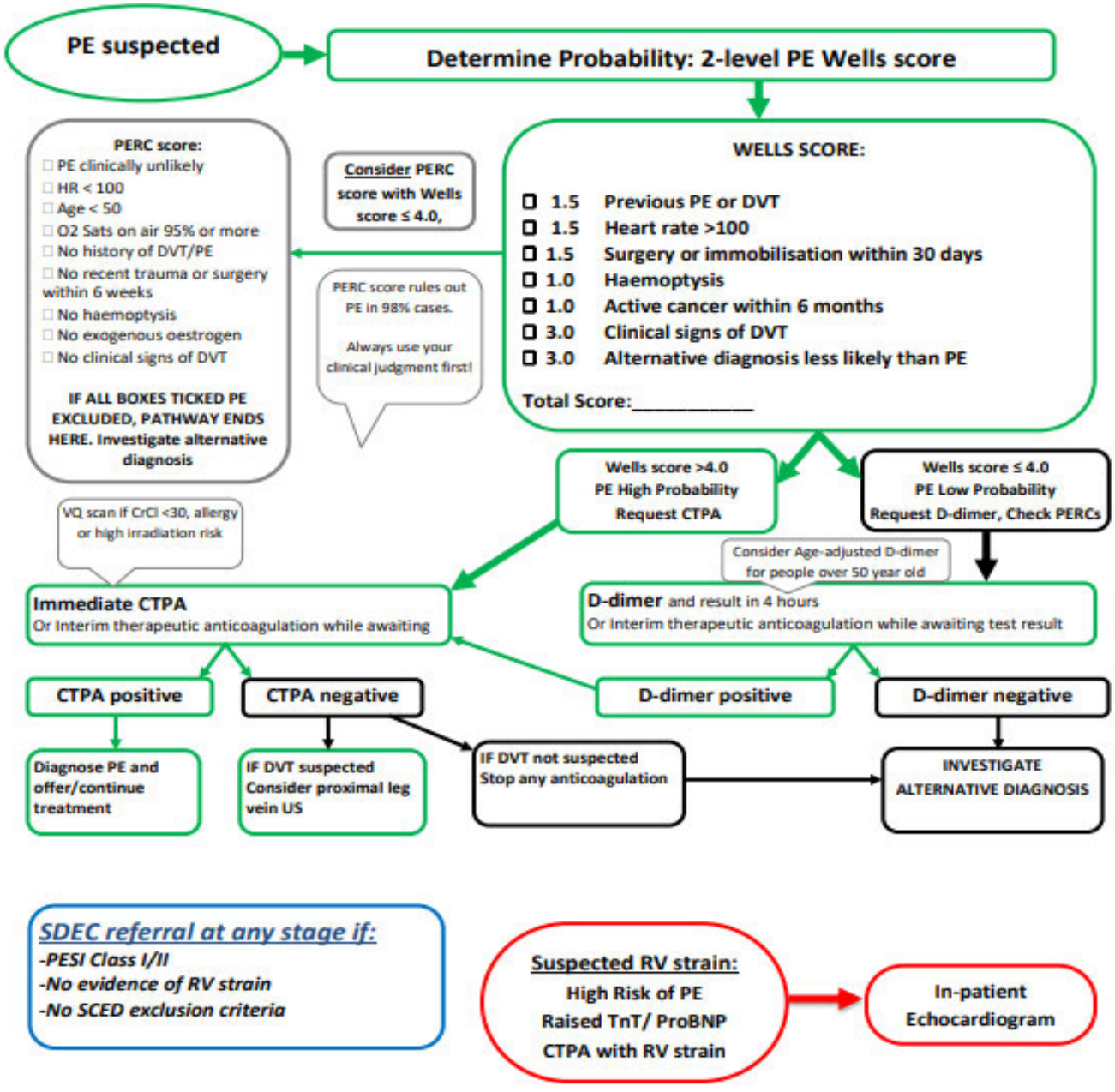
Pulmonary Embolism Pathways

(for adults (>18 years) and not applicable for pregnant patients)



Management of pulmonary embolism

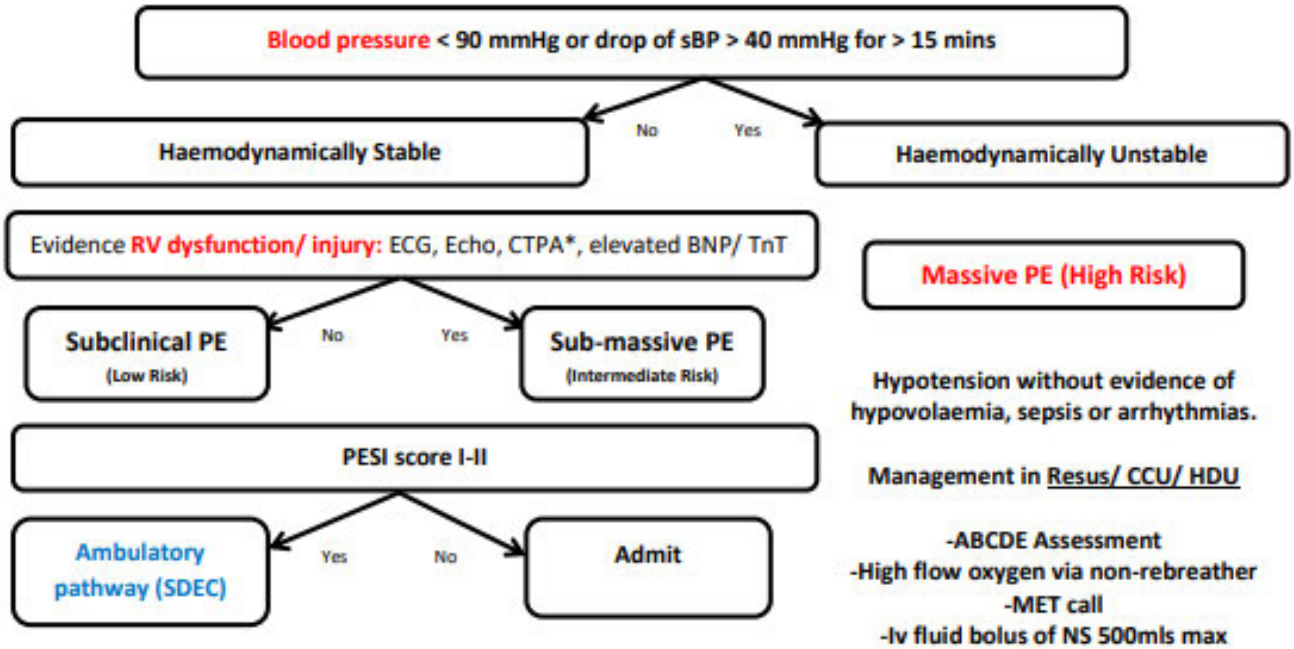
NHS East Sussex Healthcare NHS Trust

Escalation plan:

For full escalation / For inotropes/ For NIV / For ward based care / Pending (document reason).

Assessment:

ABCDE approach, Oxygen Saturation, Blood pressure,
Blood tests (FBC, U+E, LFT, Coagulation screen, troponin, pro-BNP), ECG, CXR, consider ABG



Massive PE (High Risk)

Hypotension without evidence of hypovolaemia, sepsis or arrhythmias.

Management in Resus/ CCU/ HDU

-ABCDE Assessment
-High flow oxygen via non-rebreather
-MET call
-Iv fluid bolus of NS 500mls max
- Consider inotropes/ventilation
-Immediate bedside ECHO
-Urgent CTPA if stabilized
-Inform responsible Consultant

Treatment:
1.Thrombolysis
ALTEPLASE: see Thrombolysis protocol

2. If Contraindications for Thrombolysis or patient fail to improve refer for: Catheter-Directed Thrombolysis to Cardiology in RCSH or Surgical Embolectomy to Cardiothoracic surgeons at RSCH).

SDEC pathway 7days/week

SDEC exclusion criteria:

- ☐ **High Bleeding risk**
- ☐ **Severe liver failure**
- ☐ **Severe renal dysfunction (CrC <20 ml/min)**
- ☐ **Compliance unlikely or social reasons e.g. alcoholism, homeless, IVDU**
- ☐ **Acute mental illness, cognitive impairment**
- ☐ **Unable to return/No phone**

IF ANY BOXES TICKED ADMIT

PESI score:

- ☐ **Age if > 80_____ 1/year**
- ☐ **Male sex_____ 10**
- ☐ **Cancer active or in the past_____ 30**
- ☐ **Heart Failure_____10**
- ☐ **Chronic lung disease___10**
- ☐ **Heart rate >110 bpm_____20**
- ☐ **Systolic BP < 100 mmHg_____30**
- ☐ **Respiratory Rate >30_____ 20**
- ☐ **Temperature <36C_____ 20**
- ☐ **Altered mental status_____60**

Total_____

Class	**I**	**<65**
Class	**II**	**66-85**
Class	**III**	**86-105**
Class	**IV**	**106-125**
Class	**V**	**>126**

***CTPA report should include comment on RV strain**

TREATMENT: anticoagulation (NICE 2020)

Always consult Trust guideline: Clinical Guideline for Anticoagulant Use in Adults, 2020 and BNF

- Measure baseline full blood count, renal and hepatic function, PT and APTT but start anticoagulation before results available. Review and if necessary act on results within 24 hours
- Offer anticoagulation for at least 3 months. Take into account contraindications, comorbidities and the person's preferences.
- After 3 months (3 to 6 months for active cancer) assess and discuss the benefits and risks of continuing, stopping or changing the anticoagulant with the person. See long-term anticoagulation for secondary prevention in the guideline

No renal impairment, active cancer, antiphospholipid syndrome or haemodynamic instability	Renal impairment (see the BNF)	Active cancer (receiving antimitotic treatment, diagnosed in past 6 months, recurrent, metastatic or inoperable)	Antiphospholipid syndrome (triple positive, established diagnosis)
Offer **apixaban** or **rivaroxaban** If neither suitable, offer one of: • **LMWH** for at least 5 days followed by **dabigatran** or **Edoxaban** • LMWH and a **VKA** for at least 5 days, or until INR at least 2.0 on 2 consecutive readings, then a VKA alone	CrCl 15 to 50 ml/min, offer one of: • **apixaban** • **rivaroxaban** • **LMWH** for at least 5 days then **edoxaban or dabigatran** if CrCl ≥ 30 ml/min • **LMWH or UFH and a VKA** for at least 5 days, or until INR at least 2.0 on 2 consecutive readings, then a VKA alone CrCl < 15 ml/min, offer one of: • **LMWH** • **UFH** • **LMWH or UFH and a VKA** for at least 5 days, or until INR at least 2.0 on 2 consecutive readings, then a VKA alone	Consider a DOAC If a DOAC is not suitable, consider one of: • LMWH • LMWH and a VKA for at least 5 days or until INR at least 2.0 on 2 consecutive readings, then a VKA alone NB. Offer anticoagulation for 3 to 6 months Take into account tumour site, drug interactions including cancer drugs, and bleeding risk	Offer LMWH and a VKA for at least 5 days or until INR at least 2.0 on 2 consecutive readings, then a VKA alone

CONTRAINDICATIONS TO ANTICOAGULATION

Active Bleeding	Platelets<75, or Coagulopathy
Recent GI Bleed (within 2 weeks)	Previous intracranial haemorrhage
Recent Stroke (within 2 weeks)	HAS BLED score 4 or more
Recent eye or CNS surgery (< 2 weeks)	

HAEMATOLOGY ADVICE IF:

Severe liver impairment with coagulopathy PE whilst on therapeutic anticoagulation	Allergy to Heparin or Previous Heparin induced TCP History of arterial thrombosis and or miscarriage

IVC FILTER:

If anticoagulation is contraindicated or a PE has occurred during anticoagulation treatment
Consider to discuss IVC filter insertion with IR on call (**document in discharge letter date of insertion and date of removal of IVC filter with IR follow up).**

IVC filter (circle): permanent or temporary

*Date of insertion*_____ *and date of removal*_____

Ambulatory pathway Pulmonary Embolism

SDEC 7 days a week, 08:00-16:00, discuss with SDEC nurse or AAU Consultant

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Indications:	-Low probability of PE -PESI I-II score -No Exclusion criteria	**Referrer responsible for:** ☐ requesting CTPA, ☐ providing treatment, ☐ Informing patient of diagnosis, treatment, and to expect contact from SDEC with scan appointment and further review in the Unit.
Referral:	via eSeacher referral form and e-mail to: esh-tr.AEC-CQ@nhs.net (CQ) or esht.AEC.eastbournedgh@nhs.net (EDGH)or call on Ext: 734547(CQ) or 735384(EDGH)	
SDEC exclusion criteria:	☐ NEWS >4 or PESI III-V class ☐ SBP<100 mmHg, HR > 110 ☐ Sats<94% on air, RR > 24 ☐ High Bleeding risk ☐ Severe renal dysfunction (CrC <20 ml/min) ☐ PE whilst on anticoagulation	☐ Compliance issues: social reasons e.g. alcoholism, homeless, IVDU ☐ Acute mental illness, cognitive impairment ☐ Unable to return/No contact number
PESI score: (confirm Low Risk)	☐ Age if > 80_____ 1/year ☐ Male sex_____ 10 ☐ Cancer active or in the past_____ 30 ☐ Heart Failure_____10 ☐ Chronic lung disease_____10 ☐ Heart rate >110 bpm_____20	☐ Systolic BP < 100 mmHg_____30 ☐ Respiratory Rate >30_____ 20 ☐ Temperature <36C_____ 20 ☐ Altered mental status_____60 Total_____ Class I <65 Class III 86-105 Class II 66-85 Class IV 106-125 Class V >126
Risk Factors	☐ Contraceptive pill ☐ Pregnancy or <6/52 post-partum ☐ Surgery in last 4/52 ☐ Previous VTE ☐ Known Thrombophilia ☐ Malignancy/ Cancer	☐ Air travel > 4 hrs in the last 4/52 ☐ Bedbound ☐ Obesity ☐ IVDU ☐ Family history of VTE
Assessment:	Routine observations and examination Documented Wells and PESI Scores	Full examination for unprovoked PE
Investigations:	No evidence of RV strain (ECG, TnT, or CTPA)	Routine investigations: FBC, U&E, LFTs, Coagulation profile, CXR, ECG. Consider Bone profile, PSA, etc
CTPA (or VQ scan):	Must be completed by referrer (ED)	Request Form should have: PE risk factors, Wells score and/or D-dimer & Creatinine level.
CTPA results:	Must have reported RV state	If negative seek alternative diagnosis
Patient Information:	Explain Diagnosis, Treatment, complications of PE and sides effects of anticoagulation. Complete Appendix D – Patient Counselling Checklist: VKAs & DOACs, p104	Print Appendix from "Clinical guideline of Anticoagulant Use in Adult", 2020, complete and attach to the notes.
Follow up	Insure follow up with relevant specialties or GP	

Unprovoked PE assessment and further investigations to consider		East Sussex Healthcare NHS Trust
Weight loss > 7lbs in 6 months	Yes / No	Yes = consider imaging with abdominal-pelvic CT scan/USS/endoscopy/colonoscopy
Recent abdominal pain	Yes / No	
Recent dysphagia	Yes / No	
Recent alteration in bowel habit/melena	Yes / No	
Haematuria (perform urinalysis)	Yes / No	
Bilateral DVT	Yes / No	
Unexplained PV bleeding	Yes / No	Yes = gynaecological screen
Smoker or smoked within last 5 years	Yes / No	Yes = Review CTPA for malignancy
Male > 60 years	Yes / No	Yes = PSA
Male < 60 years with urinary problems	Yes / No	Yes = PSA
Female aged 25 to 64: ?attended cervical screening	Yes / No	No = refer to GP
Female aged 50 to 70: ?attended breast cancer screening within last 3 years	Yes / No	No = GP to refer
Abnormal screening bloods (FBC/Calcium/LFTs)	Yes / No	Yes = Repeat and consider targeted further investigation
Focused clinical examination complete (including breast and/or testicular exam where indicated)	Yes / No	

Thrombolysis for Massive Pulmonary Embolism pathway

NHS East Sussex Healthcare NHS Trust

Patient Name:	Hospital ID:	DoB:	Date:

Definition of Massive PE :

An acute PE with a systolic blood pressure <90mmHg or a drop in systolic blood pressure of ≥40mmHg from baseline for a period of >15minutes, not otherwise explained by hypovolaemia, sepsis or new arrhythmia.

Decision Making Process:

For consideration for thrombolysis for Massive Pulmonary Embolism there:

- MUST be clinical signs of shock present i.e.: SBP <90mmHg
- AND strong clinical suspicion of PE

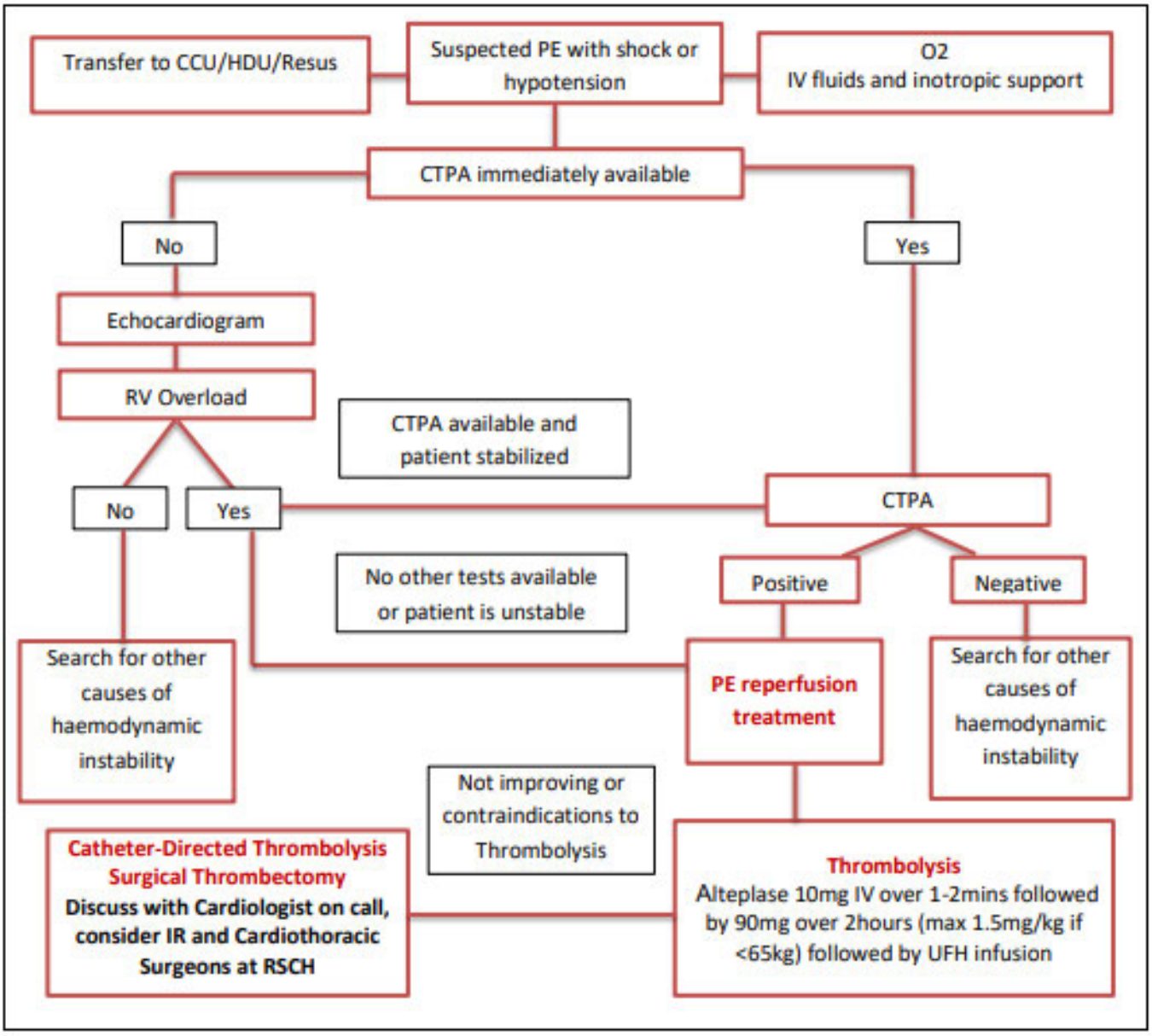
All patients with suspected massive PE need to be urgently assessed by the Medical Registrar On-Call and discussed with AAU or On-call Consultant.

Consent:

Written consent is mandatory, as per best practice guidelines. If the patient is too unwell or unable to provide written consent this must be fully documented as discussed with the relatives if appropriate. **Particular reference should be made to bleeding (approx. 10-15%), especially intracranial bleeds (approx. 2%) and death.**

Location:

Resuscitation area, Coronary Care Unit, High Dependency Unit



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COMPLETE Massive PE Thrombolysis Check List:

	YES	NO	Evidence
Diagnosis / strong clinical suspicion of PE			
Signs of shock: BP <90mmHg or systolic drop ≥40mmHg for 15mins			
CT evidence of PE (or RV Strain on ECHOCARDIOGRAPHY)			
Discussed with Medical Consultant on-call			
Patient in an acute bed (Resus/CCU/HDU)			

Absolute Contra-indications	Y	N	Relative Contra-Indications	Y	N
Haemorrhagic stroke at any time			On oral anti-coagulation with INR >1.5 or DOAC therapy		
Ischaemic stroke in last 6/12			TIA within 6/12		
Central nervous system damage, neoplasms, intracranial or intra spinal surgery at any time.			Pregnancy or within week post-partum. Termination of pregnancy within 1 week.		
Recent major trauma / surgery / head injury (within 2 months)			Refractory hypertension Systolic blood pressure >180mmHg.		
Gastro-intestinal bleeding in last 2/12			Non-compressible punctures		
Known bleeding disorder			Traumatic resuscitation		
Active bleeding			Advanced liver disease		
Aortic dissection			Infective endocarditis / pericarditis		
Allergy to Alteplase or Gentamicin			Active pulmonary TB with cavitation		
Active peptic ulceration			Oesophageal varices		
Acute pancreatitis			Arterial aneurysm		

If yes to ***ANY*** CONTRA-INDICATION discuss with Consultant.

OBTAINED PATIENTS CONSENT FOR THROMBOLYSIS	YES/NO

Absolute and relative contraindications excluded and Consent obtained by:

Signature_____ Date_____

Print Name_____ Designation_____

Medication Check List	tick
ALTEPLASE. BOLUS -10mg over 1-2mins (as per BNF) available in Resus	
ALTEPLASE. IV Infusion – 90mg over 2hours (Max. 1.5mg/kg in patients less than 65kg) (as per BNF)	
Unfractionated Heparin (delay for 8hours if has already had LMWH), check APTT stat and in 6 hrs, if APTT ≤ 1.5 give 5000u bolus and IV Infusion 16u/kg/hr *(see **Clinical Guideline for Anticoagulant use in Adults, p109-111**)*	

NEEDS ADMISSION TO CCU/ HDU FOR 24HRS MONITORING

The patient should be attached to a cardiac monitor throughout the administration of the thrombolysis.

ALTEPLASE (rt-PA) DOSAGE REGIMENS	
PE Thrombolysis (met criteria)	• Reconstitute each 50mg vial Alteplase with 25ml water for injection provided (2 vials in total) • Give Alteplase 10mg (5ml) IV bolus over 1-2 minutes then • Give Alteplase 90 mg (45ml) as an IV infusion over 2 hours using an infusion device • The total dose should not exceed 1.5mg /kg in patients with actual body weight <65kg On completion of the Alteplase infusion, check APTT and again at 6 hours: if APTT ≤ 1.5 give bolus 5000u of UFH heparin or if APTT 1.6-1.9 give 2500u of UFH heparin followed by infusion at **16 units/kg/hr.** This dose should be adjusted to maintain APTT at 2.0-2.59 **(see Clinical Guideline for Anticoagulant use in Adults, p109-111)**.
Cardiac arrest with confirmed or suspected PE	• Reconstitute 50mg vial with 25ml water for injection provided • Give Alteplase 50 mg IV bolus over 1-2 mins • Repeat after 30 minutes if patient still critical • The total dose should not exceed 1.5mg /kg in patients with actual body weight <65 kg In patients who were undergoing CPR at the time of Alteplase administration, continue CPR as per ALS guidelines for **60mins** post administration (at clinician's discretion). If return of spontaneous circulation (ROSC) is achieved then consider commencement of intravenous Unfractionated Heparin infusion **(see Clinical Guideline for Anticoagulant use in Adults, p109-111)**.

Osey Kankam, Viktoriya Clarke, Bipin Pun, Roshana Rajendram East Sussex Healthcare NHS Trust. November 2020 (Version 1). Review Date November 2023.

References:

NICE Venous Thromboembolic diseases: diagnosis, management and thrombophilia testing, 26 March 2020 NG1581 https://www.nice.org.uk/guidance/ng158.

BNF. Alteplase on-line access 23/11/20
https://bnf.nice.org.uk/drug/alteplase.html

Grace G, Ward I. Clinical Guideline for Anticoagulant Use in Adults. 2020

Blackman V, Walker D ESHT PE Thrombolysis guideline, 2020 (pending)

Konstantinides SV, et al. ESC Scientific Document Group. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS) Eur Heart J. 2020;41:543–603.

Chatterjee S, et al. Thrombolysis for pulmonary embolism and risk of all-cause mortality, major bleeding and intracranial haemorrhage: A meta-analysis. JAMA - J Am Med Assoc. 2014;

Appendix H: Equality Impact Assessment Form

Please refer to the accompanying guidance document when completing this form.

Strategy, policy or service name	Venous Thromboembolism Diagnosis, Treatment and Prevention Policy and Procedure
Date of completion	Jan 2024
Name of the person(s) completing this form	Jane Starr
Brief description of the aims of the Strategy/ Policy/ Service	This document outlines the roles, responsibilities and actions required to drive and implement effective VTE prevention across the organisation.
Which Department owns the strategy/ policy/ function	Clinical Opt
Version number	V3.0
Pre Equality analysis considerations	
Who will be affected by this work? **E.g. staff, patients, service users, partner organisations etc.**	Patients, staff
Review date	Jan 2027.
If negative impacts have been identified that you need support mitigating please escalate to the appropriate leader in your directorate and contact the EDHR team for further discussion.	To whom has this been escalated? **Name**: Click here to enter text. **Date**: Click here to enter a date.
Have you sent the final copy to the EDHR Team?	No

2. EIA Analysis

<table>
<tr><td></td><td>☺ 😐 ☹</td><td colspan="5">Evidence:</td></tr>
<tr><td>Will the proposal impact the safety of patients', carers' visitors and/or staff?

Safe: Protected from abuse and avoidable harm.</td><td>Positive

☺</td><td colspan="5">The aim is to ensure that diagnosis, treatment, and monitoring of patients reduces the risk of VTE</td></tr>
<tr><td>Equality Consideration

Highlight the protected characteristic impact or social economic impact (e.g. homelessness, poverty, income or education)</td><td>☺</td><td>Race</td><td>Gender</td><td>Sexual orientation</td><td>Age</td><td>Disability & carers</td></tr>
<tr><td></td><td>☐</td><td>☐</td><td>☐</td><td>☐</td><td>☐</td></tr>
<tr><td></td><td>Gender reassignment</td><td>Marriage & Civil Partnership</td><td>Religion and faith</td><td>Maternity & Pregnancy</td><td>Social economic</td></tr>
<tr><td></td><td>☐</td><td>☐</td><td>☐</td><td>☐</td><td>☐</td></tr>
</table>

<table>
<tr><td>Is the proposal of change effective?

Effective: Peoples care, treatment and support achieves good outcomes, That staff are enabled to work in an inclusive environment. That the changes are made on the best available evidence for all involved with due regards across all 9 protected Characteristics</td><td>Positive</td><td></td></tr>
<tr><td>Equality Consideration

Highlight the protected characteristic impact or social economic impact (e.g. homelessness, poverty, income or education)</td><td>☺</td><td>
<table>
<tr><td>Race</td><td>Gender</td><td>Sexual orientation</td><td>Age</td><td>Disability & carers</td></tr>
<tr><td>☐</td><td>☐</td><td>☐</td><td>☐</td><td>☐</td></tr>
<tr><td>Gender reassignment</td><td>Marriage & Civil Partnership</td><td>Religion and faith</td><td>Maternity & Pregnancy</td><td>Social economic</td></tr>
<tr><td>☐</td><td>☐</td><td>☐</td><td>☐</td><td>☐</td></tr>
</table>
</td></tr>
<tr><td>What impact will this have on people receiving a positive experience of care?</td><td>Positive</td><td>Reduced harm for patients</td></tr>
</table>

Equality Consideration *Highlight the protected characteristic impact or social economic impact (e.g. homelessness, poverty, income or education)*	☺	**Race**	**Gender**	**Sexual orientation**	**Age**	**Disability & carers**
		☐	☐	☐	☐	☐
		Gender reassignment	**Marriage & Civil Partnership**	**Religion and faith**	**Maternity & Pregnancy**	**Social economic**
		☐	☐	☐	☐	☐
Does the proposal impact on the responsiveness to people's needs?	Positive					
Equality Consideration *Highlight the protected characteristic impact or social economic impact (e.g. homelessness, poverty, income or education)*		**Race**	**Gender**	**Sexual orientation**	**Age**	**Disability & carers**
		☐	☐	☐	☐	☐
		Gender reassignment	**Marriage & Civil Partnership**	**Religion and faith**	**Maternity & Pregnancy**	**Social economic**
		☐	☐	☐	☐	☐
What considerations have been put in place to consider the organisations approach on improving equality and diversity in the workforce and leadership?	Positive					
Equality Consideration *Highlight the protected characteristic impact or social economic impact (e.g. homelessness, poverty, income or education)*		**Race**	**Gender**	**Sexual orientation**	**Age**	**Disability & carers**
		☐	☐	☐	☐	☐
		Gender reassignment	**Marriage & Civil Partnership**	**Religion and faith**	**Maternity & Pregnancy**	**Social economic**
		☐	☐	☐	☐	☐

Access
Could the proposal impact positively or negatively on any of the following:

• Patient Choice	Neutral	
• Access	Neutral	
• Integration	Neutral	

Equality Consideration *Highlight the protected characteristic impact or social economic impact (e.g. homelessness, poverty, income or education)*		**Race**	**Gender**	**Sexual orientation**	**Age**	**Disability & carers**
		☐	☐	☐	☐	☐
		Gender reassignment	**Marriage & Civil Partnership**	**Religion and faith**	**Maternity & Pregnancy**	**Social economic**
		☐	☐	☐	☐	☐

Engagement and Involvement How have you made sure that the views of stakeholders, including people likely to face exclusion have been influential in the development of the strategy / policy / service:	Neutral	The views of colleagues have been sought

Equality Consideration *Highlight the protected characteristic impact or social economic impact (e.g. homelessness, poverty, income or education)*		**Race**	**Gender**	**Sexual orientation**	**Age**	**Disability & carers**
		☐	☐	☐	☐	☐
		Gender reassignment	**Marriage & Civil Partnership**	**Religion and faith**	**Maternity & Pregnancy**	**Social economic**
		☐	☐	☐	☐	☐

Duty of Equality Use the space below to provide more detail where you have identified how your proposal of change will impact.	Positive	
Characteristic	**Rating** ☺ ☹ 😐	**Description**
Race	☺	
Age	😐	This policy refers to patients age 16 and over
Disability and Carers	☺	
Religion or belief	☺	
Sex	☺	
Sexual orientation	☺	
Gender re-assignment	☺	
Pregnancy and maternity	☺	A risk benefit decision would be made for individual patients- refer to Maternity policy
Marriage and civil partnership	☺	

Human Rights

Please look at the table below to consider if your proposal of change may potentially conflict with the Human Right Act 1998

Articles		Y/N
A2	Right to life	N
A3	Prohibition of torture, inhuman or degrading treatment	N
A4	Prohibition of slavery and forced labour	N
A5	Right to liberty and security	N
A6 &7	Rights to a fair trial; and no punishment without law	N
A8	Right to respect for private and family life, home and correspondence	N
A9	Freedom of thought, conscience and religion	N
A10	Freedom of expression	N
A11	Freedom of assembly and association	N
A12	Right to marry and found a family	N
Protocols		
P1.A1	Protection of property	N
P1.A2	Right to education	N
P1.A3	Right to free elections	N

Appendix I: VTE Data imputing Process

VTE Data Inputting Process

East Sussex Healthcare NHS Trust

On a daily basis Ward Clerks to extract VTE compliance data from the [redacted]

↓

Ward Clerks input the VTE Data onto PAS

↓

If the patient is admitted out of hours, Ward Clerks are to retrieve the data and input it at a later date

↓

CIS.Development extract the data from PAS

↓

CIS.Development send the weekly report to relevant staff

When looking for VTE data for reporting, sources may include:

[redacted]

Ward Clerks are not to leave the data in the "complete later" section as it will not be counted on the weekly reports.