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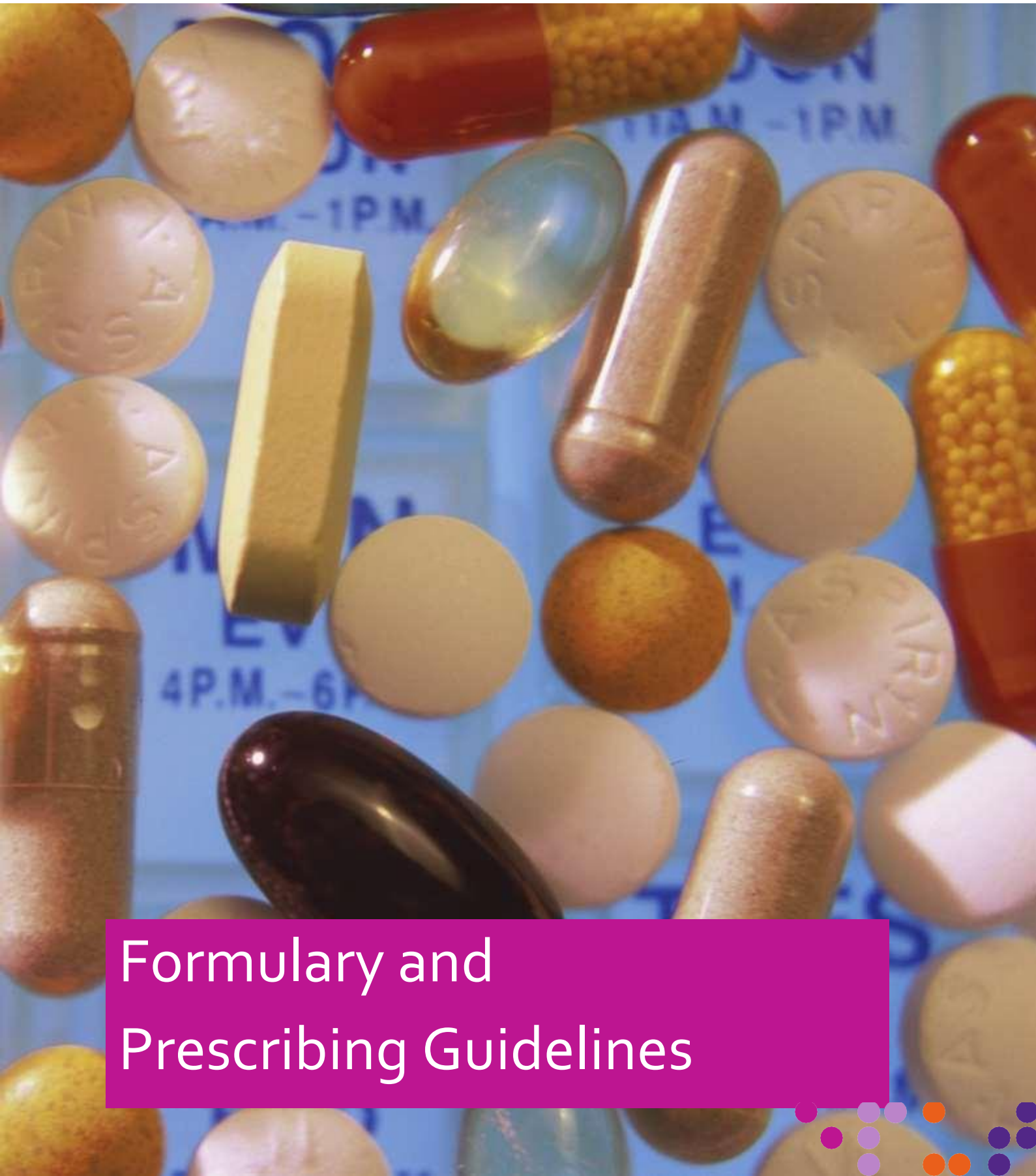
SECTION 14: ANTICOAGULANTS



Formulary and Prescribing Guidelines

14.1 Introduction

Anticoagulants are amongst the most frequently identified medicines causing preventable harm and admission to hospital. Managing the risks associated with anticoagulants can reduce the chance of patients being harmed in the future.[1]

When anticoagulants are prescribed guidance should be sought from the anticoagulation service in the local acute Trust. It is not expected that EPUT services will initiate these medicines, but maintenance and monitoring of treatment is expected. All prescribers who initiate, continue or adjust dosage of anticoagulants shall have the necessary work competencies as defined by the NPSA [1] (www.npsa.nhs.uk/health/alerts)

For further information refer to Trust Clinical Guideline for the Management of Patients on Anticoagulant Medicines in Inpatient Wards (CG83), and Trust Clinical Guideline on Physical Healthcare (CG55).

Listed below are the steps that should be followed to ensure that treatment with anticoagulants is managed appropriately.

- Information should be provided to the patient prior to the start of anticoagulant therapy and /or prior to discharge, which is patient-held and includes written doses. Oral Anticoagulation Therapy booklets (OAT) are available through the pharmacy department if the patient doesn't already hold one. All relevant sections should be completed.

- A clear indication for the anticoagulant therapy and duration of treatment must be recorded in the patient notes and on the Prescription Administration Chart (Drug Chart).

- Prescribe doses in mg (milligrams) and not numbers of tablets.

- Prescribe the least number of tablets needed to be taken each day

- Prescribe a constant daily dose where possible

- Discontinuation of an anticoagulant or a change in dose should be done in liaison with the local anticoagulation clinic.

- If a patient self-administers medicines during their stay the doses to be taken should be confirmed in writing.

- Ensure there is a stop-date or review date for anticoagulant therapy, where initiated or dose changed by EPUT.

14.2 Oral Anticoagulants

There are five oral anticoagulants licensed for use in the UK: warfarin, apixaban, dabigatran, edoxaban and rivaroxaban. Anticoagulants should be prescribed in line with local acute Trust guidelines.

Direct-acting Oral Anticoagulants (formerly known as NOACs): rivaroxaban; dabigatran: apixaban; Edoxaban, no routine INR monitoring is required for patients on DOAC because

INR tests are unreliable when patient is on a DOAC.

Patients on warfarin require the INR to be monitored regularly and maintained at the indicated therapeutic level.

- For most indications the target INR is usually 2.5 (2.0-3.0), but in some cases a higher target INR is indicated. INR should always be maintained at <5.Where INR levels are above 5 advice should be sought from the Local Acute Trust Anticoagulation Service and corrective action must be taken.
- Prescribers should check carefully for interactions when prescribing these medicines. Where a medicine interacting with warfarin has been prescribed, or the dose changed additional INR testing should be arranged.
- Avoid use of both 5mg and 500 microgram (0.5mg) Warfarin tablets together. Ensure 0.5mg tablets are prescribed and administered in preference to half tablets.
- Ensure INR is within the appropriate therapeutic range at discharge from services.
- These drugs are not usually suitable to be included in monitored dosage systems as dose changes cannot be accommodated

14.3 : Inpatient prescribing for patients on warfarin

If a service user prescribed warfarin is admitted to an in-patient unit:

- Check the service user's anticoagulant record book before prescribing. (These can be ordered from Pharmacy if the patient does not have one)
- Complete the Anticoagulant Treatment Record Card ensuring ALL sections are completed
- Take a baseline INR and decide on the frequency of INR checks
- Decide on the dose (which may vary) to be administered and prescribe on the Anticoagulant Treatment Record Card, having checked for interactions, contra-indications and cautions
- Ensure the anticoagulant is also prescribed on the In-patient treatment card with reference to the Anticoagulant Treatment Record Card so it is not overlooked during medicine administration rounds. (The dose will not be prescribed and administration will not be recorded on the In-patient treatment card).
- Ensure the nursing staff are clear as to the care and observation of the patient

Inpatient monitoring for patients on warfarin

- The dose should be monitored as per the Anticoagulant Treatment Record Card. This can vary from every 1-7 days, but should not exceed 7 days between INR checks.

In-patient monitoring for patients on any anticoagulant

- The patient should be observed for bruising and other side effects (such as bleeding gums) and if this is found the doctor should be contacted. A body map of the bruising should also be completed.

- Anticoagulant clinic and GP monitoring appointments should be attended wherever possible, and details of the treatment while an in-patient should be provided.

- Missed doses: If a dose is missed but remembered on the same day it should be administered and a note made of the time of administration on the treatment card. If the dose is not remembered until the next day, omit the dose and continue with the prescription for that day. Do not administer a double dose.
- If an incorrect dose is administered, contact the doctor. It may be necessary to seek advice from the anticoagulant clinic.

Duration of Treatment and Review

- For Atrial Fibrillation review the need for anticoagulation and the quality of anticoagulation at least annually, or more frequently if clinically relevant events occur affecting anticoagulation or bleeding risk.[6]

- Venous thrombo-embolism (VTE) should generally be treated for either three months or indefinitely, depending on the long-term risk of recurrence, the risk of bleeding and by patient preference.[7]

- For prevention of VTE following major elective orthopaedic surgery (i.e. knee or hip replacement) ensure DOACs are stopped after the documented (as in discharge) or licensed duration of treatment period is reached.

- These reviews should be facilitated by EPUT and carried out by the local acute trust anticoagulation service.

Management of High INR (>5) or Haemorrhage

- Refer to the latest BNF guidance, and obtain advice from the local anticoagulant service.

Discharge from EPUT if patient is on warfarin

- The patient must have an anticoagulant therapy record book (“yellow book”) updated at the date of discharge, an alert card and a patient information leaflet

- Ensure the patient has a date for their next anticoagulant check, and that they and/or their carer are clear about the dose to be taken, especially if it has changed.

Direct-acting Oral Anticoagulants (DOACs)

Dabigatran, Apixaban, Rivaroxaban, Edoxoban

- These drugs are increasingly being used as alternatives to warfarin therapy.

- They do not require any specific INR monitoring, however, the patient should be checked for signs of bleeding or anaemia.

- Dosage depends on renal function.

14.4 Low Molecular Weight Heparins (LMWH)

Enoxaparin, dalteparin, tinzaparin

Low molecular weight heparins have been identified as an area of risk by the National Patient Safety Agency (NPSA) and are the subject of a Rapid Response Report, NPSA/2010/RRR014. The following guidance should be followed when prescribing these medicines to ensure patient safety.

- Patient weight must be used as the basis for calculating the required treatment dose of LMWH. The weight must be accurately recorded in kilograms (kg) in the patient's notes. Patients should be weighed at the start of therapy and, where applicable, during treatment, if this is warranted.

- Renal function should be considered when prescribing treatment doses of LMWHs. The renal function test should not delay initiation of the first dose but every effort must be made to base subsequent dosing on these results. A pharmacist should be consulted for advice on prescribing in individuals with reduced renal function. Thrombocytopenia and hyperkalaemia are potential side effects of heparin therapy and should be monitored for if treatment is prolonged

- Essential information such as dose, weight, renal function, indication and duration of treatment should be communicated at transfer of care (e.g. by discharge letters) and used to ensure that future doses are safe.

- Doses should be checked based on patient information by prescribers and pharmacists when LMHWs are reviewed or dispensed.

14.4.1 Recommended Doses

Enoxaparin is available as inhixa® ▼ and Clexane® brands
Care should be taken during dose calculation using different strengths

Clexane® available as:
Clexane® Syringes 2,000 IU (20 mg)/0.2 ml solution for injection in pre-filled syringes

Clexane® Syringes 4,000 IU (40 mg)/0.4 ml solution for injection in pre-filled syringes

Clexane® Syringes 6,000 IU (60 mg)/0.6 ml solution for injection in pre-filled syringes

Clexane® Syringes 8,000 IU (80 mg)/0.8 ml solution for injection in pre-filled syringes

Clexane® Syringes 10,000 IU (100 mg)/1 ml solution for injection in pre-filled syringes

Clexane® Forte Syringes 12,000 IU (120 mg)/0.8 ml solution for injection in pre-filled syringes

Clexane® Forte Syringes 15,000 IU (150 mg)/1 ml solution for injection in pre-filled syringes

Clexane® Multidose Vial 30,000 IU (300 mg)/3 ml solution for injection

Inhixa®▼ available as:

Inhixa 2,000 IU (20 mg) in 0.2 mL solution for injection in pre-filled syringe ▼
Inhixa 4,000 IU (40 mg) in 0.4 mL solution for injection in pre-filled syringe ▼
Inhixa 6,000 IU (60 mg) in 0.6 mL solution for injection in pre-filled syringe ▼
Inhixa 8,000 IU (80 mg) in 0.8 mL solution for injection in pre-filled syringe ▼
Inhixa 10,000 IU (100 mg)/1 mL solution for injection in prefilled syringe▼
Inhixa 12,000 IU (120mg)/0.8mL solution for injection ▼
Inhixa 15,000 IU (150mg)/1 mL solution for injection▼
Inhixa 30,000 IU (300 mg)/3 mL solution for injection in multidose vial▼

Indication	Dosing regimen
Prophylaxis of venous thromboembolic disease	2,000 IU (20 mg) SC once daily
Treatment of DVT and PE	100 IU/kg (1 mg/kg) body weight SC once daily
Treatment of unstable angina and NSTEMI	100 IU/kg (1 mg/kg) body weight SC once daily
Treatment of acute STEMI (patients under 75) Treatment of acute STEMI (patients over 75)	1 x 3,000 IU (30 mg) IV bolus plus 100 IU/kg (1 mg/kg) body weight SC and then 100 IU/kg (1 mg/kg) body weight SC every 24 hours No IV initial bolus, 100 IU/kg (1 mg/kg) body weight SC and then 100 IU/kg (1 mg/kg) body weight SC every 24 hours

14.4.2 Dose Calculation for Treatment of DVT and PE

Dosage: Enoxaparin 1.5mg/kg ONCE daily

Product	Weight (kg)	Weight (stones/lbs)	Dose (mg)	Volume (ml)
Enoxaparin 60mg Syringe				
	40	6st 4 lbs	60 od	0.60*
Enoxaparin 80mg Syringe				
	45	7st 1 lb	68 od	0.70*
	50	7st 12 lbs	75 od	0.75*
Enoxaparin100mg Syringe				
	55	8st 9 lbs	83 od	0.85*
	60	9st 6 lbs	90 od	0.90*
	65	10st 3lbs	98 od	1.00*
Enoxaparin 120mg Syringe				
	70	11st 0 lbs	105 od	0.70*
	75	11st 11lbs	113 od	0.75*
	80	12st 8lbs	120 od	0.80*
Enoxaparin 150mg Syringe	85	13st 5lbs	128 od	0.85*
	90	14st 2lbs	135 od	0.90*
	95	14st 13lbs	143 od	0.95*
	100	15st 10lbs	150 od	1.00*

* These figures have been rounded to the nearest 0.05ml

Where 120mg or 150mg Enoxaparin prefilled is not available it is acceptable to use multiple dose of 60mg/80mg or 100mg if necessary until it can be acquired.

Example

Patient weights 70kg therefore; 70 x 1.5 = **105mg** of enoxaparin required Enoxaparin **(150mg/ml) = 105mg/150 = 0.7ml**
Enoxaparin **(100mg/ml) = 105mg/100 = 1.05ml**

For further information contact your ward pharmacist and/or refer to the Trust Clinical Guideline for the Management of Patients on Anticoagulant Medicines in Inpatient Wards (CG83), and Trust guideline CG55 – Clinical Guideline on Physical Healthcare.

14.5 NICE Guidelines

NG 89: Venous thromboembolism in over 16s: reducing the risk of hospital-acquired deep vein thrombosis or pulmonary embolism.[8]

Assess all patients to identify the risk of venous thromboembolism and bleeding.

Acute psychiatric patients

The section “Interventions for people with psychiatric illness” in NG89 gives the following recommendations:

Assess all acute psychiatric patients to identify their risk of VTE and bleeding:

- As soon as possible after admission to hospital or by the time of the first consultant review
- Using a tool published by a national UK body, professional network or peer-reviewed journal. The most commonly used risk assessment tool for hospital patients is the Department of Health VTE risk assessment tool.

Reassess all people admitted to an acute psychiatric ward for risk of VTE and bleeding at the point of consultant review or if their clinical condition changes.

Consider pharmacological VTE prophylaxis with LMWH for people admitted to an acute psychiatric ward whose risk of VTE outweighs their risk of bleeding.

Consider pharmacological VTE prophylaxis with fondaparinux sodium if LMWH is contraindicated for people admitted to an acute psychiatric ward whose risk of VTE outweighs their risk of bleeding.

Continue pharmacological VTE prophylaxis for people admitted to an acute psychiatric ward until the person is no longer at increased risk of VTE.

Lower limb immobilisation

NICE NG89 and its quality standard[11] gives the following recommendations. People aged 16 and over who are discharged with lower limb immobilisation are to be assessed to identify their risk of venous thromboembolism (VTE). Consider pharmacological VTE prophylaxis with LMWH or fondaparinux sodium for people with lower limb immobilisation whose risk of VTE outweighs their risk of bleeding. Consider stopping prophylaxis if lower limb immobilisation continues beyond 42 days.

NG158: Venous thromboembolic diseases: diagnosis, management and thrombophilia testing. [7]

NICE NG158 and its quality standard[11] gives the following recommendations.

People aged 18 and over taking anticoagulation treatment after a venous thromboembolism are to have a review at 3 months and then at least once a year if they continue to take it long term.

Assess and discuss the benefits and risks of continuing, stopping or changing the anticoagulant with people who have had anticoagulation treatment for 3 months (3 to 6 months for people with active cancer) after a proximal DVT or PE. Follow the recommendations on shared decision making and supporting adherence in the NICE guidelines on medicines optimisation, medicines adherence and patient experience in adult NHS services.

Review general health, risk of VTE recurrence, bleeding risk and treatment preferences at least once a year for people taking long-term anticoagulation treatment or aspirin.

NICE has produced a **visual summary** of the recommendations on diagnosis and initial management of suspected deep vein thrombosis (DVT) and pulmonary embolism (PE).

For patients who present with signs or symptoms of DVT, such as a swollen or painful leg, assess their general medical history and do a physical examination to exclude other causes.

For patients who present with signs or symptoms of PE, such as chest pain, shortness of breath or coughing up blood, assess their general medical history, do a physical examination and refer for a chest X-ray to exclude other causes immediately.

DVT: Urgency of treatment if investigation is delayed

Offer patients with suspected deep vein thrombosis an **interim therapeutic dose** of anticoagulation therapy while awaiting the result, if diagnostic investigations are expected to take **longer than 4 hours** from the time of first clinical suspicion. This is to avoid adverse effects if a quick confirmation test is not available or possible because there is risk of pulmonary embolism.

Refer to NICE NG158 for advice on when it would be appropriate to stop interim therapeutic anticoagulation, and to consider alternative diagnoses, once diagnostic tests are available.

For patients with suspected deep vein thrombosis have all diagnostic investigations completed within 24 hours of first clinical suspicion, to ensure prompt treatment if the diagnosis is confirmed, and to avoid unnecessary repeat doses of anticoagulants if the diagnosis is excluded.

PE: Urgency of treatment if investigation is delayed

Offer patients with suspected pulmonary embolism an **interim therapeutic dose** of anticoagulation therapy while awaiting the result, if diagnostic investigations are expected to be delayed. The consequences of missing a diagnosis of pulmonary embolism are severe and if a PE is left untreated there is a high risk of mortality. For people with a 'likely' PE Wells score (more than 4 points), interim anticoagulation therapy should be offered if diagnostic investigations cannot be done **immediately**. For people with an 'unlikely' PE Wells score (4 or less), interim anticoagulation therapy should be offered if the D-dimer test results cannot be obtained **within 4 hours**.

Refer to NICE NG158 for advice on when it would be appropriate to stop interim therapeutic anticoagulation, and to consider alternative diagnoses, once diagnostic tests are available.

Refer also to Trust guideline CG83 – “Management of patients on anticoagulant medicines in inpatient units”.

Refer also to Trust guideline CG55 – “Clinical guideline on physical healthcare”, for guidance on Venous Thromboembolism risk.

14.6 Antidote for oral anticoagulants

- For DOACS : The product information for DOACs includes guidance on the management of bleeds and bleeding complications. Specific reversal agents are available for dabigatran (Praxbind▼, idarucizumab) and apixaban and rivaroxaban (Ondexxya▼, andexanet alfa) but there is currently no specific authorised reversal agent available for Edoxaban[9]
- For warfarin: Antidote is Phytomenadione, all services administering warfarin should have access to Phytomenadione injection 10mg/ml (Vitamin K injection which can be administered orally). Patients with an INR >5·0 but who are not bleeding should have 1–2 doses of warfarin withheld and their maintenance dose should be reduced. Oral vitamin K may be given to patients with an INR of 5·0–8·0 if they are judged to be at high risk of bleeding. The cause of the elevated INR should be investigated. Patients with an INR >8·0 and who are not bleeding should receive 1–5 mg of oral vitamin K. (unlicensed use)[10]. Intravenous vitamin K produces a more rapid correction of the INR than oral vitamin K and should be used in preference in the bleeding patient. Advice on appropriate use of reversal agents should be sought from the Acute Trust Haematologist.

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