Wrightington, Wigan and Leigh NHS Foundation Trust

Title of Guideline	**ANTICOAGULANT GUIDELINES**
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Division & Specialty	Medicine - Haematology
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Explicit definition of patient group to which it applies	Adult patients who are on or being considered for anticoagulation medication
Abstract	Guidelines for initiation, maintenance and reversal of warfarin, direct oral anticoagulants, low molecular weight heparin and unfractionated heparin.
Statement of evidence base of the guideline Evidence Base (1-5)	5
Consultation Process	Reviewed by Haematologists, Pharmacists and other clinical staff who frequently manage patients on anticoagulation.
Target Audience	All clinical staff managing adult patients

1a	Meta analysis of RCT
1b	At least 1 RCT
2a	At least 1 well designed controlled study without randomisation
2b	At least 1 other well designed quasi experimental study
3	Well –designed non-experimental descriptive studies (ie comparative / correlation and case studies)
4	Expert committee reports or opinions and / or clinical experiences of respected authorities
5	Recommended best practise based on the clinical experience of the guideline developer

This guideline has been registered with the trust. However, clinical guidelines are guidelines only. The interpretation and application of clinical guidelines will remain the responsibility of the individual clinician. If in doubt contact a senior colleague or expert. Caution is advised when using guidelines after the review date.

1. Introduction

Anticoagulants are drugs that increase the time it takes for a person's blood to clot, by altering coagulation factors within the blood.

Anticoagulants are one of the classes of medicines most frequently identified as causing preventable harm and admission to hospital.

These incidents may be avoided by:

- Considering each patient's individual risks verses the benefits before starting anticoagulation and try to correct potential risk factors.

- Adequately documenting the reasons for anticoagulation, which drug is being used and for how long in the case notes.

- Discussing the anticoagulant treatment with the patient and providing them with adequate verbal and written information so they can make an informed choice.

- Ensuring that all relevant information is provided to the patient, the anticoagulation clinic (if appropriate) and the primary care team.

This guideline aims to promote a safe practice for the use of anticoagulants within this Trust.

Although some of the information may be applicable to children this guideline is not intended to cover Paediatrics. If a paediatric patient needs to be considered for anticoagulation please contact a Consultant Haematologist for specific advice.

Within this Trust if paper Drug Boards are in use, all anticoagulant medications should be prescribed in the 'Anticoagulation' section.

Warfarin is the most commonly prescribed Vitamin K Antagonist (VKA) anticoagulant. Alternative VKA anticoagulants should only be started by clinicians experienced in their use. If a patient is admitted to the Trust on a different VKA please consult the ward pharmacist for advice about dose adjustments.

2. Indications for Anticoagulation

Condition	Usual Duration	Anticoagulants
Pulmonary Embolism or Proximal DVT	6 months[1]	Apixaban, Dabigatran, Edoxaban, Rivaroxaban, Warfarin
Symptomatic calf vein DVT (not extending into popliteal vein)	6-12 weeks	Apixaban, Dabigatran, Edoxaban, Rivaroxaban, Warfarin
Cancer related thrombosis	6 months[1]	Dalteparin (Enoxaparin if eGFR <30mls/min)
Recurrent DVT or PE while off anticoagulation	Long Term	Apixaban, Dabigatran, Edoxaban, Rivaroxaban, Warfarin
Recurrent DVT or PE while on adequate anticoagulation	Long Term	Discuss with Haematology
Atrial Fibrillation[2] not caused by mitral valve stenosis	Long Term	Apixaban, Dabigatran, Edoxaban, Rivaroxaban, Warfarin (if due to valve disease, only warfarin can be used)
Awaiting Cardioversion	4 weeks before and 4 weeks after cardioversion	Apixaban, Dabigatran, Edoxaban, Rivaroxaban, Warfarin
Mural thrombus	3 months	Warfarin
Cardiomyopathy	Long Term	Warfarin
Mechanical prosthetic heart valve or mitral valve stenosis and AF	Long Term	Warfarin
Bioprosthetic heart valve	3 months then review	Warfarin
Peripheral artery occlusion/graft	Individual basis (Vascular team to decide)	Warfarin

[1] Longer duration may be required if there are on-going risk factors for recurrence (e.g. active cancer or impaired mobility)

[2] If CHA_2DS_2-VASC score (see appendix 1) is ≥1 for men and ≥2 for women

3. Contraindications for Anticoagulation

It is vital to weigh up the bleeding risks verses the benefits of anticoagulation for every patient and this should be reviewed at least annually, as risk factors may change with time.

For patients with Atrial Fibrillation it is recommended by NICE to use the HAS-BLED score (see appendix 2) to assess an individual's risk of bleeding. If the bleeding risk is considered to be high then any modifiable risk factors should be addressed and corrected before anticoagulation therapy is started.

Absolute contraindication to anticoagulation for patients with AF:

- Known large oesophageal varices or active peptic ulcer
- Platelet count <50 x 10^9/L – (refer to Haematology if the cause is unknown)
- Within 72 hours of major surgery with risk of severe bleeding – (defer and reassess risk post-operatively)
- Recent organ biopsy – (delay between 12-72 hours after haemostasis is achieved depending on the bleeding risk)
- Recent trauma or surgery to the head, eye or spine
- Known allergy or hypersensitivity to the anticoagulant – (consider an alternative)
- Acute clinically significant bleeding – (defer and reassess stroke verses bleeding risk within 3 months)
- Thrombotic stroke within past 2 weeks – (defer until at least 2 weeks after the event)
- Decompensated liver disease
- Infective endocarditis – (Cardiology to decide if/when anticoagulation is appropriate)
- Uncontrolled severe hypertension (BP > 180/110)
- Untreated proliferative retinopathy
- Pregnancy or within 48 hours post-partum

Relative contraindications to anticoagulation for patients with AF:

- Previous intracranial haemorrhage over 3 months ago – (Seek the advice of a stroke specialist)

- Recent major extracranial bleed within the last 6 months where the cause has not been identified or treated – (defer decision for at least 6 months)

- Recent documented peptic ulcer within past 3 months – (defer until ulcer is adequately treated and continue Proton Pump Inhibitor (PPI) therapy while on anticoagulation)

- Recent history of recurrent iatrogenic falls causing injury – (discuss risks verses benefits with a cardiologist)

- Dementia or marked cognitive impairment with poor medication compliance and no access to carer support

- Pre-existing coagulation disorder – (discuss case with a Haematologist)

Contraindications for patients requiring anticoagulation for non-AF causes

- Patients requiring anticoagulation for indications other than AF, who have any of the above absolute or relative contraindications, should be discussed on an individual basis with a senior clinician.

- The decision about anticoagulation should be reviewed if there is a change in the patient's condition.

4. Guidance Regarding Which Anticoagulation to Prescribe

Some indications for anticoagulation only have one recommended type of anticoagulation, in which case this should be the standard option unless there is a particular contraindication (e.g. drug allergy).

Venous Thromboembolic Events

Patients suspected or diagnosed with a Pulmonary Embolism or Deep Vein Thrombosis, who do not have underlying cancer, can be considered for a Direct Oral AntiCoagulant (DOAC). The DOACs have been approved by NICE guidance and can be a cost effective alternative to Warfarin. For further information regarding these indications please refer to the separate policies available on the Trust Intranet.

Atrial Fibrillation

Current NICE guidelines (NG196) recommend DOACs over warfarin for patients with newly diagnosed AF for who there are no contraindications.

Switching Anticoagulants

- Patients can switch anticoagulants if they develop side-effects or find aspects of the anticoagulation therapy interfering with their life-styles (e.g. unable to attend anticoagulation clinics).

- Patients who are established on Warfarin for over 3 months, who then have poor INR control (Time in Therapeutic Range <65%) should be considered for switching to a DOAC, if the indication is within their license.

- Please consult the medicine SPC's regarding switching from one anticoagulant to another.

5. Counselling a Patient Prior to Starting Oral Anticoagulation Therapy

Patients need a clear explanation of the treatment and the implications it will have on their lifestyles.

The initial responsibility for this lies with the clinician deciding that the patient may benefit from anticoagulation.

More detailed discussions can sometimes be delegated to other healthcare workers (such as a pharmacist or Anticoagulant Nurse).

Check recent blood results (including Full Blood Count, Urea and Electrolytes, PT and aPTT) and consider correcting any abnormalities before starting anticoagulation.

If the patient is already prescribed medication that can increase the risk of bleeding, especially antiplatelet agents, Non-Steroidal Anti-Inflammatories (NSAIDs) and steroids they should be discontinued where possible. If these medications are to continue it should be clearly documented why they need to continue and for how long.

It is imperative that any decisions made regarding anticoagulation and antiplatelet agents are clearly communicated to the anticoagulation team or professional responsible for monitoring the patient's anticoagulation.

<u>General:</u>

- Explain about the underlying condition that is an indication for anticoagulation therapy
- Explain about the intended duration of treatment (see Indications for Anticoagulation table)
- Explain that anticoagulants increase the time it normally takes blood to clot, therefore any injury may bleed more.
- If the patient develops bleeding that won't stop, even if the amount of blood loss seems small, then they should seek medical attention and omit their anticoagulation until told to restart.
- **If the patient sustains a head injury that makes them lose consciousness, or causes obvious external injury to their head/face then they should seek urgent medical attention, even if they feel fine at the time of the injury.**
- To reduce the risk of injury, patients on an anticoagulant should be encouraged to review their lifestyle and modify it where necessary. This may include wearing gardening gloves, switching to an electric razor, avoiding full contact sports.
- If a patient on anticoagulation requires surgery or dental work, then they must inform the healthcare staff caring for them that they are taking an anticoagulant. This may need to be omitted for a few days prior to the procedure.

DOACS:

- The DOACs work by stopping a specific clotting factor that would normally help our bodies to form blood clots.
- The DOACs do not require regular monitoring, as they have a much more predictable effect in people's bodies than warfarin. However, as they are removed from our bodies by the kidneys it is recommended to have occasional blood tests to make sure the kidneys are working normally. The dose of the DOAC may need to be reduced in patients with reduced renal function.
- Some medication can increase or decrease the effects of DOACs so it is important to check the product literature when prescribing a new drug to make sure there are no significant interactions. If a drug that could alter the effects of a DOAC has to be prescribed then please discuss with a Haematologist for further advice.
- DOACs are not significantly affected by dietary changes or alcohol, however we recommend alcohol consumption within the government guidelines as excessive alcohol consumption is an independent risk factor for bleeding.

Warfarin:

- Warfarin works by stopping our bodies from turning Vitamin K into clotting factors that enable us to form blood clots.
- Warfarin levels in a person's body can be very variable; therefore anyone taking warfarin will need to have regular blood tests every few weeks. The dose of warfarin will be adjusted according to the blood tests.
- Warfarin can be affected by lots of different medications; therefore anyone taking warfarin that has changes to their usual medication should have another blood test 2 - 4 days later.
- Warfarin can be affected by a person's diet; therefore anyone taking warfarin should avoid sudden dietary changes and avoid alcohol consumption above national recommended limits or in sudden large quantities.
- If warfarin levels are too high then a patient may need a dose of Vitamin K (given orally) to help correct the warfarin. Therefore the hospital must have a reliable way of contacting the patient at short notice.

Give the patient the time and opportunity to accept or decline anticoagulation therapy

Once a patient has agreed to start an oral anticoagulant please refer to the appropriate section below for initiation guidance.

6. Starting a Patient on a DOAC

Each of the DOACs have different doses depending on the indication for anticoagulation. It is important to check the product literature or the British National Formulary (BNF) if you are uncertain about the dose.

Each DOAC has a lower dose for patients with impaired renal function, therefore a calculated creatinine clearance using the Cockcroft-Gault formulae is recommended prior to starting a DOAC.

If a higher initial loading dose is required (i.e. Apixaban or Rivaroxaban for the treatment of VTEs) the date when maintenance should start needs to be clearly documented in the notes (and drug board if applicable). The maintenance dose should also be communicated clearly, especially if this is to be done by a different healthcare professional.

Pharmacy and the Anticoagulation Department have product literature and patient alert cards specific to the different DOACs that can be given to patients, in place of the 'yellow books'. Advise patients to carry the Alert Card with them to show health care professionals.

The DOACs do not need to be routinely monitored; however their dosing may be adjusted depending on renal function. Therefore for patients on a DOAC long-term their GP should be advised to check renal function on these patients in accordance with NICE Chronic Kidney Disease guidelines and adjust the dose according to the product literature.

The DOACs can be affected by liver impairment and this guideline recommends that patients starting a DOAC should have their LFTs checked within the past 3 months.

The DOACs have fewer drug interactions compared to warfarin; however it is important to check for potential interactions when starting a DOAC, or a new medicine if the patient is already on a DOAC.

DOACs are not licensed for use in pregnancy and there is limited evidence with regards to breastfeeding. Therefore DOACs should not be prescribed to women in these circumstances.

Prescribe a PPI for patients on steroids and/or Non-Steroidal Anti-Inflammatory Drugs.

7. Starting a Patient on Warfarin

Patients requiring warfarin for atrial fibrillation should ideally be referred to the Outpatient Anticoagulation Clinic where trained nurses have time to complete this process in detail.

Patients who require urgent anticoagulation therapy that cannot wait until an outpatient clinic appointment should be managed according to the points below. If the patient is an inpatient the ward pharmacist may be able to help with this process.

- Give the patient a Yellow NPSA Oral Anticoagulant Therapy important information for patients pack (available from the Anticoagulation Department)
    - For the Oral Anticoagulation Therapy booklet
        - Fill in the patient's information on the first 4 pages
        - Talk the patient through the booklets sections making sure the patient understands the information;
            - How do I take my anticoagulant
            - How to get repeat prescriptions
            - The potential side effects of warfarin
            - What to do if you require dental work or surgery
            - How medication can affect warfarin and what drugs to avoid, including herbal preparations
            - How diet can affect warfarin
            - Discuss effects on pregnancy and periods for women of child-bearing potential
        - Highlight the different coloured warfarin tablets which correspond to different strengths (NB we do not dispense Pink 5mg Warfarin tablets in this Trust).
        - Explain to the patient how the local monitoring clinics work
        - Answer any questions the patient may have about this treatment
    - For the Anticoagulation Alert Card
        - Fill in the required information
        - Advise the patient to carry this card with them at all times
    - For the smaller Oral Anticoagulant Therapy Record Book
        - Fill in the required information
        - Explain that this will be the method that their dosing will be adjusted based on the blood tests. The book will also be a record of when they are next due a blood test
        - Advise that the patient will need to bring the book to the anticoagulation clinic appointments
- Check the patient's current medication
    - Consider discontinuing current antiplatelet agents as dual therapy can significantly increase the risk of bleeding. There are only a few reasons why a patient should be on oral anticoagulation and an antiplatelet agent, if unsure please check with a Cardiologist or Haematologist.

        - **It is imperative that any decisions made regarding concurrent antiplatelet and anticoagulation therapy are communicated clearly to the Anticoagulant Department or the professional responsible for monitoring the patient's anticoagulation**
    - Prescribe a PPI for patients on steroids and/or Non-Steroidal Anti-Inflammatory Drugs

- Prescribe an appropriate loading regime of warfarin depending on the indication (see below).
    - If rapid loading is required then concomitant Low Molecular Weight Heparin must also be prescribed.

- Monitor INR and adjust the dose of warfarin according to the loading regime.

- Ensure the patient has an outpatient follow up appointment with an anticoagulation clinic once they are discharged from your care.

- Make sure anticoagulation therapy is noted in correspondence to the patient's GP (e.g. discharge summary or clinic letter).

<u>Low Dose Loading Regime</u>

This regime should only be used for patients where rapid anticoagulation is not required (e.g. patients with Atrial Fibrillation). It can take several weeks before the INR is in the target range.

1. Prescribe warfarin 3mg daily for 7 days (2mg daily for patients who are taking amiodarone, antibiotics or other interacting medication and those with known renal, liver or cardiac impairment).

2. Check INR in one week, then use table below. If the patient is in hospital with ongoing medical problems and/or interacting drugs are being prescribed, consider checking INR earlier than 7 days.

3. Recheck the INR and dose accordingly. If a patient maintains a stable INR with no dose changes the time to next test can be slowly increased up to 12 weeks

INR	Warfarin Dose Change	Time to next test
<1.8	Increase by 1mg a day	1 week
1.8 – 2.5	Continue current dose	2 weeks
>2.5	Decrease by 1mg	1 week

<u>Rapid Loading Regime</u>

This regime should be used for patients who need to achieve therapeutic anticoagulation within a few days. It is no longer indicated for patients with Atrial Fibrillation unless they have symptoms of thromboembolism.

The following dosing schedule aims to achieve maintenance INR of 2 to 3

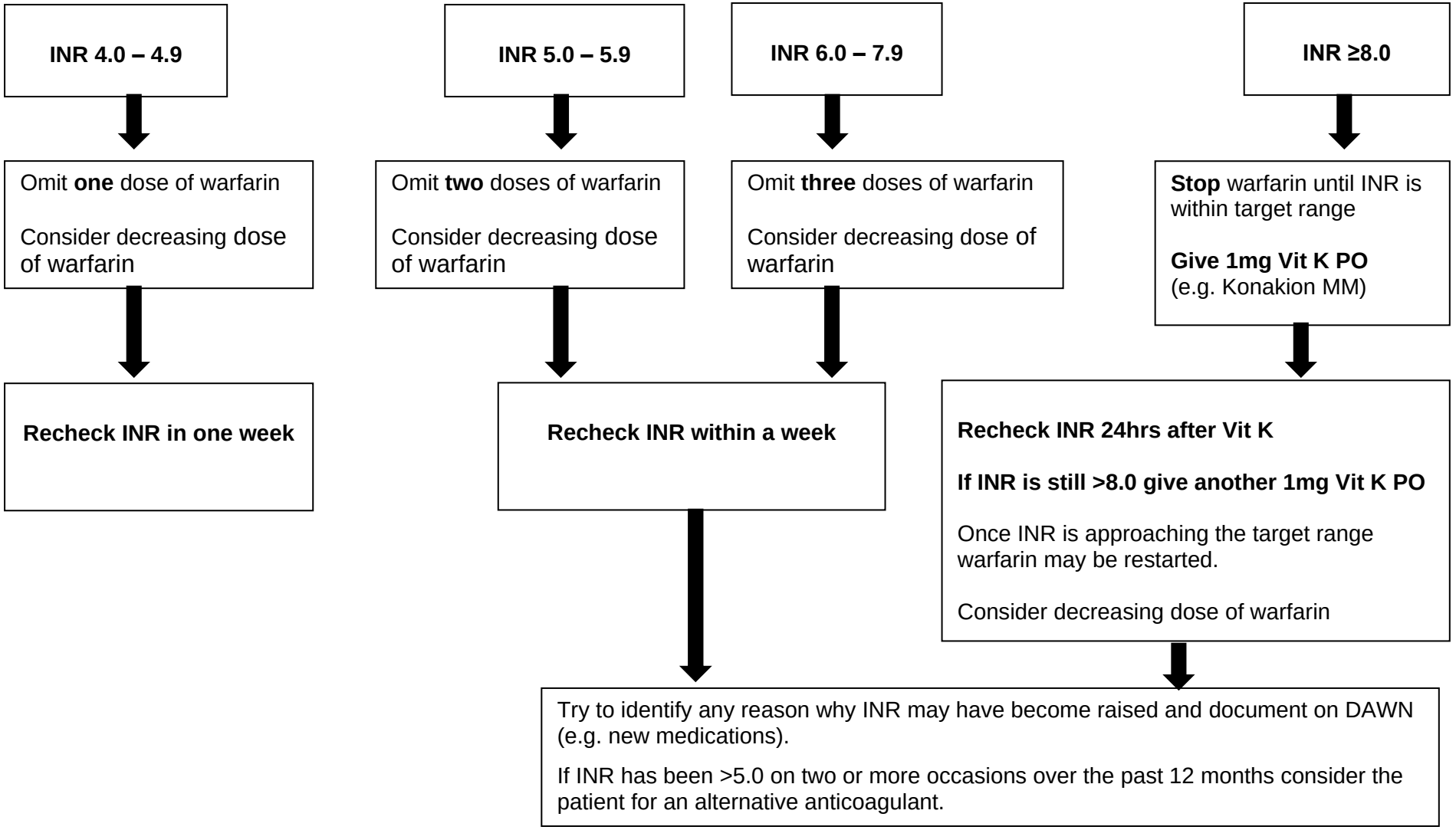
Day	INR	Dose of Warfarin
1	< 1.4	10mg 5mg if **any** of the following: • Age >75yr • Weight <50kg • Raised baseline INR • Hepatic and or severe renal failure • Malnourished • Debilitated • On interacting drugs that increase warfarin activity
2	< 1.8 = 1.8 > 1.8	5mg 1mg 0mg
3	< 1.7 1.8 – 2.1 2.2 – 2.5 2.6 – 2.9 3.0 – 3.3 3.4 – 3.6 >3.6	10mg 5mg 4mg 3mg 2mg 1mg 0mg
4	<1.4 =1.4 =1.5 1.6 – 1.7 = 1.8 =1.9 2.0 – 2.1 2.2 – 2.3 2.4 – 2.6 2.7 – 3.0 3.1 – 3.5 3.6 – 4.0 4.1 – 4.5 >4.5	Refer to pharmacist for advice 8mg 7mg / 8mg alternate days 7mg 6mg / 7mg alternate days 6mg 5mg / 6mg alternate days 5mg 4mg / 5mg alternate days 4mg 3mg / 4mg alternate days 3mg Miss out one day's dose, then give 2mg Miss out two day's doses, then give 1mg
5 onward		**Monitor INR daily until in range and stable**

Management of patients on warfarin with a raised INR

Any patient with a raised INR should be asked if they have had any bleeding symptoms since their last dose of warfarin (including nose bleeds, blood in their urine or blood in stools).

If they have bleeding symptoms then IV Vitamin K is recommended (which requires hospital attendance if outpatient)

If the INR on a near patient test is unrecordable, consider it to be high and organise an urgent venous blood test to confirm



8. Ongoing Warfarin Management

If a patient is admitted to hospital on warfarin or they have developed a stable INR after starting warfarin during the current admission follow this guide to help with dosing.

Warfarin Monitoring in Hospital

- If a patient is admitted to hospital already on warfarin and there are no reasons to discontinue it, then prescribe their usual dose. This will be recorded in the patient's 'yellow book' or contact the anticoagulation department if that is unavailable.

- Check the patient's INR once a week if the patient is clinically stable

- If the INR is within target range the warfarin doses can be prescribed for the following week on the anticoagulation section of the drug board

- If the patient's clinical picture changes or they have medication changes the INR should be monitored more frequently

- Try to avoid daily INRs and a different daily dose each day. Due to the long half-life of warfarin it takes several days to gain an accurate picture of whether a dose is too high or low.

- Warfarin doses in the community are calculated over a week to give an average dose (e.g. 2mg for 5 days a week and 3mg for 2 days a week = 2.29mg/day average). Therefore if the INR is out of range make an appropriate adjustment to the average weekly dose, not just the last daily dose the patient received.

- Try to avoid omitting warfarin doses unless the INR is >4.0 or if the patient is bleeding.

- Try to avoid big increments in the dose of warfarin to 'boost' the INR into a therapeutic range. It is safer to make a smaller adjustment and give LMWH cover for those patients at high risk of thrombotic events.

Discharging from Hospital

If a patient was already on warfarin prior to the hospital admission, then please contact their local anticoagulation department to organise further INR monitoring **before** the patient is discharged. These patients do not need a new anticoagulant clinic appointment.

If a patient has been newly started on warfarin during this hospital admission, then a Anticoagulation Clinic Referral Form (available on the intranet) needs to be completed and faxed to the Anticoagulation Clinic (Fax: 2820, Phone: 4175).

Procedure for the administration of Vitamin K by Community React Team

- Anticoagulation and Haematology Lab to contact CRT between the hours of 5pm and 7pm Monday to Sunday by email wwl-tr.WWL-SPA@nhs.net and then phone CRT to ensure they have received the e mail and confirm instructions if the INR is greater than 8. If a visit cannot be completed the referral will need to go to out of hours G.P service by the referring agent.

- Both the referral form and prescription (see appendix and 5) need to be filled in with the details of the Vitamin K dosage if the referral is direct from anticoagulation service. Referrals from the lab require a referral (see appendix 8) and CRT doctor will then prescribe the Vitamin K.

- The Anticoagulant service must contact the patient to ensure NO WARAFRIN is taken on that evening and questioned as to recent medical history (i.e illnesses, new medication, bruising or bleeding). They should be advised to expect a visit from CRT to administer the vitamin K capsule and details of the plan of care for the next 3 days. Referrals from the Haematology lab will require CRT to ring the patient and ask the following above questions.

- Supplies of oral vitamin K capsules must be available (drug store room) and consist of bottles containing 3 x 1mg capsules, with an instruction leaflet for each patient. CRT will ensure that the instructions leaflet is provided. (see appendix 7).

- The CRT nurse will visit the patient within 4 hours after receiving the written referral and DNR4 prescription. CRT nurse will administer the prescribed dose of vitamin K following the instructions and leave the instructions and the remaining capsules if safe to do so. Otherwise, the remaining medication will need to be brought back to CRT drug storeroom and be discarded as per trust policy.

- The CRT nurse will remind the patient NOT TO TAKE warfarin that evening, if the patient has taken their warfarin, still administer the Vitamin K, document that the patient has taken the warfarin, and inform the anticoagulant team the following day by email (appendix 7) or the CRT doctor who prescribed the vitamin K that evening.

- CRT nurse will complete the administration care plan on System One.

- If the patient appears unwell or haemorrhagic (excess bruising or bleeding) and needs further medical attention:-

  a) Administer the prescribed dose of Vitamin K
  b) Transfer the patient to RAEI with a hospital transfer form documenting the administration of vitamin K (see appendix 6)
  c) Document the patients visit on System One.
  d) Inform anticoagulation service the following day by email/phone call.

- The following day the patient will need a repeat INR. Please ask the patient for the yellow anticoagulant book and this must be sent with the blood sample to the pathology laboratory REAI on an urgent blood request form. Please e mail the anti-coagulate service the following day to inform them of the referral (see appendix 7).

- If the INR needs to be taken the following day if at weekend please check with anticoagulation service referring for instructions or CRT doctor prescribing the vitamin K.

9. Antiplatelet Agents and Anticoagulants

Combination therapy of antiplatelet agents and anticoagulants will significantly increase the risk of bleeding. These combinations should only be used where the benefits clearly outweigh the risks.

When prescribing antiplatelet agents (including Aspirin, Clopidogrel, Ticagrelor, Prasugrel) it should be clearly documented whether anticoagulation should be continued and the duration of each medicine.

Dual antiplatelet therapy should not be used in combination with a DOAC.

Dual antiplatelet therapy and warfarin can be used in certain circumstances, but this should only be recommended by a Cardiologist or Haematologist.

The use of Proton Pump Inhibitors may reduce the risk of gastrointestinal bleeding and should be considered for all patients requiring antiplatelet agents and an anticoagulant.

10. Low Molecular Weight Heparins (LMWH)

This group of medicines are administered sub-cutaneously and act in a similar way to the DOACs targeting a specific part of the clotting pathway.

This Trust primarily uses Dalteparin (brand name – Fragmin) for prophylaxis against and treatment of VTEs. However, Enoxaparin (brand name – Clexane) is used for patients who require therapeutic doses and have an eGFR less than 30mls/min (see below).

Check FBC, U&Es, PT and aPTT before starting a LMWH and try to correct any abnormalities where possible.

LMWH can be prescribed at the same time as starting warfarin, or if the patient's INR is sub-therapeutic and additional anticoagulation cover is required. LMWH should be discontinued once the patient has achieved a therapeutic INR (e.g. 2 or above).

LMWH should **not** be prescribed with a DOAC as they both have rapid onsets of action and could result in an increased risk of bleeding.

Treatment Dose Dalteparin:

Weight (Kg)	Dose (International Units)
Less than 46	7,500
46 - 56	10,000
57 - 68	12,500
69 - 82	15,000
83 and over	18,000

Monitoring LMWH Anticoagulant Effect:

LMWHs do not normally require monitoring however in certain circumstances it may be appropriate to measure their anticoagulant effect. This is done through a blood test called 'Anti-Xa'.

<u>Target Levels for Anti-Xa:</u>

Trough Anti Xa level = 0.1-0.2 units/ml (taken just before next dose of LMWH)

Peak Anti Xa level = 0.5-1.0 units/ml (taken 3-4 hours after last dose of LMWH)

Treatment Dose LMWH Special Circumstances:

1. Renal Failure (eGFR <30mls/min)

Patients with an eGFR <30mls/min should be prescribed Enoxaparin instead of Dalteparin. They may require Anti-Xa monitoring and should be referred to a Haematologist for further advice.

Do not use either Enoxaparin or Dalteparin is a patient's eGFR is <15mls/min unless agreed by a Haematologist. LMWHs can accumulate in renal impairment and increase the risk of bleeding.

Treatment Dose Enoxaparin (for patients who have eGFR <30mls/min):

Weight (Kg)	Dose (mg)
35-44	40mg
45-54	50mg
55-64	60mg
65-74	70mg
75-84	80mg
85-94	90mg
95-104	100mg
105-114	110mg
115-124	120mg
>125	Seek specialist advice

2. Pregnant Patients

Patients who are pregnant and require treatment dose LMWH should be referred to the on-call Obstretric Registrar for advice. They usually have the standard total daily dose given as two equal half-doses and Anti-Xa monitoring as their body weight alters during the pregnancy.

There are separate guidelines for pregnant patients suspected or diagnosed with a VTE which are available on the Trust Intranet.

3. Hyperkalaemia (High Potassium)

LMWHs can suppress adrenal secretion of aldosterone which can lead to hyperkalaemia. This risk is highest in patients with Diabetes Mellitus, chronic renal impairment and pre-existing metabolic acidosis.

If a patient on treatment dose LMWH develops hyperkalaemia please contact a Haematologist for further advice.

4. Thrombocytopaenia (Low Platelets)

LMWH can cause Heparin Induced Thrombocytopaenia (HIT) where a patient develops antibodies that consume platelets and can cause thrombosis despite being on an anticoagulant.

Routine monitoring of platelet count is not indicated for patients on LMWH, however if a patient develops a new thrombosis, a skin reaction at the injection site or has a drop in platelet count by >30% then HIT should be considered.

For further information see 'Heparin Induce Thrombocytopaenia' guidelines on the Trust Intranet.

5. Patients with Cancer who Develop a VTE

Patients with a solid tumour who develop a VTE benefit from extended use of Dalteparin compared to Warfarin. The first month of Dalteparin is given at the standard dose. From month two onwards the dose should be adjusted according to the table below.

Treatment Dose Dalteparin for Cancer Patients - Month Two Onwards:

Weight (Kg)	**Dose (International Units)**
Less than 56	7,500
57 - 68	10,000
69 - 82	12,500
83 - 98	15,000
99 and over	18,000

The recommended duration of treatment for patients with cancer who develop a VTE is six months; however a longer duration may be appropriate if the risk of further VTEs remains high.

If a patient is on chemotherapy and becomes thrombocytopaenic the dose of Dalteparin may need omitting or reducing:

- Platelets <50 x 10^9/L = Stop Dalteparin and restart when platelets >50 x 10^9/L

- Platelets 50 - 100 x 10^9/L = Reduce daily dose of Dalteparin according to table:

Weight (Kg)	**Normal Dose (IU)**	**Reduced Dose (IU)**
Less than 56	7,500	5,000
57 - 68	10,000	7,500
69 - 82	12,500	10,000
83 - 98	15,000	12,500
99 and over	18,000	15,000

- Platelets >100 x 10^9/L = Give normal dose of Dalteparin

11. Unfractionated Heparin (UFH)

Unfractionated Heparin is a short acting anticoagulant that is given as an intravenous infusion. It is used in circumstances where rapid discontinuation of anticoagulation may be required.

The clinical effect can be variable so regular monitoring of the aPTT is required and dose adjustments may be needed. Patients requiring UFH infusions should normally be managed on wards that have high nurse to patient ratios such as the Coronary Care Unit (CCU) or High Dependency Unit (HDU).

Starting an UFH Infusion

- Check baseline FBC, U&Es, LFTs, PT and aPTT
- Use Heparin (Pump-Hep) which contains 1000units/ml of Heparin Sodium in 10 or 20ml vials.
- Draw up 20mls (20,000units) of Heparin solution into a syringe and use a suitable infusion pump.
- Prescribe bolus dose of 5,000units over 5 minutes at start of infusion (rate = 60ml/hour).
- Prescribe Heparin 1,000units/ml at an **hourly** rate according to the patient's weight (see table).
- **The prescription should clearly state, 'CONTINUOUS INFUSION'.**

Initial Heparin Infusion Rate

Weight	Rate (ml/hour of 1000units/ml solution)	Dose (units over 24 hours)
41-50 kg	0.8	19 200
51-60 kg	1.0	24 000
61-70 kg	1.2	28 800
71-80 kg	1.4	33 600
81-90 kg	1.6	38 400
> 90kg	1.7	40 800

- The aPTT and aPTT Ratio should be repeated after 4-6 hours and the infusion rate adjusted accordingly (see table below):

Adjusting Heparin Infusion rate:

aPTT (seconds)	aPTT ratio	Infusion rate adjustment	Recheck APTT
< 37	<1.2	Give 5000 unit bolus **and** increase infusion by 0.4ml/hour	After 4-6 hours
37 – 47	1.2 – 1.4	Increase by 0.2ml/hour	After 4-6 hours
47 – 79	1.5 – 2.5	No Change	After 12-24 hours
80 – 117	2.6 – 3.7	Decrease by 0.1ml/hour	After 4-6 hours
118 – 136	3.8 – 4.4	Decrease by 0.2ml/hour	After 4-6 hours
> 136	> 4.4	Stop for one hour **then** decrease by 0.3ml/hour	After 4-6 hours

These dose adjustments are appropriate for patients on <u>continuous</u> heparin infusions. It should be noted that due to the short half-life of heparin any stopping of the infusion will lead to reduced aPTT ratio results, which can lead to inappropriate increasing of heparin dose.

Great care should be taken when interpreting results - that these are based on patients actually receiving continuous heparin.

- The aPTT and aPTT ratio should be repeated every 4-6 hours after every dose change. If the patient is well established on a stable Heparin dose then monitoring can be reduced to every 12-24 hours.

- Repeat FBC 24 hours after starting the infusion and then every 2-3 days to assess for thrombocytopaenia. See 'Heparin Induced Thrombocytopaenia' guidelines on Trust Intranet for further information.

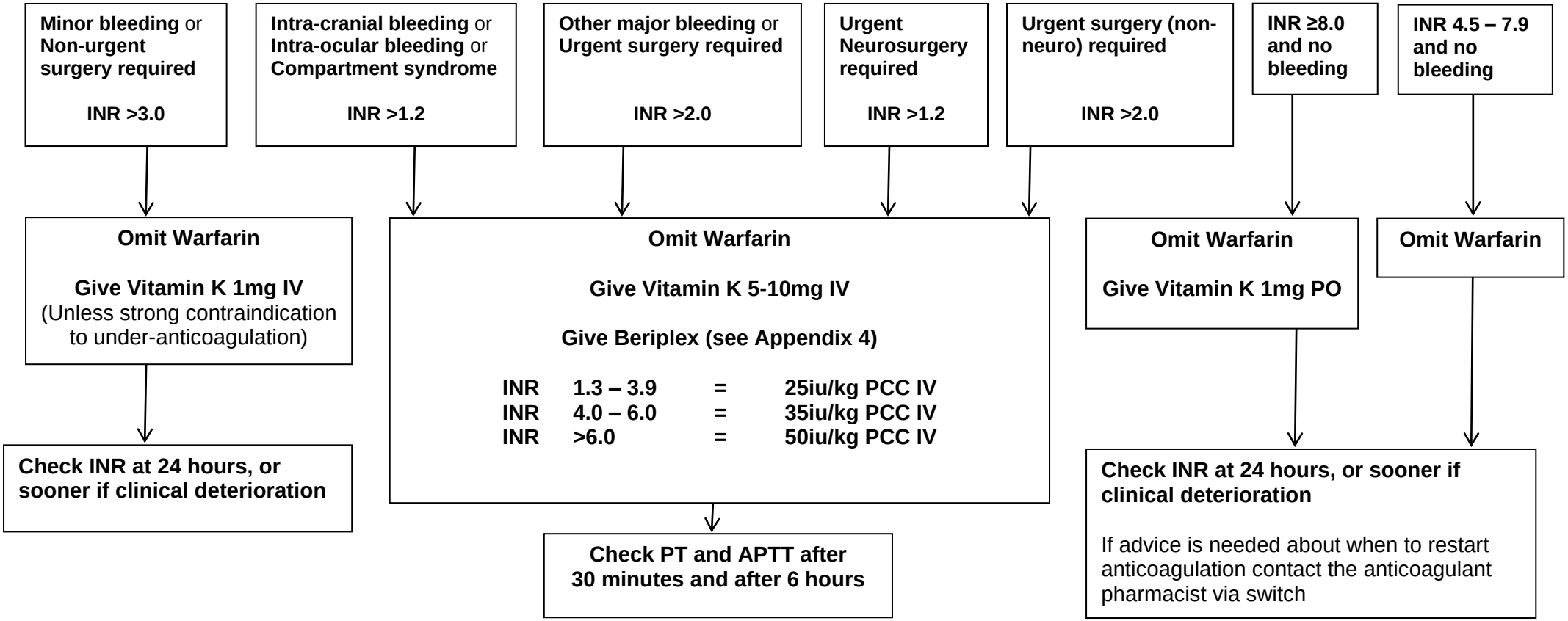
12. Reversal of Anticoagulation

Patients on anticoagulation may require reversal if they have major or critical site bleeding, or if they require surgery. There are some general measures that should be considered for all patients on anticoagulation; however there are also specific antidotes for different ones.

General Measures

- Stop the anticoagulant and record when the patient last received it
- Check FBC, PT, aPTT, Fibrinogen, U&Es, LFTs and Group & Save
- If major bleeding or critical site bleeding consider Tranexamic Acid 1gram IV bolus
- If major bleeding activate major haemorrhage protocol (see transfusion guidelines on the trust Intranet)
    - Transfuse Platelets to keep platelets >50 x 10^9/L
    - Transfuse FFP to keep aPTT and PT within 1.5x normal
    - Transfuse Cryoprecipitate to keep fibrinogen >1g/L

Reversal of Warfarin or Other VKAs



High Risk Patients: Patients with any of these conditions may require closer attention and earlier intervention, if in doubt contact the on-call Haematologist via switchboard

- Age >70
- Renal disease
- Concurrent illness (e.g. infection)
- Previous anticoagulant-related bleeding
- Hypertension
- Recent surgery
- Thrombocytopaenia
- Cerebrovascular disease
- Cardiac failure
- Other coagulopathy
- On medication that can affect clotting (e.g. aspirin, platelet antagonists)
- Liver disease
- Body weight <50kg
- History of peptic ulceration/GI bleeding

Reversal of Dabigatran

- **If surgery is planned over 48hours and patient is not bleeding:**
  - Omit the Dabigatran and monitor the patient

- **If surgery is planned within 24hours or patient is bleeding:**
  - Give Idarucizumab (Praxbind) 5grams (2 x 2.5gram vials) IV as slow bolus. This is available from A&E resus fridge at Royal Albert Edward Infirmary. Please discuss this with on-call Consultant Haematologist before prescribing.

Reversal of Edoxaban

- **If surgery is planned over 24hours and patient is not bleeding:**
  - Omit the Edoxaban and monitor the patient

- **If surgery is planned within 24hours or patient is bleeding:**
  - Surgery should ideally be delayed for 24 hours since the last tablet to minimise anticoagulant effect. If surgery cannot wait or the patient is bleeding discuss the patient with on-call Consultant Haematologist. Beriplex can be used at a dose of 50units/kg.

Reversal of Apixaban

- **If surgery is planned over 48hours and patient is not bleeding:**
  - Omit the Apixaban and monitor the patient

- **If surgery is planned within 24hours or patient is bleeding:**
  - Surgery should ideally be delayed for 48 hours since the last tablet to minimise anticoagulant effect. If surgery cannot wait or the patient is bleeding discuss the patient with on-call Consultant Haematologist. Beriplex can be used at a dose of 50units/kg.

- **If patient has life threatening GI bleeding**
  - Andexanet alfa can be used to reverse the anticoagulation effects. See Table below for dosing regimens.

Reversal of Rivaroxaban

- **If surgery is planned over 24hours and patient is not bleeding:**
  - Omit the Rivaroxaban and monitor the patient

- **If surgery is planned within 24hours or patient has non-GI bleeding:**
  - Surgery should ideally be delayed for 24 hours since the last tablet to minimise anticoagulant effect. If surgery cannot wait or the patient is bleeding discuss the patient with on-call Consultant Haematologist. Beriplex can be used at a dose of 50units/kg.

- **If patient has significant GI bleeding**
  - Andexanet alfa can be used to reverse the anticoagulation effects. See Tables below for dosing regimens.

Andexanet Alfa

Andexanet Alfa (Ondexxya) is a reversal agent for FXa inhibitors and is licensed for use in patients who have taken Apixaban or Rivaroxaban. NICE have given approval for it's use in patients who have life threatening GI bleeding and have been taking one of these two DOACs. It is not approved for use in patients with intracranial bleeding or who require surgery. This is available from A&E resus fridge at Royal Albert Edward Infirmary. Please discuss this with on-call Consultant Haematologist and Gastroenterologist before prescribing, because it is a high-cost medicine.

Andexanet Alfa Dosing:

FXa Inhibitor	**Last Dose**	**Timing of last Dose**	
		<8 hours or unknown	**≥8 Hours**
Apixaban	**≤5mg**	Low dose	Low dose
	>5mg or unknown	High dose	
Rivaroxaban	**≤10mg**	Low dose	Low dose
	>10mg or unknown	High dose	

Andexanet Alfa Regimens:

	Initial IV Bolus	**Continuous IV infusion**	**Total number of 200mg vials**
Low Dose	400mg at a rate of 30mg/min	4mg/min for 120 minutes (480mg)	5
High Dose	800mg at a rate of 30mg/min	8mg/min for 120 minutes (960mg)	9

Administer the infusion via a 0.2 or 0.22micron filter using a syringe pump. Please refer to the Injectable Medicines Guide (available through Wally) for further information on how to reconstitute and administer.

<u>Reversal of LMWH</u>

- **If bleeding is severe or at a critical site:**
  - Give IV Protamine Sulphate 50mg as a slow bolus over 10-15 minutes
  - This is only a partial reversal agent of LMWHs and can cause hypotension or anaphylactoid reactions

<u>Reversal of UFH</u>

- As UFH has a short half-life it is usually sufficient to stop the infusion
- If bleeding is severe or at a critical site:

- Give 1mg Protamine Sulphate for every 100 units of heparin given over previous hour.
    - Halve Protamine dose if heparin infusion has been stopped for over one hour
    - Quarter Protamine dose if stopped for two hours.

13. Head Injuries and Anticoagulation

All patients on warfarin presenting to the Accident & Emergency Department with a head injury, however minor, should have their INR measured. Patients on alternative anticoagulation should have a coagulation screen sent, although the results may not correlate with bleeding risk in the same way that INR does with warfarin.

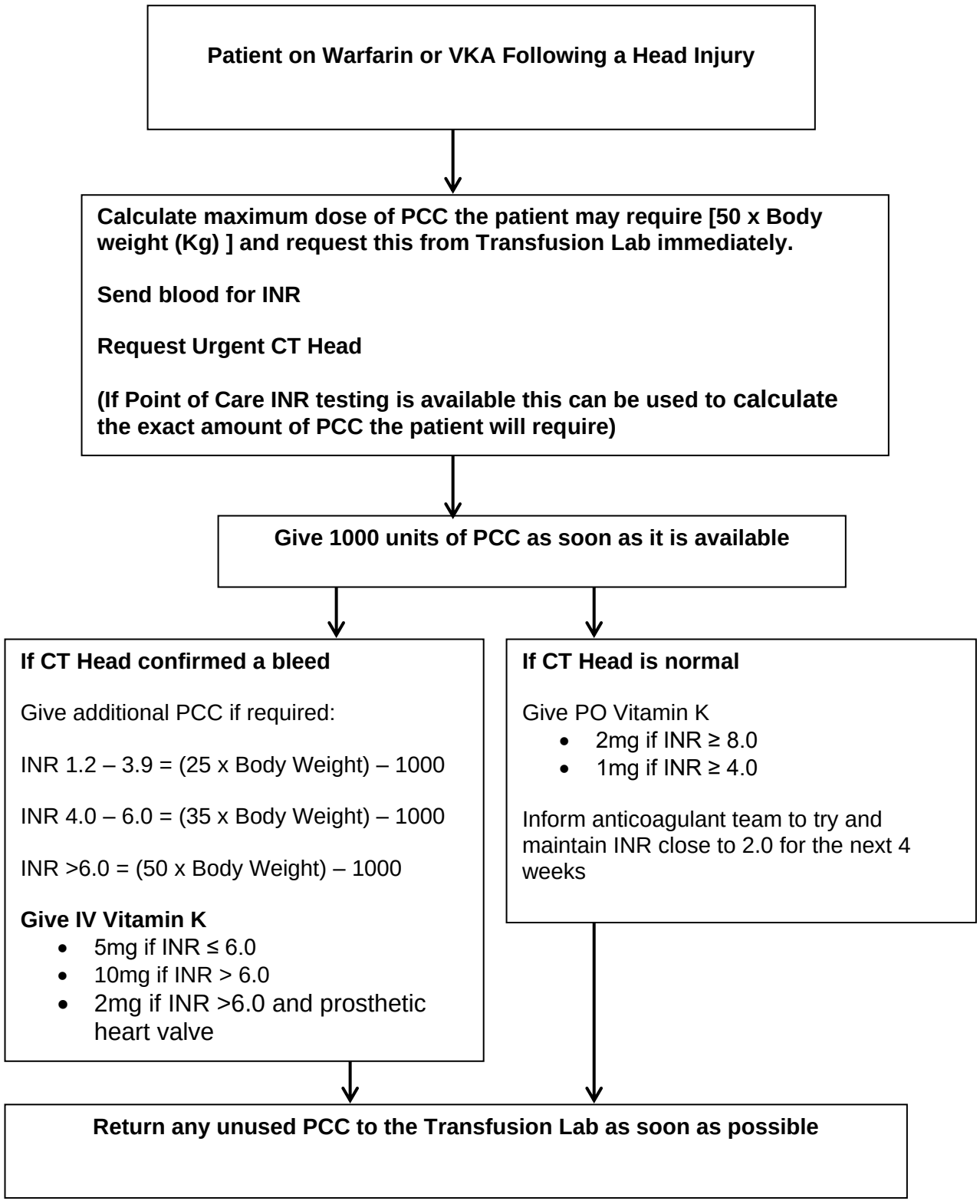
Individuals with loss of consciousness, amnesia or reduced Glasgow Coma Scale following a head injury should have an immediate CT scan of their head. Patients on anticoagulation are more likely to have a cerebral bleed with minor injury and should have an even lower threshold for a CT scan**. In general if the head injury was sufficient to cause facial or scalp laceration, bruising or persistent headache then a patient on anticoagulation should have an urgent CT Head.**

Any patient on anticoagulation therapy, who has had a head injury and where there is a strong suspicion of intracerebral bleeding, should have their anticoagulation reversed as quickly as possible. This may mean giving treatment to reverse the anticoagulation before blood test results are back and before CT scans have been performed.

Patients who are on warfarin for prosthetic heart valves and who sustain a head injury can have their anticoagulation reversed safely with Prothrombin Complex Concentrate (PCC). They may also require Vitamin K to help correct high INRs, but a lower dose of 2mg IV may be more appropriate.

Delayed intracranial bleeding can occur in patients on anticoagulation even when the initial CT scan is normal. In view of this patients on warfarin with supra-therapeutic INRs should have them corrected with Oral Vitamin K. It is also recommended to maintain their INR as close to 2.0 as possible for 4 weeks after a significant head injury.

Any patient on anticoagulation who sustains a significant head injury should have the risks verses benefits of anticoagulation reviewed prior to discharge from hospital. Patients on anticoagulation for atrial fibriallation alone who sustain a significant head injury or who are felt to be at increased risk of falls in the future should have their anticoagulation discontinued until the risk has reduced.


Patient on Warfarin or VKA Following a Head Injury
Calculate maximum dose of PCC the patient may require [50 x Body weight (Kg)] and request this from Transfusion Lab immediately.
Send blood for INR
Request Urgent CT Head
(If Point of Care INR testing is available this can be used to calculate the exact amount of PCC the patient will require)
Give 1000 units of PCC as soon as it is available
If CT Head confirmed a bleed
Give additional PCC if required:
INR 1.2 – 3.9 = (25 x Body Weight) – 1000
INR 4.0 – 6.0 = (35 x Body Weight) – 1000
INR >6.0 = (50 x Body Weight) – 1000
Give IV Vitamin K
5mg if INR ≤ 6.0
10mg if INR > 6.0
2mg if INR >6.0 and prosthetic heart valve
If CT Head is normal
Give PO Vitamin K
2mg if INR ≥ 8.0
1mg if INR ≥ 4.0
Inform anticoagulant team to try and maintain INR close to 2.0 for the next 4 weeks
Return any unused PCC to the Transfusion Lab as soon as possible

Appendix 1. CHA_2DS_2-VASC score

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

Appendix 2. HAS-BLED score

	Condition	Points
H	Hypertension: (uncontrolled, >160 mmHg systolic)	1
A	Abnormal renal function: Dialysis, transplant, Cr >200 µmol/L Abnormal liver function: Cirrhosis or Bilirubin >2x Normal or AST/ALT/AP >3x Normal	1 1
S	Stroke: Prior history of stroke	1
B	Bleeding: Prior Major Bleeding or Predisposition to Bleeding	1
L	Labile INR: (Unstable/high INRs), Time in Therapeutic Range < 60%	1
E	Elderly: Age > 65 years	1
D	Prior Alcohol or Drug Usage History Medication Usage Predisposing to Bleeding: (Antiplatelet agents, NSAIDs)	1

Appendix 3. Cockcroft-Gault Creatinine Clearance (CrCl) Formulae

$$\text{Creatinine Clearance (mls/min)} = \frac{(140 - \text{Age}) \times \text{Mass (kg)} \times \text{Constant}}{\text{Serum Creatinine (µmol/L)}}$$

(Where Constant is 1.23 for males and 1.04 for females)

Appendix 4. Beriplex Prescribing Information

Beriplex is a mixture of human clotting factors and is licensed for the urgent reversal of warfarin therapy.

It is stored as a dry powder and needs to be reconstituted prior to administration.

For reversal of warfarin the dose of Beriplex is dependent on the INR and the patient's weight (see Table below).

Beriplex is stored in the Accident and Emergency department and is also available from the Blood Bank.

Infusion Rate

- Patients less than 65kg = 4ml/min (240ml/hr)
- Patients greater than 65kg = 8ml/min (480ml/hr)

Beriplex Dosing Guide

Body Weight (Kg)	INR 2.0 – 3.9		INR 4.0 – 6.0		INR >6.0	
	Dose 25 IU/Kg		Dose 35 IU/Kg		Dose 50 IU/Kg	
30	30ml	750 units	42ml	1050 units	60ml	1500 units
35	35ml	875 units	49ml	1225 units	70ml	1750 units
40	40ml	1000 units	56ml	1400 units	80ml	2000 units
45	45ml	1125 units	63ml	1575 units	90ml	2250 units
50	50ml	1250 units	70ml	1750 units	100ml	2500 units
55	55ml	1375 units	77ml	1925 units	110ml	2750 units
60	60ml	1500 units	84ml	2100 units	120ml	3000 units
65	65ml	1625 units	91ml	2275 units	130ml	3250 units
70	70ml	1750 units	98ml	2450 units	140ml	3500 units
75	75ml	1875 units	105ml	2625 units	150ml	3750 units
80	80ml	2000 units	112ml	2800 units	160ml	4000 units
85	85ml	2125 units	119ml	2975 units	170ml	4250 units
90	90ml	2250 units	126ml	3150 units	180ml	4500 units
95	95ml	2375 units	133ml	3325 units	190ml	4750 units
100	100ml	2500 units	140ml	3500 units	200ml	5000 units
105	100ml	2500 units	140ml	3500 units	200ml	5000 units
110	100ml	2500 units	140ml	3500 units	200ml	5000 units
115	100ml	2500 units	140ml	3500 units	200ml	5000 units
120	100ml	2500 units	140ml	3500 units	200ml	5000 units

Full instructions are available via the SPC: http://www.medicines.org.uk/emc/medicine/21147

****Allergies. **** …… …… ……..

DNACPR in place? **YES NO**

Wrightington, Wigan and Leigh Teaching Hospitals
NHS Foundation Trust

Appendix 5: DNR4

DNR 4 **REQUEST FOR COMMUNITY NURSE TO ADMINISTER PRESCRIBED MEDICATION**

Patient's Name: ……
Address: …….
……..
Date of Birth……..
NHS Number ……

GP: ……
Address: ……...
……
Tel. No: ……

Date & Time Prescribed	Medication to be administered	Date to be commenced	Dosage	Frequency of Administration	Route of Administration	Date to be Discontinued *(If applicable)*	Print Name	Signature of Prescriber*

Appendix 6:

Hospital At Home
Transfer To Hospital

Wrightington, Wigan and Leigh Teaching Hospitals NHS Foundation Trust

Contact Tel No: 01942 822642	Contact Fax No: 01942 264440		
Patient's Name: Address:	Date of Birth:	Age:	
	NOK Advised of Admission?	YES	NO
	NOK Name:		
	Contact Number:		

Presenting Complaint / Reason Patient Is Being Referred For Hospital Assessment

Initial Reason For Referral to Hospital At Home

Patient's Medical History

Medication	**Allergies**
	Have you any LATEX associated allergies? Yes ☐ No ☐
Healthcare Associated Infections	**Observations**

Name:	Signature:	Date:

Wrightington, Wigan and Leigh Teaching Hospitals
NHS Foundation Trust

Fact Sheet

Vitamin K (Phytomenadione)

This vitamin is the antidote to Warfarin/Sinthrome and is given to patients on anticoagulant therapy to prevent bleeding.

It is being given to you because your blood result (INR) is out of your therapeutic range and needs to be reduced to prevent bruising or bleeding,

To administer

1. Snip off the top of the capsule with scissors.

2. Squeeze out the contents of the capsule directly into your mouth, on the inside of your cheek.

3. You may then need a glass of water if the taste is unpleasant.

Your INR will be checked again tomorrow and further advice given if necessary. If you are advised that the remaining capsule/s is/are not required, please throw it away by cutting the top off and squirting the contents down the sink and then put the capsule/s in a rubbish bin.

If you have any queries, please feel free to contact:

The Anticoagulant Nurses

Telephone 01942 822964

Monday to Friday 9:00 am to 5:00 pm

If you have any problems with bleeding overnight, you must contact the ‘out of hours’ GP Service or your nearest Accident and Emergency Department for further advice.

Appendix 8: Anti-coag nurses handover letter

NHS
Wrightington, Wigan and Leigh Teaching Hospitals
NHS Foundation Trust

Email

To:	**Email:**
From: Community React Team	**Phone: 01942 481221** **Email: wwl-tr.wwl-spa@nhs.net**
Pages:	**Date:**
Re:	**CC:**

	Urgent		**For information**		**Please comment**

Dear Anti Coagulation Nurses,

The Community React Team have been out to visit the above patient to administer Vitamin K _____, as requested by _____, due to INR being _____.

We have obtained a repeat INR today. If you require any further information, please contact us on the above numbers.

Thank You,

Kind Regards

Appendix 9: Haematology email sheet

Pathology at Wigan and Salford		Haematology Doc title: **Community React Team Email sheet**	
Q-Pulse Ref: HH-CF-361	Q -Pulse Revision No: 1	Authorised By: A Kennedy	Page **35** of **36**

To: Community React Team
Claire House
Ince
Wigan
WN3 4NW
Tel: 01942 481221
Email: wwl-tr.wwl-spa@nhs.net

Date		From	Haematology – 01942 822146
Number of pages including cover sheet:		1	

Patient Details	
Patient Name:	
Date of Birth:	
Hospital Number:	
Address:	
Telephone Number:	

REMARKS
Urgent
The above patient had an INR obtained today and the result is :   Please could Hospital at Home team visit and complete appropriate/assessment treatment following WWL anticoagulation Guidelines.   Please fax Hospital at Home team on the above number.   Regards.

PRIVACY AND CONFIDENTIALITY NOTICE
The information contained in this facsimile message is legally privileged and confidential information intended only for the individual or entity named above. If you, the reader of this message are not the intended recipient you are hereby notified that you should not further disseminate, distribute or copy this telecopy. In addition, if you have received this telecopy in error, please immediately notify us by telephone and return the original message to us at Haematology Department, Royal Albert Edward Infirmary, Wigan Lane, Wigan, WN1 2NN. Thank you. If this FAX dose not arrive complete or if there are any queries regarding this result, please telephone the Haematology Department on 01942 822146.