Direct Oral Anticoagulants (DOACs) for DVT and PE in adults: Local pathways

NHS Wiltshire Clinical Commissioning Group

Prescribing criteria for Rivaroxaban (Xarelto®), Dabigatran, Apixaban or Edoxaban in the treatment of Deep Vein Thrombosis (DVT) and Pulmonary Embolism (PE) and prevention of recurrent DVT and PE in adults

Rivaroxaban (Xarelto®) is the first-line option

Hospital VTE treatment pathways

- The hospital treatment pathways found via the links below advise the GP how to deal with suspected VTE according to which local hospital trust the patient is to be sent to for further investigation
- The treatment pathways should be used in conjunction with our other DOAC documents found on the local formulary websites

RUH (Bath)

http://nww.ruh-bath.nhs.uk/For_Clinicians/clinical_guidelines/documents/medicine/ACUTE-027_Deep_Venous_Thrombosis.pdf

http://nww.ruh-bath.nhs.uk/For_Clinicians/clinical_guidelines/documents/medicine/ACUTE-034_Pulmonary_Emoblus.pdf

SFT (Salisbury)

- A large range of documents regarding VTE can be accessed via: http://www.icid.salisbury.nhs.uk/CLINICALMANAGEMENT/THROMBOPROPHYLAXIS/Pages/IndexPage.aspx
- The DVT pathway can be found here: http://www.icid.salisbury.nhs.uk/ClinicalManagement/Thromboprophylaxis/Pages/SuspectedDVT.

Please note that the anticoagulation service at Salisbury district hospital recommend rivaroxaban (off-label) for the treatment of extensive superficial thrombophlebitis for patients at high risk of DVT

GWH (Swindon)

- See treatment pathway overleaf

Pulmonary Embolism

- NICE recommends all of the DOACs as possible treatments for adults with pulmonary embolism and to prevent further deep vein thrombosis or pulmonary embolism as follows:

  - Rivaroxaban (2013): http://www.nice.org.uk/guidance/ta287
  - Dabigatran (2014): http://www.nice.org.uk/guidance/ta327
  - Apixaban (2015): https://www.nice.org.uk/guidance/ta341
  - Edoxaban (2015): https://www.nice.org.uk/guidance/ta354

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GWH OP DVT Treatment Flowchart

Patient (NHS Swindon or NHS Wiltshire) attends Ambulatory Care Unit at GWH for initial assessment including FBC, Urea and electrolytes, eGFR, LFT's D-Dimer, Wells score and +/- Doppler ultrasound. If appropriate commence anticoagulation until result of Doppler scan known. Anti-coagulant options pre diagnosis is:

- LMWH
- Rivaroxaban (don't use this option if you think the patient would need to be on warfarin if the scan is positive).

Scan positive

Refer to anticoagulant clinic for on-going anticoagulation with either Rivaroxaban or warfarin. Continue anticoagulant until patient is seen by anticoagulant team

Scan negative

Patients referred back to GP for further investigation, anticoagulation discontinued

Consider rivaroxaban or warfarin for each patient:

If Rivaroxaban is being considered, use the other DOAC documents on the formulary websites to ensure that it is prescribed safely, that the NICE criteria are fulfilled and that the optimum treatment is chosen with the patient (also see page 3).

Rivaroxaban:
NICE TA261 for DVT and NICE TA287 for PE recommend:

Rivaroxaban is an option for the treatment of DVT and PE and prevention of recurrent DVT and PE in adults.

Both rivaroxaban and warfarin are available as options for the treatment of all VTE patients.

Rivaroxaban will be considered first-line.

Considerations – warfarin may be more appropriate:

1.) For patients with a Cr CL below 30ml/min or eGFR below 30ml/min/1.73m^3.

Refer to other formulary DOAC documents for further advice in any patient with renal impairment (or the SPC).

Treat with Rivaroxaban

- Fully counsel patient re: anticoagulation
- Prescribe **Rivaroxaban 15mg b.d issuing a 21 day pack (42 tabs)**
- Issue patient with information leaflet and alert card
- **For Swindon patients: Arrange to review patient in the anticoagulant clinic in 3 weeks' time to reduce the dose of Rivaroxaban to 20mg daily issuing a further 28 days prescription.**
- **For Wilts patients : Arrange appointment with GP in 3 weeks' time to reduce dose and check compliance**
- Transfer care to GP for further supplies
- For all patients fax all details to patients GP

Treat with Warfarin

- Fully counsel patient re: anticoagulation, including information leaflet and alert card
- Prescribe warfarin and continue with anticoagulant initiated pre-diagnosis until INR>2 on two consecutive occasions.

Following this:

Either: Review patient in the anticoagulant clinic

Or: Arrange for follow up with patients GP and or D/N services to monitor INR's and review treatment.

Long-term LMWH may be an option for certain patient groups as advised by specialist anticoagulant services.

For patients that don't tolerate Rivaroxaban, Apixaban is the 2nd line and Edoxaban 3rd line DOAC alternative. See SPC for dosage details.

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Considerations when choosing the right anticoagulant to use

Should I admit or not?

- Do you have reason to suspect serious renal failure? *Patient not suitable for ambulatory treatment,* refer for hospital assessment
- Do you suspect serious (pelvic) DVT or PE? *Medical assessment in hospital required +/- consideration of catheter directed thrombolysis etc.*
- Does the patient have ongoing bleeding or serious anaemia? *Seek specialist advice*

Will a DOAC be ok for this patient?

- Do you think the patient has active cancer? *Use a LMWH until the situation is clear*
- Does the patient have significant mucosal bleeding? (eg. Heavy periods, frequent rectal bleeding / haematuria*) Apixaban preferred*
- Does the patient already suffer with dizziness / hypotension / troublesome headaches? *Apixaban preferred*
- Is the patient on any medications which might alter DOAC effectiveness (eg. Anti-epileptics, dronedarone)? Use LMWH and then load with warfarin

Allergies:

- Rash is an infrequent side effect of rivaroxaban but when it happens it can be severe / progressive – seek specialist advice
- Paradoxical thrombosis + a fall in platelet count can occur with LMWH – seek specialist advice
- Lactose intolerance / diarrhoea – rivaroxaban / apixaban may worsen symptoms –Use LMWH instead and seek specialist advice

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Use of rivaroxaban for suspected DVT & PE (pre-diagnosis) in adults

- Current management of venous thromboembolism (VTE) requires the initiation of a low molecular weight heparin (LMWH) (e.g. dalteparin) for rapid anticoagulation whilst awaiting diagnostic workup. Once diagnosis is confirmed, a DOAC such as rivaroxaban or a vitamin K antagonist such as warfarin is initiated to treat the DVT or PE
- Many CCG areas in England have started to use DOACs such as rivaroxaban pre-diagnosis as it is much more convenient for the patient and in terms of staff resource
- Rivaroxaban removes the need for initial treatment with LMWH, and so replaces a two stage therapy with a single oral component
- Local haematologists in the BaNES/Swindon/Wiltshire area support the use of rivaroxaban in this manner
- In new patients, rivaroxaban should be the preferred option in those with a suspected DVT (unless contraindicated- see SPC) while awaiting and subject to diagnostic confirmation. For suspected PE discuss anticoagulation options with the clinician on referral for advice
- If the patient in question has a known diagnosis of cancer they should be anticoagulated with a LMWH (e.g. dalteparin) rather than rivaroxaban
- An informed discussion should take place between the clinician and the patient about the risks and benefits of rivaroxaban compared with LMWHs pre-diagnosis of VTE prior to the initiation of therapy

Procedure to follow:

- **Please refer to your local acute trusts diagnostic work up guidelines to ensure that the correct samples are done before initiating anticoagulation: **Ensure that baseline U&Es are done****
- **If DVT is likely** and ultrasound scan **is not** available within 4 hours, prescribe rivaroxaban 15mg bd for up to 7 days (depending on when the scan will take place) ie 14 x 15mg tablets . Check renal function. Remember to stop treatment if the diagnosis of DVT is disproved.
- **If DVT is unlikely** and ultrasound scan is not available within 4 hours, but a D-dimer test is positive, do as above in the "DVT is likely" statement.

Do NOT use rivaroxaban if:

- ***Patient already on DOACs/LMWHs or warfarin for other conditions***
- ***Renal impairment****: Rivaroxaban should be used with caution in patients with severe renal impairment (15 to 30ml/min) and may need a dose adjustment <u>after</u> the initial BD dosing in the first 3 weeks. Rivaroxaban is not recommended in patients with a CrCL <15ml/min**.** See SPC for further information: (http://www.medicines.org.uk/emc) or discuss with medicines information or anticoagulant specialist*
- ***Rivaroxaban is not an option if there is a chance of pregnancy*** *(or until negative pregnancy test)* ***or if breastfeeding****. Seek advice for such patients from a specialist.*

Ensure patient knows to ask their community pharmacist for an anticoagulant patient alert card

Once diagnosis is confirmed:

- <u>Dose:</u> **WEEK 1 TO 3:** 15mg twice daily with food for 21 days
- **WEEK 4 ONWARDS:** followed by 20mg once daily with food (total treatment of at least 3 months)
- <u>Duration of treatment</u> for confirmed DVT varies depending on clinical presentation. A shorter duration of therapy (at least 3 months) should be based on transient risk factors (e.g. recent surgery, trauma, immobilisation) and longer durations should be based on permanent risk factors or idiopathic DVT or PE. If unprovoked, review at 3 months and consider lifelong anticoagulation.
- All patients who need to be considered for lifelong anticoagulation should be referred to / discussed with a haematologist