County Durham and Darlington DVT Pathway Information

1. Patients with a diagnosis of suspected or confirmed DVT will be offered a choice of treatment of either oral rivaroxaban or enoxaparin and warfarin if clinically appropriate. To help you with this there are now two patient held records, one for rivaroxaban and one for enoxaparin, along with some supporting information.

2. Rivaroxaban can be used in place of enoxaparin and warfarin and there are cost savings when used short term for DVT and also potential benefits for patients and healthcare professionals. Clinicians are recommended to make themselves familiar with rivaroxaban before prescribing it.

3. Patients with suspected DVT should receive diagnostic interventions within 24 hours. Ultrasound scans are available 7 days a week and should be booked via 111.

4. Please note that patients with a negative initial ultrasound scan, but a positive d-dimer will have their treatment stopped until the results of the second scan are known – please see the Further Information section.

Duration of Treatment

Unless you are happy this is a provoked distal DVT we strongly recommend you seek advice on duration of treatment and further investigations either by referring to haematology or communicating with your local haematologist.

The NICE clinical guideline on venous thromboembolic disease recommends the following:

Short-term treatment (3 months) is recommended for those with transient risk factors such as recent surgery and trauma, and longer treatment for permanent risk factors or idiopathic (unprovoked) deep vein thrombosis.

Distal DVT (below the knee) usual duration of treatment is 3 months

Proximal DVT (above the knee), and those with permanent risk factors or idiopathic (unprovoked) deep vein thrombosis treat for 6 months or in some cases longer.

Consider extending the treatment for patients with unprovoked proximal DVT if their risk of DVT recurrence is high and there is no additional risk of major bleeding. Discuss with the patient the benefits and risks of extending their DVT treatment.

Patients who choose Rivaroxaban

Patients with a diagnosis of suspected or confirmed DVT will be offered a choice of treatment of either oral rivaroxaban or enoxaparin and warfarin if clinically appropriate. To help you with this there are now two patient held records, one for rivaroxaban and one for enoxaparin, along with some supporting information.

Rivaroxaban can be used in place of enoxaparin and warfarin and there are cost savings when used short term for DVT and potential benefits for patients. Clinicians are expected to make themselves familiar with the content of the summary of product characteristics for all drugs in the DVT pathway before prescribing.

To ensure immediate treatment, patients entering the rivaroxaban pathway will be supplied with either a starter pack of rivaroxaban 14 x 15mg tablets or will need a prescription of four tablets of rivaroxaban 15 mg until diagnosis and required treatment course is confirmed. For those patients diagnosed with a DVT, subsequent supplies of rivaroxaban will be by prescription.

For safety reasons, if the starter pack is used it is essential that this is recorded in their medical record.

The patient will also carry the DVT patient held record and the NOAC patient alert card which should be given to the patient with the starter packs, or will be supplied by the pharmacy if a prescription is given. In addition patients should also be counselled to let other health care professionals, such as dentists, involved in their care know that they are taking rivaroxaban.

Patients who do not wish to take rivaroxaban should be offered enoxaparin and warfarin.

Patients entering the DVT pathway should be provided with adequate information to give informed consent to their choice of treatment, please see the attached aide memoir for information.

Any patient who is already anti-coagulated should not enter the rivaroxaban DVT pathway and you should seek specialist advice**. For the avoidance of any doubt, patients must not be prescribed rivaroxaban and warfarin.**

Please familiarise yourself with prescribing information contained in the current version of the BNF. More extensive prescribing information can be found in the summary of product characteristics (SPC), along with a copy of the patient information leaflet, both of which can be found here:

www.medicines.org.uk/EMC/searchresults.aspx?term=Rivaroxaban&searchtype=QuickSearch

Please also consider the following website as an information resource on rivaroxaban which is MHRA approved:

www.xarelto-info.co.uk/

Serious reactions must be reported to the MHRA via the yellow card scheme.

Treatment of DVT

Dosage

The recommended dose for the initial treatment of acute DVT is **15 mg twice daily for the first three weeks, followed by 20 mg once daily for the remainder of the treatment period*.**

Patients should be advised to take rivaroxaban with food to improve absorption of the tablets.

If the patient is to remain on rivaroxaban longer term, renal function should be checked every 6 months, or sooner if the patient becomes clinically unwell.

**In patients with reduced creatinine clearance of between 15 – 49 ml/min, a reduction of the dose from 20 mg once daily to 15 mg once daily should be considered if the patient's assessed risk for bleeding outweighs the risk for recurrent DVT. Do not enter patient into DVT Pathway if creatinine clearance is below 30 ml/min. NB Please use creatinine clearance rather than eGFR (most medical software systems have an automatic creatinine clearance calculator eg look under Clinical Tools within SystmOne).*

Missed Doses

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

If a dose is missed during the once daily treatment phase (day 22 and onwards), the patient should take rivaroxaban immediately, and continue on the following day with the once daily intake as recommended. The dose should not be doubled within the same day to make up for a missed dose.

Interactions with other medicinal products

The use of Xarelto is not recommended in patients receiving concomitant systemic treatment with azole-antimycotics (such as ketoconazole, itraconazole, voriconazole and posaconazole) or HIV protease inhibitors (e.g. ritonavir).

For full details of interactions see the summary of product characteristics: www.medicines.org.uk/emc/medicine/

Common side effects

The summary of product characteristics states that the risk of bleeding may be increased in certain patient groups, for example those with uncontrolled severe arterial hypertension and/or those taking other treatments that affect haemostasis such as NSAIDs, aspirin, platelet aggregation inhibitors or other antithrombotic agents. For patients at risk of GI bleeding, gastric protection with a PPI should be considered.

For full details of adverse reactions and contraindications see the summary of product characteristics:

www.medicines.org.uk/emc/medicine/

Management of bleeding and overdose

Should minor bleeding complications arise in a patient taking rivaroxaban, delay the next dose of rivaroxaban or discontinue treatment if appropriate, after DVT risk assessment. If bleeding is problematic, consider tranexamic acid 1g orally up to 6 hourly until cessation of bleeding, but suggest you seek secondary care advice. Moderate to severe bleeding requires urgent hospital admission.

Please click on the following link for more information:

Xarelto 15mg film-coated tablets - Summary of Product Characteristics (SPC) - (eMC)

Patients who choose Enoxaparin

If DVT is likely and enoxaparin is clinically appropriate, calculate the dose of enoxaparin and inject the patient.

Arrange an ultrasound scan within 24 hours.

If DVT is confirmed, the patient should be initiated on warfarin and continued on enoxaparin until the INR is within the therapeutic range with a targeted INR range of between 2.0 to 3.0.

Continue prescribing warfarin for duration of treatment. For patients who have an unprovoked DVT please see 'Further Investigations' section.

If the patient doesn't have a DVT, further investigations may be required for an alternative diagnosis.

Further information (applies to rivaroxaban and enoxaparin/warfarin):

Patients with a negative ultrasound scan, but a positive D-dimer

You should **stop treatment** with either rivaroxaban or enoxaparin until the repeat ultrasound scan 6-8 days later (which you should arrange by telephoning 111). This is because the patient will have one of the three scenarios below:

1. Not have a DVT at all,
2. have an isolated calf vein DVT that would not have extended, or
3. have an isolated calf vein DVT that would have extended

Giving anticoagulation for the week is unnecessary for 1 and 2. In 3, continuing treatment would very likely stop extension for the week it is given (making the second scan pointless as it will be negative). When anticoagulation is then stopped the clot may then extend proximally and remain untreated - one week of anticoagulation being insufficient.

A repeat scan should be booked via 111 for 6–8 days after the initial scan and this should be recorded on the second page of the patient held record.

Patients with Active Cancer

LMWH remains the first choice treatment for preventing venous thromboembolism in people with cancer. NICE stated that rivaroxaban should not be excluded as a treatment option for preventing venous thromboembolism in people with cancer and it may be a pragmatic option in some cases. Please note that rivaroxaban is contra-indicated in malignant neoplasms at high risk of bleeding e.g. upper gastrointestinal malignancies.

There is limited evidence to compare the effect of rivaroxaban in patients with cancer and DVT to the standard treatment of low molecular weight heparin. No direct head to head studies have been conducted as yet and an indirect comparison submitted to NICE suggested that rivaroxaban would be less effective in preventing VTE recurrence but would induce fewer major bleeding events.

Compression Stockings

After deep vein thrombosis affecting a lower limb, NICE used to recommend offering compression stockings. This recommendation has now changed and NICE now says:

Do not offer elastic graduated compression stockings to prevent post-thrombotic syndrome or VTE recurrence after a proximal DVT. This recommendation does not cover the use of elastic stockings for the management of leg symptoms after DVT.

Iliofemoral DVT

NICE Guidance suggests that for patients with Iliofemoral DVT, catheter-directed thrombolytic therapy for patients should be considered. In these circumstances, contact secondary care.

D-dimer result

This should be asked for urgently in a patient who is DVT unlikely on presentation (Wells score 1 pt or less). In this situation where the d-dimer result is unavoidably going to be delayed until the next day, then it would be sensible for the physician to weigh up the risk/benefits of giving a one off dose of rivaroxaban or enoxaparin, and if this ok then it may be appropriate to give an interim dose whilst waiting for the result.

Further Investigations

Please remember that there are a multitude of other causes for a raised d-dimer in absence of DVT and you should consider further investigations.

Patients with clinical signs of superficial thrombophlebitis affecting the proximal long saphenous vein should have an ultrasound scan to exclude concurrent DVT.

NICE says the following regarding investigations for cancer and thrombophilia testing;

Investigations for cancer

Offer all patients diagnosed with unprovoked DVT who are not already known to have cancer the following investigations for cancer:

- a physical examination (guided by the patient's full history)
- a chest X-ray
- blood tests (full blood count, serum calcium and liver function tests)
- urinalysis

and consider further investigations for cancer with an abdomino-pelvic CT scan (and a mammogram for women) in all patients aged over 40 years with a first unprovoked DVT who do not have signs or symptoms of cancer based on initial investigation.

NICE guidance NG12 states that DVT is associated with several cancers including urogenital, breast, colorectal and lung; carry out an assessment for additional symptoms, signs or findings that may help to clarify which cancer is most likely and consider urgent investigation or refer under the two week wait rules.

Unless you are happy this is a provoked distal DVT we strongly recommend you seek advice regarding further investigations either by referring to haematology or communicating with your local haematologist.

Thrombophilia testing

- Do not offer thrombophilia testing to patients who are continuing anticoagulation treatment.
- Consider testing for antiphospholipid antibodies in patients who have had unprovoked DVT if it is planned to stop anticoagulation treatment.
- Consider testing for hereditary thrombophilia in patients who have had unprovoked DVT or and who have a first-degree relative who has had DVT or if it is planned to stop anticoagulation treatment.
- Do not offer thrombophilia testing to patients who have had provoked DVT.
- Do not routinely offer thrombophilia testing to first-degree relatives of people with a history of DVT and thrombophilia.

For more information please go to: CDDFT Pathology Handbook and look under “Thrombophilia Screen”

Unless you are happy this is a provoked distal DVT we strongly recommend you seek advice regarding further investigations either by referring to haematology or communicating with your local haematologist.

Give Patients Informed Consent in their Choice of Treatment

All NOACS recommended by NICE are an option for treating and preventing recurrent DVT and should be made available if required for individual patients. County Durham and Darlington APC recommend rivaroxaban as the first line NOAC for DVT based on experience, cost and consistency for the DVT pathway.

Patients entering the DVT pathway should be provided with adequate information to give informed consent to their choice of treatment. You may find it useful to cover the following points:

LMWH plus warfarin

Pros

- Well established treatment which is very effective
- Process of bleeding reversal is more familiar

Cons

- Initial injections with LMWH
- Warfarin requires on-going monitoring at an INR clinic which may be inconvenient for some patients
- Warfarin has many drug and non-drug interactions which can impact on many patients
- Dose depends on INR result and can often vary
- Risk of bleeding

Rivaroxaban

Pros

- Use in DVT has been supported by respected bodies such as NICE and the Scottish Medicines Consortium. It has shown to be as effective as warfarin in DVT.
- Oral preparation with no injections
- Simple dosage regimen
- Significantly fewer drug and non-drug interactions than warfarin
- No need to attend monitoring clinics
- Reduced incidence of intracranial bleeding compared to warfarin
- Short half life

Cons

- A newer treatment with less experience than with LMWH and warfarin
- Increased risk of GI bleeding compared to warfarin
- Process of bleeding reversal is less familiar with no established antidote (yet)