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| Primary Care Prescribing Pathway: Rivaroxaban for the Treatment of Deep Vein Thrombosis |
| Dr Rob White |
| 3rd March 2014 |

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| Title: | DVT Primary Care Prescribing Pathway |
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| Name of originator/author: | Dr Rob White |
| Name of responsible team: | KCCG Urgent Care/Prescribing |
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| Review date: | 3rd September 2014 |
| Target audience: | General Practice |

Before commencing NOAC anticoagulation please ensure that patient is not already taking anticoagulation. This non-exhaustive list provides examples to check:

Orally: Warfarin, Acenocoumarol, Phenindione, Dabigatran, Apixaban, and Rivaroxaban

Parenteral- Heparin, Dalteparin, Enoxaparin, Tinzaparin.

If any doubts please contact numbers given or check BNF

**Introduction**

The purpose of this guideline is to support primary care in the use of rivaroxaban in the treatment and diagnosis of deep vein thrombosis (DVT) in the community . Rivaroxaban is recommended as an option for the treatment of DVT in the NICE technology guidance 261 issued July 2012.

<http://guidance.nice.org.uk/TA261>

The main benefits of rivaroxaban over traditional Vitamin K antagonist treatments (such as warfarin) is a more predictable effect, with fewer drug and food interactions and a wider therapeutic window . The therapeutic effect of rivaroxaban is measured clinically without specific drug or coagulation testing. This has benefits to the patients over the usual treatments in reducing blood testing, travelling and dietary restrictions. Financial savings or cost neutrality by use of these agents has been calculated by cost reduction to the healthcare system as a whole which is offset against the increased cost of the drugs. Benefits include reduction in the expense of coagulation testing as well as clinician time, freeing nursing appointments, reducing home visiting and patient travelling, as well as dealing with “out of range” INRs.

Rivaroxaban has an incidence of significant haemorrhage of about 3%. The EINSTEIN-DVT study demonstrated a comparable number of clinically relevant bleeding episodes to those treated with enoxaparin and vitamin K antagonist. The extension study (EINSTEIN-EXT) experienced a higher rate of clinically non-major bleeding but the comparator was placebo and not active control. (CIOS Formulary fact sheet: Rivaroxaban for the treatment and prevention of recurrent DVTs and PEs)

<https://www.eclipsesolutions.org/cornwall/info.aspx?paraid=192>

There is no specific antidote for rivaroxaban. Management is by drug omission and resuscitation, but in life threatening haemorrhage reversal of the drug effect may be attempted by the administration of prothrombin complex concentrate. Local guidance has been developed regarding this with education given to medical staff.

**Primary care management of DVT**

This pathway should be read and used in conjunction with the relevant service specifications covering DVT assessment and management in primary care. Patient choice of anticoagulation should always be offered and discussed including risks vs. benefits of each agent. If rivaroxaban is initiated, patient counselling and guidance should be undertaken, and a patient alert card issued.

This pathway specifically covers the treatment of adults with suspected or confirmed DVT who are suitable to be treated with rivaroxaban. This pathway should be used in conjunction with the two-level Wells score and D-dimer testing with or without ultrasound imaging. This pathway can be offered by a two routes; solely primary care managed with bloods and scanning arranged directly as per protocols available on Acute GP and RMS websites, or by DVT clinic:

<http://acutegp.com/pathways/deep-vein-thrombosis/>

This pathway does not cover children or young people under the age of 18, or women who are pregnant or breast feeding. For cancer patients specialist advice should be sought via the DVT clinic or haematology department. The pathway will assume that prescribers will use a drug’s summary of product characteristics to inform decisions made with individual patients.

[http://www.medicines.org.uk/EMC/medicine/25586/SPC/Xarelto+20mg+film-coated+tablets/](http://www.medicines.org.uk/EMC/medicine/25586/SPC/Xarelto%2B20mg%2Bfilm-coated%2Btablets/)

The pathway consists of a number of parts:

* DVT patient pathway - informed by NICE guidance
* Rivaroxaban for DVT treatment - prescribing information
* DVT investigation and treatment proforma

For patients who present with a chronically swollen leg of greater than 28 days with no change in symptoms, it is appropriate to book straight to scan with no anticoagulation.

**Post-operative patients on Rivaroxaban already with suspected DVT.**

(Patients will usually be on the prophylactic dose post hip/knee replacement of 10mg daily)

If 4-hour scan is available just book to scan- no change in anticoagulation. If the patient has not taken that day’s rivaroxaban dose then stop it and start Dalteparin s/c at appropriate weight -related dose and arrange scan. Treat until scan gives appropriate course of action (no need to D-dimer).

If the patient has already taken that day's dose of rivaroxaban then increase
to therapeutic dose i.e. 30mg (15mg bd) and arrange scan. Treat until scan gives appropriate course of action (no need to D-dimer).

**DVT PATIENT PATHWAY** (Ref NICE CG 144 (June 2012)

<http://guidance.nice.org.uk/CG144>

* Please refer to DVT dosing regime and counsel patient about dose change at week 4 onwards.
* Please refer to duration of treatment
* Issue patient with alert card (Yellow anticoagulation card or *Xarelto* card).
* All patients presenting with VTE should have full clinical history and examination undertaken with aim of detecting underlying conditions contributing to the development of thrombosis and assessing suitability for antithrombotic therapy
* Unselective screening for cancer in patients with DVT is not recommended
* Patients who have a negative or inadequate initial scan but have a persistent clinical suspicion of DVT or symptoms do not settle should have a repeat ultrasound scan

Please refer to DVT dosing regimen and council patient about dose change at week 4 onwards

Please refer to duration of treatment

Issue patient with alert card

**Patient presents with symptoms and signs of DVT**

Examination to exclude other causes

**TO BOOK SCAN RING VASCULAR STUDIES**

**NEXT AVAIALABLE**

**SLOT WILL BE ALLOCATED**

**01872 255186**

**DVT Likely**

Two-level DVT Wells ≥ 2 points

**DVT Unlikely**

Two level DVT Wells 1 point or less

D-dimer test

(include Wells score on blood form)

Start oral

Anticoagulation\*

Two level Wells score

(see proforma)

D-dimer

positive

D-dimer

negative

Scan

(Localised policy whole leg is scanned so no scan 6-8 days later if scan negative)

Start oral

Anticoagulation\*

Scan

Not DVT

Scan

positive

Scan

negative

DVT

NOT

DVT

Scan

positive

Scan

negative

DVT

NOT

DVT

STOP

Oral

Anticoagulation

\*NOTE

* If scan can be performed in 4 hours issue a delayed script and advise only to commence if scan positive
* If wait for scan>4 hours, start treatment

This guide is used to support the appropriate use of rivaroxaban for the treatment of DVT by GPs .

It includes the following information:

* Indications
* Counselling checklist
* Dosing recommendations
* Initiation whilst waiting a scan
* Review
* Populations at higher risk of bleeding
* Perioperative management
* Pregnancy breast feeding
* Overdose
* How to manage bleed complications.

**Indications for Rivaroxaban covered by this document**

Treatment of DVT and prevention of recurrent DVT and pulmonary embolism (PE) following an acute DVT in adults

**Rivaroxaban patient alert card and patient information**

The prescriber must provide a patient alert card to each patient prescribed rivaroxaban 15mg or 20mg (contained within the patient booklet *A patient’s guide to Deep Vein Thrombosis treatment –available from manufacturer or CCG).* The patient alert card will inform treating clinicians and dentists about the patient’s anticoagulation treatment and will contain emergency contact information . Patients should be instructed to carry alert card at all times and present it to all health care providers.

**Counselling checklist**

1. patient alert card-go through each point, keep at hand

Dose and duration of treatment

Possible side effects and what to do

Impact on dental treatment

Advise on planning pregnancy or becoming pregnant

Effect on sport and travel

When and how to seek medical help

1. Importance of compliance
2. non-reversibility of rivaroxaban and bleeding risk
3. Missed dose advice
4. Avoid OTC aspirin/NSAID
5. Take with food
6. Need for GP to continue script
7. Expect dose change from 15mg twice daily to 20mg once a day after 3 weeks

**DVT dosing recommendations**

**WEEK 1 T0 3-** Initially treat with **15mg twice daily with food** for the first 3 weeks

**WEEK 4 ONWARDS**- The initial treatment is followed by **20mg once daily with food** for duration

(See separate dose adjustment for renal impairment)

**Duration of treatment**

* **3 months’ treatment**- *Confirmed proximal DVT- continue the maintenance dose of rivaroxaban for three months. Short term (3 months) is recommended for those with transient risk factors such as recent surgery and trauma. After 3 months’ treatment at maintenance dose, assess the risk and benefits of continuing treatment. Unprovoked proximal DVT –Consider extending beyond 3 months if their risk of VTE recurrence is high and there is no additional risk factor of major bleeding. Discuss with the patient the risk vs. benefits and risk of extending their treatment.*
* **Longer duration of treatment-** *Consider longer treatment for permanent risk factors or idiopathic (unprovoked) deep vein thrombosis if their risk of VTE recurrence is high and there is no additional risk of major bleeding. Discuss with the patient the benefits and risks of extending their treatment. Seek advice from haematology if unsure. Experience with rivaroxaban in this indication for more than 12 months is limited.*

**General risk factors for VTE recurrence**

|  |  |  |  |
| --- | --- | --- | --- |
| **Thrombophilia** | **History/FH of VTE** | **Pregnancy/recent child birth** | **Bedridden> 3 days** |
| **Age>60 years** | **Recent surgery 4 wks.** | **IV drug abuser** | **Smoker** |
| **Obesity** | **Travel >4hrs last 5 wks.** | **HRT or Oral contraception** | **Cancer** |
| **Acute medical illness** |  |  |  |

**Patients with renal impairment**

|  |  |  |
| --- | --- | --- |
| **Normal or mild renal impairment****eGFR>50** | **Day 1-21** | **15mg twice daily for 3 weeks** |
| **Day 22 and onwards** | **then 20mg once daily for duration** |
| **Moderate to severe renal impairment** **eGFR15-49** | **Day 1-21** | **15mg twice daily for 3 weeks** |
| **Day 22 and onwards** | **then 20mg once daily for duration. A reduction of dose to 15mg once daily should be considered if assessed risk of bleeding outweighs risk of recurrent DVT and PE** |
| **Severe renal impairment** **eGFR <15** | **Not recommended** |

Patients with renal impairment are at higher risk of haemorrhage. Rivaroxaban should be used with caution in patients with renal impairment taking concomitant potent inhibitors of CYP3A4 (e.g. systemic azole-antimycotics (such as ketoconazole, itraconazole, voriconazole and posaconazole) or HIV protease inhibitors (e.g. ritonavir) or dronedarone

**Initiation of Rivaroxaban Whilst Awaiting Scan**

* **DVT is likely-** For those patients in whom the diagnosis of DVT is likely based on two-level Wells score, and for whom a leg vein ultrasound scan **is not** available within 4 hours, 1 week (14x15mg tablets) treatment with rivaroxaban should be initiated. For those patients for whom a DVT is likely based on the two-level wells score and a leg vein scan **is** available within 4 hours, a prescription for 1 week (14x15mg tablets) treatment with rivaroxaban should be issued with instruction only to have dispensed and start treatment if the scan is positive. GP communication with the patient must be the same day. Check renal function.
* **DVT is unlikely-** For those patients in whom the diagnosis of DVT is unlikely based on the two-level Wells score, and for whom leg vein scanning is not available within 4 hours , but a D-dimer test is positive , 1 week (14x15mg tablets) treatment with rivaroxaban should be initiated. For those patients for whom a DVT is unlikely based on the two-level wells score and a leg vein scan **is** available within 4 hours, but the D-dimer is positive a prescription for 1 week (14x15mg tablets) treatment with rivaroxaban should be issued with instruction only to have dispensed and start treatment if the scan is positive . GP communication with the patient must be the same day. Check renal function.

**Missed Dose:**

* **Twice daily treatment period** (15mg twice daily for 3 weeks) : if a dose is missed , the patient should take rivaroxaban immediately to ensure intake of 30mg rivaroxaban per day. Continue with the regular 15mg twice daily on the following day.
* **Once daily treatment period** (beyond three weeks): If a dose is missed, the patient should take rivaroxaban immediately and continue on the following day with once daily intake as recommended. The dose should not be doubled within the same day to make up a missed dose.

**Review of patients**

Once a diagnosis of DVT is confirmed patients should be reviewed near the end of their 3 month period. For those patients who continue onto longer duration of treatment, they should be reviewed at least every 3-6 months, depending on individual circumstances.

**Populations Potentially at Higher Risk of Bleeding**

Any unexplained fall in haemoglobin or blood pressure should lead to a search for a bleeding site.

Several sub-groups of patients are at increased risk of bleeding and should be carefully monitored for signs and symptoms of bleeding complications:

* *Patients with hepatic impairment-* Rivaroxaban is contraindicated in patients with hepatic disease-associated coagulopathy and clinically relevant bleeding risk, including cirrhotic patients classified as Child Pugh B and C.
* *Patients concomitantly receiving other medicinal products-* Rivaroxaban is not recommended with systemic azole-antimycotics (such as ketoconazole, itraconazole, voriconazole and posaconazole) or HIV protease inhibitors (e.g. ritonavir ) or dronedarone
* *Take care with drugs effecting haemostasis-* Such as NSAIDs, acetylsalicylic acid, platelet aggregation inhibitors or other antithrombotic agents. **Consider GI prophylaxis with a daily proton pump inhibitor (PPI), especially in those on drugs effecting haemostasis, older persons and/or those with additional risk factors.**
* *Patients with other haemorrhagic risk factors such as-*uncontrolled severe arterial hypertension (systolic >180 diastolic >115) – active ulcerative GI disease, recent GI ulcerations, vascular retinopathy, recent intracranial/intracerebral or genitourinary haemorrhage, intraspinal or intracerebral vascular abnormalities, recent brain, spinal or ophthalmic surgery, bronchiectasis or history of pulmonary bleeding, congenital or acquired bleeding disorders .

*If there are concerns over bleeding risk, please always seek help from the contact numbers.* However further guidance may be gained from “risk scores” such as HAS-BLED score for major bleed

<http://www.mdcalc.com/has-bled-score-for-major-bleeding-risk/>

This has only been validated in atrial fibrillation so is only useful for non-quantitative guidance.

**Pregnancy/Breastfeeding**

Rivaroxaban is contraindicated in this group. Women of child-bearing potential should be counselled about the risks of pregnancy.

**Peri-operative Management**

If an invasive procedure or surgical intervention is required, rivaroxaban should be stopped at least 24 hours before the intervention if possible, and based on the clinical judgement of the physician. If the procedure cannot be delayed the increased risk of bleeding should be assessed against the urgency of the intervention. Rivaroxaban should be restarted as soon as possible after the procedure allowing for the clinical situation and adequate haemostasis.

**Overdose**

Limited absorption of rivaroxaban leads to a ceiling effect and no increase in average plasma exposure in doses of 50mg and above. The use of activated charcoal is appropriate to reduce absorption in overdose.

**How to Manage Bleeding Complications**

**There is currently very limited clinical experience with the use of products to reverse the effects of rivaroxaban and no specific antidote.** Should a bleeding complication occur the next dose should be delayed or treatment discontinued as appropriate. Individual bleeding management may include *symptomatic treatment*, such as mechanical compression, surgical intervention, fluid replacement. *haemodynamic support,* blood product or component transfusion. *For life threat bleeding,* that cannot be controlled by above measures, administration of a specific procoagulant reversal agent should be considered; prothrombin complex concentrate (PCC), activated prothrombin complex concentrate (APCC) or recombined factor VIIa (r-FVIIa)

Rivaroxaban is a Black Triangle drug therefore all suspected adverse drug reactions should be reported.

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| Kernow CCG: DVT Primary Care Prescribing Pathway-Using RivaroxabanVersion 1.0 March 14 |

1. **Patient information**

|  |  |  |  |
| --- | --- | --- | --- |
| NAME |  | DOB |  |
| ADDRESS |  | NHS No |  |
| GP |  | Tel |  |

**B. Pre-test probability of DVT D. Suitable for primary care**

**Two level DVT Wells Score management with rivaroxaban?**

|  |  |
| --- | --- |
| Clinical Feature | points |
|  Active cancer in the last 6/12 | **+1⁮** |
| Paralysis, paresis or recent leg plaster | **+1⁮** |
| Recent bedridden for 3/7 or more, or major surgery within 4/52 | **+1⁮** |
| Tenderness along the distribution of the deep venous system | **+1⁮** |
| Entire leg (calf and thigh) swollen | **+1⁮** |
| Calf swelling 3cm larger than asymptomatic side | **+1⁮** |
| Pitting oedema confined to/worse in symptomatic leg | **+1⁮** |
| Collateral superficial veins (non-varicose) | **+1⁮** |
| Previously documented DVT | **+1⁮** |
| An alternative diagnosis is at least as likely as a DVT |  **-2⁮** |
| **Total score** |  |
| **Clinical probability simplified score** | **Points** |
| **DVT likely** | **2 or more points** |
| **DVT unlikely**  | **1 point or less** |

|  |  |
| --- | --- |
| **Clinical feature** | **Tick** |
| **Yes-proceed to consider treatment** | **⁮** |
| **No-due to one or more of the following reasons below (or another reason)****Refer to secondary care. Consider low molecular weight heparin DVT clinic etc.** | **⁮** |
| Pregnancy or breast feeding/post-partum | **⁮** |
| Age <18 years | **⁮** |
| Currently on warfarin or low molecular weight heparin | **⁮** |
| Symptoms of PE | **⁮** |
| Potential bleeding lesions e.g. GI ulcers, GU, pulmonary, intracranial/spinal or GI bleed < 4/52 ago, varices. CNS vascular abnormalities, aneurysm, trauma/surgery, vascular retinopathy, bronchiectasis (not exclusive list) | **⁮** |
| Hepatic disease associated with coagulopathy | **⁮** |
| Congenital or acquired bleeding disorders | **⁮** |
| Systolic BP >180 or diastolic BP >115 | **⁮** |
| Active cancer within 6 months (consider low molecular weight heparin DW secondary care) | **⁮** |
| Anticipated compliance problems even with support (e.g. mental illness or alcohol/drug misuse) | **⁮** |
| Severe renal impairment (CKD stage 5)eGFR <15 | **⁮** |
| Azole antifungals (e.g. fluconazole, itraconazole etc.) HIV protease inhibitor or dronedarone | **⁮** |

**C. D-Dimer test result**

|  |  |
| --- | --- |
| Taken in practise | **Y or N** |
| Positive**⁮** | Negative**⁮** | No result**⁮** | Not app’**⁮** |

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**NEXT AVAIALABLE**

**SLOT WILL BE ALLOCATED**

**01872 255186**

**E. Treating venous thromboembolism (VTE): Rivaroxaban dosing:**

|  |  |  |
| --- | --- | --- |
| Normal or mild renal impairmenteGFR>50 | Day 1-21 | 15mg twice daily for 3 weeks |
| Day 22 and onwards | then 20mg once daily for duration |
| Moderate to severe renal impairment eGFR 15-49 | Day 1-21 | 15mg twice daily for 3 weeks |
| Day 22 and onwards | then 20mg once daily for duration. A reduction of dose to 15mg once daily should be considered if assessed risk of bleeding outweighs risk of recurrent DVT and PE |
| Severe renal impairment eGFR <15 | Not recommended |

**F. Mechanical prophylaxis**

Proximal deep vein thrombosis

Offer below-knee graduated compression stockings with an ankle pressure greater than 23mmHg (class 3 stockings, or class 2 if these are poorly tolerated) to patients with proximal DVT a week after diagnosis or when swelling is reduced sufficiently and there is no contraindication and :

* Advise the patients to continue wearing the stockings for **at least 2 years**
* Ensure the stockings are **replaced two or three times a year** or according to manufacturer’s instructions
* Advise patients that stockings only need to be  **worn on affected leg**

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* Advise patients that stockings only need to be  **worn on affected leg**

**H. Results and Observations**

|  |  |
| --- | --- |
| **Date of scan** | **Result** |
|  | **No DVT****⁮** | **Confirmed DVT****⁮** |

**G. Further help and advice about management and Tx DVT please go to Acute GP website or between 09.00-18.00 7 days can also ring also DVT clinic.**

<http://acutegp.com/pathways/deep-vein-thrombosis/>

Acute GP

**01872 25 3566**

**DVT clinic**

**Phone/fax** 01872 25 **3597**