NHS FORTH VALLEY

RIVAROXABAN AS TREATMENT FOR DEEP VEIN THROMBOSIS AND PULMONARY EMBOLISM IN ADULTS

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Consultation and Change Record – for ALL documents

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Date	**Author**	**Change**	**Version**
16/01/2013	RN	Minor textual changes	1.1
18/03/13	RN	Addition of acute PE as indication for treatment with rivaroxaban	1.2

Indications

Rivaroxaban (Xarelto ®) is licensed and approved for the treatment of deep vein thrombosis (DVT) and pulmonary embolus (PE) along with prevention of recurrent DVT and pulmonary embolism (PE) following an acute VTE in adults.

Rivaroxaban is the first line therapy for patients with new presentation DVT and PE in NHS Forth Valley

Rivaroxaban is NOT to be used in patients with VTE associated with active cancer, IVDU patients or during pregnancy. Such patients are to be treated with LMWH.

Patients *already* established on VKA for treatment of VTE should remain on VKA unless there is a good reason to change

Treatment of DVT and PE and prevention of recurrent DVT and PE

The recommended dose for the initial treatment of confirmed acute DVT or PE is 15 mg twice daily for the first three weeks followed by 20 mg once daily for the continued treatment and prevention of recurrent DVT and PE, as indicated in the table below.

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	Dosing schedule	Maximum daily dose
Day 1-21	15 mg twice daily	30 mg
Day 22 and onwards	20 mg once daily	20 mg

Duration of Therapy

The duration of therapy should be individualised after careful assessment of the treatment benefit against the risk for bleeding. Short duration of therapy (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. Experience with Rivaroxaban in this indication for more than 12 months is limited.

Recommendation:

Provoked DVT (following surgery, trauma, immobilisation) – 3 months therapy

Spontaneous DVT (First or subsequent thrombosis) – 6 months therapy

Provoked PE (following surgery, trauma, immobilisation) – 6 months therapy

Spontaneous PE (First or subsequent thrombosis) – 12 months therapy

Any extension of therapy beyond twelve months to be discussed with a consultant haematologist.

Missed Dose

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.

Thrombosis when on Rivaroxaban

Patients who develop a subsequent DVT when taking rivaroxaban should be regarded as treatment failures and managed with LMWH and warfarin. Patients who develop a pulmonary embolus when on rivaroxaban should have the drug stopped and be managed with LMWH and warfarin.

Renal Impairment

Mild renal impairment (eGFR 30 – 59ml/min) – No dose adjustment

Moderate renal impairment (eGFR 15-29ml/min) dose= 15 mg twice daily for 3/52 then 20mg OD. Consider reducing from 20mg to 15mg OD if patient's bleeding risk outweighs risk for recurrent DVT or PE.

Severe renal impairment (eGFR of <15ml/min) - Rivaroxaban should not be prescribed.

Converting from Warfarin to Rivaroxaban

For patients treated for DVT and prevention of recurrent DVT and PE, Vitamin K Antagonist (VKA) treatment should be stopped and rivaroxaban therapy should be initiated once the INR is 2.5. ≤

When converting patients from VKAs such as warfarin to Rivaroxaban, INR values will be falsely elevated after the intake of rivaroxaban. The INR is **not** valid to measure the anticoagulant activity of Rivaroxaban, and therefore should not be used

Converting from Clexane to Rivaroxaban

Rivaroxaban should be started 0-2 hours before the next scheduled administration of Clexane.

INR MEASUREMENT IS NOT APPROPRIATE TO MEASURE THE ANTICOAGULANT ACTIVITY OF RIVAROXABAN AND THEREFORE SHOULD NOT BE USED FOR THIS PURPOSE.

Treatment with Rivaroxaban does **not** require routine coagulation monitoring.

Populations at Potentially Higher Risk of Bleeding

Patients with renal impairment – See above

Patients with hepatic impairment – Rivaroxaban is contraindicated in patients with a coagulopathy related to hepatic disease and a relevant bleeding risk, including cirrhosis (Child Pugh B+C)

Patients on other medicinal products

Rivaroxaban should not be prescribed with azole-antimycotics such as ketoconazole, itraconazole, voriconazole and posaconazole.

Care should be taken with drugs that affect haemostasis such as NSAIDs, aspirin and other antithrombotic agents or platelet aggregation inhibitors.

Perioperative Management

If an invasive procedure or surgical intervention is required Rivaroxaban should be stopped at least 24 hours prior to the intervention if possible. If the procedure cannot be delayed the increased risk of bleeding due to Rivaroxaban should be assessed against the urgency of the intervention.

Rivaroxaban should be restarted as soon as possible after the invasive procedure or surgical intervention provided the clinical situation allows and adequate haemostasis has been achieved.

Overdose

Due to limited absorption a ceiling effect with no further increase in plasma exposure is expected at ingested doses of Rivaroxaban of 50mg and above. Activated charcoal may be used to reduce absorption if clinically indicated. Due to high plasma protein binding Rivaroxaban is not considered dialysable.

How to Manage Bleeding Complications

If a patient taking Rivaroxaban develop bleeding problems treatment should be discontinued until the bleeding resolves. There is no specific antidote to rivaroxaban so bleeding should be managed as follows:

- **Minor Bleeding** (ie bleeding with no haemodynamic compromise or fall in Hb)

    1) Stop Rivaroxaban
    2) Apply external compression/elevation if bleeding is external.
    3) Check coagulation screen – rivaroxaban does not prolong PT or APTT at therapeutic levels but may if therapeutic level is exceeded.
    4) If bleeding does not stop consider treatment with Prothrombin Complex Concentrate that contains FX – ie BERIPLEX 50ug/kg IV

- **Major Bleeding** (ie bleeding with features of hypotension, tachycardia, reduced urine output and fall in Hb)

  1) Stop Rivaroxaban
  2) Active Fluid Resuscitation
  3) Check coagulation screen – rivaroxaban does not prolong PT or APTT at therapeutic levels but may if therapeutic level is exceeded.
  4) If bleeding does not stop consider treatment with Prothrombin Complex Concentrate that contains FX – ie BERIPLEX 50ug/kg IV

IN THE CASE OF MAJOR BLEEDING ON RIVAROXABAN OR IF THE USE OF BERIPLEX IS BEING CONSIDEREDTHE PATIENT SHOULD BE DISCUSSED WITH THE DUTY CONSULTANT HAEMATOLOGIST.

FURTHER ADVICE CAN BE OBTAINED FROM DR RODERICK NEILSON, CONSULTANT HAEMATOLOGIST AT 01324 567084

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