Formulary Fact Sheet:
Rivaroxaban for the treatment of DVTs and prevention of recurrent DVTs and PEs

NHS
Cornwall and Isles of Scilly

The purpose of this fact sheet is to provide advice to clinicians considering the use of rivaroxaban for the treatment of a deep vein thrombosis and/or prevention of a recurrent deep vein thrombosis or pulmonary embolism. Note that dabigatran is not licensed for this indication.

Current Practice

For the treatment of acute VTE, current practice would be to initiate warfarin in conjunction with a parenteral low molecular weight heparin (LMWH) such as dalteparin, dosed according to body weight. This should be administered for at least five days or until the INR has been ≥2 for at least 24 hours, whichever is longer. The target INR is 2.5, although a range of 2.0 to 3.0 is acceptable, and treatment should continue for at least three months.

What does NICE say?

NICE Technological Appraisal Guidance 261 (July 2012) supports the use of rivaroxaban as an option for treating deep vein thrombosis and preventing recurrent deep vein thrombosis and pulmonary embolism after a diagnosis of acute deep vein thrombosis in adults.

- ***Evidence***

The EINSTEIN-DVT trial was the key trial supporting the clinical effectiveness of rivaroxaban in the manufacturer's submission. This was a non-inferiority trial that demonstrated that rivaroxaban was as effective as the LMWH enoxaparin followed by a vitamin K antagonist for preventing recurrent venous thromboembolism, but did not have the disadvantages of an injected treatment followed by an oral treatment with the need for regular monitoring with blood tests. Key limitations included the fact that this was an open-label trial, and excluded several important patient groups; those at high risk of bleeding, those with CrCl <30ml/min, clinically significant liver disease, high blood pressure (systolic >180mmHg, diastolic>110mmHg), and patients for whom vitamin K antagonists are not appropriate (other than patients with cancer.)

- ***Safety***

EINSTEIN-DVT demonstrated that patients treated with rivaroxaban experienced a comparable number of clinically relevant bleeding episodes to those treated with enoxaparin and a vitamin K antagonist. The extension study (EINSTEIN-Ext) demonstrated that patients treated with rivaroxaban experienced a higher rate of clinically relevant non-major bleeding but the comparator was placebo and not active control.

- ***Duration of treatment***

Treatment duration depends on bleeding risk and other clinical criteria; 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. The summary of product characteristics further states that experience with rivaroxaban in this indication for more than 12 months is limited.

- ***Dose***

For the initial treatment of acute deep vein thrombosis, the recommended dosage of rivaroxaban is 15 mg twice daily for the first 21 days followed by 20 mg once daily for continued treatment and prevention of recurrence.

A reduced dosage of 15 mg twice daily for 21 days followed by 15 mg once daily should be used in people with moderate (creatinine clearance 30–49 ml/min) or severe (creatinine clearance 15–29 ml/ min) renal impairment.

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- ***Cost***

Rivaroxaban costs £2.10 per 15 mg or 20 mg tablet. The cost of treatment is estimated to be £235.86, £427.61 and £811.13 for 3, 6 and 12 months of treatment respectively.

Cornwall Area Prescribing Committee (CAPC) Decision

Rivaroxaban has been deemed to be 'specialist initiated' for this NICE approved indication by the CAPC. Patients assessed through the RCHT DVT clinic will receive initial treatment, the choice of which will depend on individual suitability. If rivaroxaban is prescribed, the clinic will provide the first three weeks of the BD dosing regime and then bring the patient back at day 21 for a week of the daily regime. There will then be a communication to the GP requesting that they take over the prescribing. Whilst experience is gained with this drug, it will be used primarily in those patients with transient risk factors requiring short term treatment (3 months).

GPs may identify existing individual patients who may gain more benefit from rivaroxaban than from their current drug regimen. This may be related to compliance factors and/or tolerability issues, ease of administration or challenges relating to INR monitoring or stability. In these cases GPs may wish to switch patients to rivaroxaban.

- The SPC for rivaroxaban states that for patients treated for DVT and prevention of recurrent DVT and PE, VKA treatment should be stopped and rivaroxaban initiated (at the appropriate dose) once the INR is ≤ 2.5.
- Two dosages exist: 20mg daily (or 15mg daily in moderate to severe renal impairment.)
- For complicated patients, please seek advice from an MAU consultant or consultant haematologist.

Informed Decision Making

The decision about whether to start treatment with rivaroxaban should be made after an informed discussion between the clinician and patient about the risks and benefits compared with their current oral anticoagulation therapy, with particular reference to the level of INR control.

- Discuss the rationale for the switch
- Consider any new dose and monitoring requirements, potential new adverse effects and interactions

The risk of potential adherence problems or confusion would need to be taken into account when switching therapies (e.g. elderly, cognitively impaired, language problems) and every effort should thus be made to ensure that the dosing regimen is as simple as possible. Potential drug interactions need to be considered. Refer to the product SPC for full details, but significant interactions could occur with ketoconazole, itraconazole, voriconazole, posaconazole, HIV protease inhibitors, dronedarone, phenytoin, carbamazepine, phenobarbital and St. John's Wort for example.

Monitoring

Routine INR monitoring is not required nor indicated during rivaroxaban therapy. This may be an issue for some patients and clinicians who rely on knowing an INR level to gauge effectiveness of treatment. Patients should be advised that in the event of haemorrhage or significant acute illness to OMIT their rivaroxaban and seek urgent assessment by, and advice from a doctor. Patients should be advised to carry an appropriate anticoagulant alert card. The current yellow NPSA Oral Anticoagulant Therapy card may be useful, or alternatively the rivaroxaban (Xarelto) patient card.

References

NICE (2012): http://www.nice.org.uk/nicemedia/live/13805/60040/60040.pdf
Rivaroxaban (Xarelto) SPC: http://www.medicines.org.uk/emc/