Rivaroxaban for preventing atherothrombotic events in people with coronary or peripheral disease - NICE technology appraisal (TA) 607 (17 October 2019)

Summary:

Rivaroxaban 2.5mg tablets twice daily, plus aspirin 75mg daily, is recommended within its marketing authorisation, as an option for preventing atherothrombotic events in adults with coronary artery disease (CAD) or symptomatic peripheral artery disease (PAD) who are at high risk of ischaemic events. Importantly patients **did not** have an indication for full therapeutic anticoagulation i.e. atrial fibrillation or venous thromboembolism.

For people with CAD, high risk of ischaemic events is defined as:

- aged 65 or over, or
- atherosclerosis in at least 2 vascular territories (such as coronary, cerebrovascular, or peripheral arteries), or
- two or more of the following risk factors:
  - current smoking
  - diabetes
  - kidney dysfunction with an estimated glomerular filtration rate (eGFR) of less than 60ml/min
  - heart failure
  - previous non-lacunar ischaemic stroke

Clinicians (from primary or secondary care) should assess the person's risk of bleeding before considering rivaroxaban. Treatment should only be started after an informed discussion with them about the risks and benefits of rivaroxaban, weighing up the risk of atherothrombotic events against the risk of bleeding. The risks and benefits of continuing treatment with rivaroxaban should be regularly reviewed (annually or sooner if bleeding issues or change in clinical circumstances).

Efficacy outcome:

A primary outcome event of cardiovascular death, stroke, or myocardial infarction occurred in 4.1% patients who were assigned to rivaroxaban plus aspirin, 4.9% who were assigned to rivaroxaban alone, and 496 (5.4%) who were assigned to aspirin alone. For the comparison of rivaroxaban (2.5 mg twice daily) plus aspirin with aspirin alone, the hazard ratio for the primary outcome was 0.76 (95% confidence interval [CI], 0.66 to 0.86; P<0.001). For the comparison of rivaroxaban (5 mg twice daily) alone with aspirin alone, the hazard ratio was 0.90 (95% CI, 0.79 to 1.03; P=0.12).

Safety Outcome

Over the course of the trial the most commonly reported adverse reaction was bleeding including epistaxis (4.5 %) and gastrointestinal (GI) tract haemorrhage (3.8 %). Contraindications include active clinically significant bleeding; concomitant treatment with any other anticoagulants; concomitant treatment of CAD or PAD with aspirin in patients with previous haemorrhagic or lacunar stroke, or any stroke within a month; hepatic disease associated with coagulopathy and clinically relevant bleeding risk including cirrhotic patients with Child Pugh B and C; pregnancy; and breast-feeding – see SPC for full list.

NET clinical benefit

Net clinical benefit was defined as cardiovascular death, stroke, myocardial infarction, fatal bleeding, or symptomatic bleeding into a critical organ. Net clinical benefit was 4.7% per year in the rivaroxaban plus aspirin group vs. 5.9% per year in the aspirin alone group (HR 0.80, 95% CI 0.7 to 0.91;p<0.001).

Written by Paul Wright Lead Pharmacist – Cardiology, November 2021, Haematology board approval Dec 2021
Approved by WELMOCC: Date of Review: September 2024 – or sooner if clinically indicated

Additional information:
Rivaroxaban is not recommended in patients receiving concomitant systemic treatment with azole-antimycotics or HIV protease inhibitors. These are strong inhibitors of both CYP3A4 and P-gp and may increase rivaroxaban plasma concentrations to a clinically relevant degree (2.6 fold on average) and lead to an increased bleeding risk. Please – see SPC for full list

Patient factors:
Use in renal impairment: No dose adjustment necessary in mild or moderate renal impairment (CrCl 30-80ml/min) NICE recommends at least annual monitoring of eGFRcreatinine for adults, children and young people with or at risk of chronic kidney disease, in addition the MHRA recommends CrCl monitoring for Rivaroxaban. Local guidance recommends 6 monthly testing for moderate renal impairment. Avoid starting rivaroxaban if CrCl <30ml/min. If on established treatment and CrCl reduces to <30ml/min consider ceasing treatment with rivaroxaban if being used for preventing atherothrombotic events in adults with CAD or symptomatic PAD.

Additional information:

- Patients who require systemic anticoagulation (e.g. for mechanical valves, stroke prevention in atrial fibrillation, antiphospholipid etc) should **NOT** be prescribed rivaroxaban 2.5mg twice daily dosing - instead appropriate dosing of anticoagulation should be given.
- Patients taking rivaroxaban should be encouraged to carry an anticoagulation card at all times (available in the product box) or to wear a medic-alert bracelet.
- Counselling to be undertaken by the prescriber and consider referral to community pharmacist for "new medicines service".
- In the event of a significant bleed, the patient should be referred to A & E for supportive measures.
- Other healthcare professionals should be made aware that rivaroxaban is prescribed, for any patients who are to undergo invasive treatments, including elective surgery and dental treatment as dose(s) may need to be missed depending on bleeding risks associated with surgery.
- Missed dose advice should be discussed at initiation: If a dose is missed the patient should continue with regular dose as recommended at the next scheduled time. The dose should not be doubled to make up missed doses.
- If a patient has been assessed as being appropriate for a multi-compartment compliance aid (MCA), often known as a dosette box, consideration can be given to including rivaroxaban tablets as they do not have special storage requirements.

References:

Summary of product characteristics: Xarelto 2.5mg film-coated tablets. Bayer, last updated 5/02/2021, accessed 12/7/2021. Available online at https://www.medicines.org.uk/emc/product/3410/smpc

Eikelboom JW, Connolly SJ, Bosch J et al. Rivaroxaban with or without Aspirin in Stable Cardiovascular Disease. (2017) *N Engl J Med*; **377**:1319-1330, DOI: 10.1056/NEJMoa1709118

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2021https://www.nice.org.uk/guidance/ng203/chapter/Recommendations#frequency-of-monitoring

BNF Prescribing in renal impairment. https://bnf.nice.org.uk/guidance/prescribing-in-renal-impairment.html. Accessed 1.01.2022

Primary Care Prescriber Information RIVAROXABAN https://gp.walthamforestccg.nhs.uk Accessed 12/01/2022

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