Prescribing RIVAROXABAN for stroke prevention in (non-valvular) atrial fibrillation (AF)

Note: Rivaroxaban is also licensed for the acute treatment and secondary prevention of Venous Thromboembolism (VTE) and preventing atherothombotic event after acute management of Acute Coronary Syndrome (ACS). Guidance for use for these indications can be found at: Cardiovascular Disease Guidelines

Rivaroxaban▼ (Xarelto®) is a direct oral anticoagulant (DOAC) licensed for use for stroke prevention in non-valvular atrial fibrillation (SPAF). The National Institute for Health and Care Excellence (NICE) has approved the use of rivaroxaban as an option for SPAF, in patients with additional stroke risk factors.

In South London, rivaroxaban should be considered as an option, in line with its licensed indications, for stroke prevention in patients with non-valvular atrial fibrillation and a CHA_2DS_2 VASc score ≥ 2 (consider for men with CHA_2DS_2VASc score ≥ 1), except those patients in whom rivaroxaban is contra-indicated.

Additional resources have been developed to support implementation including:

- PAN London Position Statement for stroke prevention in AF: PAN London Position Statement on SPAF
- Screening checklist and Notification of initiation of a DOAC for SPAF. This document **must be completed and sent to the General Practitioner (GP) on initiation:** SPAF Notification of Initiation
- Transfer of prescribing responsibility to primary care for DOACs. This document **must be completed and sent to the GP when transferring the prescribing responsibility** in accordance to South London guidelines: SPAF Transfer of Care

Rivaroxaban should only be initiated by clinicians with expertise in managing anticoagulant therapy. The initiating clinician / organisation is responsible for ensuring patient follow up and providing a supply of rivaroxaban for the first three months of treatment. During this time, efforts should be made to reinforce adherence and address any adverse effects.

Transfer of prescribing responsibility to patients own GP

Following the initial 3 month period, patients may be considered for transfer back to the patient's own GP, provided the agreed transfer of care guidance is followed. If rivaroxaban is prescribed for unlicensed indications outside the scope of local guidance, prescribing responsibility will remain with the initiating clinician.

Contraindications (for full details see BNF or SPC)	**Cautions** (for full details see BNF or SPC)
• Hypersensitivity to the active substance or to any of the excipients • Clinically significant active bleeding • Any lesion or condition considered a significant risk factor for major bleeding e.g. current or recent gastrointestinal ulceration, presence of malignant neoplasms at high risk of bleeding, recent brain or spinal injury, recent brain, spinal or ophthalmic surgery, recent intracranial haemorrhage, known or suspected oesophageal varices, arteriovenous malformations, vascular aneurysms or major intraspinal or intracerebral vascular abnormalities • Rare hereditary conditions such as galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption as **Xarelto** contains lactose • Patients with prosthetic heart valves requiring anticoagulant treatment - the effect of rivaroxaban has not been studied in this patient group • Hepatic disease associated with coagulopathy and clinically relevant bleeding risk including cirrhotic patients with Child Pugh B and C • Established renal failure (CrCl< 15 ml/min*) • Pregnancy and/ or breast feeding • For contra-indications for use with other medicines see overleaf	• Patients with an increased bleeding risk such due to: - Congenital or acquired bleeding disorders - Uncontrolled severe hypertension, - Other gastrointestinal disease without active ulceration that can potentially lead to bleeding complications (e.g. inflammatory bowel disease, oesophagitis, gastritis and gastroesophageal reflux disease), vascular retinopathy, bronchiectasis or history of pulmonary bleeding • Liver enzymes are elevated > twice the upper limit of normal • Moderate (CrCl 30-49ml/min) or severe (CrCl 15-29 ml/min) renal impairment • For cautions for use with other medication – see overleaf

Note: BNF=British National Formulary**; SPC=**Summary of Product Characteristics

*** Estimated Glomerular Filtration Rate (eGFR) should NOT be used to guide dosing decisions. Creatinine clearance must be estimated using the Cockcroft-Gault equation calculator or refer to the South London creatinine clearance information sheet.**

Dosing

The recommended dose is 20 mg once daily with food, at the same time each day. No dose adjustment is required in the elderly.

- Reduce dose to 15mg daily in patients with moderate (CrCl 30-49mL/min) or severe (CrCL 15-29mL/min) renal impairment.

For patients identified as at risk of upper GI bleeding the co-prescription of a proton pump inhibitor *(e.g. lansoprazole/omeprazole) may be considered.*

This guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

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South East London Area Prescribing Committee. A partnership between NHS organisations in South East London: Bexley/ Bromley/ Greenwich/ Lambeth/ Lewisham & Southwark Clinical Commissioning Groups (CCGs) & GSTFT/KCH/SLAM/Oxleas NHS Foundation Trusts & Lewisham & Greenwich NHS Trust

Monitoring

International normalised ratio (INR) monitoring is not required for patients taking rivaroxaban. However, clinical surveillance is recommended throughout the treatment period in line with good anticoagulation practice.

- All patients prescribed rivaroxaban should be reviewed **at least annually** to assess benefits and risks of on-going therapy, weighing the risk for thrombotic events against bleeding risk using CHA_2DS_2VASc and HASBLED score.
- Patients should be monitored for signs of bleeding or anaemia; treatment should be stopped if severe bleeding occurs.
- A baseline renal function test is required and consequent re-testing should take place at least annually (frequency determined by the patient's baseline renal function as guided by the initiating clinician).

Side effects (for full details see the BNF or SPC)

- Bleeding occurs commonly during treatment with rivaroxaban and patients should be monitored for signs of bleeding or anaemia. In the ROCKET-AF study, the major bleeding rate with rivaroxaban 3.6% per annum. Patients should be advised to seek medical advice if they experience persistent or frequent episodes of bleeding. Patients experiencing severe bleeding should seek urgent medical advice.
- Other common side effects include: dyspepsia, diarrhoea, nausea, vomiting, hypotension, oedema, tachycardia, thrombocytopenia, syncope, dizziness and headache.

Rivaroxaban *is a black triangle drug - any adverse effect must be reported to the MHRA using the yellow card system and via the local incident reporting system*

Drug Interactions (for full details on drug interactions – see BNF or SPC)

Drug / Drug class	Recommendation
Other anticoagulant agents (e.g. unfractionated heparin (UFH) or heparin derivatives, low molecular weight heparins, oral anticoagulants)	Concomitant use is contraindicated due to increased risk of bleeding, except when UFH is given at doses necessary to maintain a patent catheter or if switching with other anticoagulants
Use of fibrinolytic agents for the treatment of acute ischaemic stroke	May be considered by hyper-acute stroke units if the clinician can be certain that there is no anticoagulant effect present based on laboratory testing of clotting
Aspirin and other antiplatelet agents	Increased risk of bleeding – use with caution; should be stopped if clinically appropriate (seek advice from cardiologist); if required to continue close monitoring required and gastro-protection is advised
Non-steroidal anti-inflammatory drugs (NSAIDs)	Increased risk of bleeding if used long-term. Avoid where possible; if required use at the lowest dose and for the shortest duration possible; close monitoring required and gastro-protection is advised
Any other medicinal products affecting haemostasis	May increase the risk of bleeding when used concomitantly, close monitoring required
CYP3A4 or P-glycoprotein inducers - such as St. John`s wort (Hypericum perforatum), rifampicin, phenobarbital, carbamazepine or phenytoin	Concomitant use will result in decreased rivaroxaban plasma concentrations, and the SPC recommends avoiding co-administration unless patients can be closely monitored for signs and symptoms of thrombosis. The co-administration of rivaroxaban with any of these agents should only be considered under specialist haematology supervision
Systemic azole-antimycotics (such as ketoconazole, voriconazole, itraconazole or posaconazole)	Concomitant use is not recommended due to increased plasma rivaroxaban levels
HIV Protease inhibitors (e.g. lopinavir/ritonavir, indinavir)	Concomitant use is not recommended due to increased plasma rivaroxaban levels
Clarithromycin, erythromycin, fluconazole	Concomitant use of clarithromycin, erythromycin and fluconazole slightly increase rivaroxaban levels. This is not clinically significant in normal renal function, but may be significant in patients with renal impairment. In these patients alternative antibiotic therapy is preferred. Avoid use in CKD stage 4/5
Dronedarone	Not recommended for concomitant treatment with rivaroxaban

Roles and responsibilities

Initiating clinician / organisation	Patient's own GP
• To initiate / guide the initiation of rivaroxaban in line with NICE and local guidance • To supply rivaroxaban for the first 3 months of treatment • To provide counselling to improve adherence and address any early adverse effects • If treatment is required for longer than three months; to transfer care to the GP in line with local transfer of care guidance	• To ensure use of rivaroxaban is in line with the NICE / local guidance • To agree to take over prescribing responsibility when the patient is stable on therapy (at least 3 months after initiation and in line with the transfer of care guidance) • To agree to take over prescribing earlier in patients with complex medication supply issues e.g. patients using medication compliance aids (MCA) or housebound patients • To emphasise the importance of adherence to rivaroxaban therapy and address any patient concerns

• To ensure the patients GP and current anticoagulant service is informed about the cessation of warfarin therapy (if previously treated with warfarin). • To transfer care to the GP in line with local transfer of care guidance	• To assess benefits and risks of on-going therapy at least annually using CHA_2DS_2Vasc / HASBLED score • To ensure monitoring of renal and hepatic function is undertaken as directed by the initiating clinician and at least annually. If results fall outside normal range then refer to contraindication, caution and dosing sections in the prescribing guidelines and/or seek specialist advice as appropriate • To monitor on-going risk of bleed and if appropriate, seek specialist advice

Additional information

1. Patients taking rivaroxaban should be encouraged to carry an anticoagulation card (available from initiating clinician / anticoagulation clinics) at all times or to wear a medic-alert bracelet.
2. There is no specific reversal agent should a patient experience a bleed on rivaroxaban. In the event of a significant bleed, the patient should be referred to A & E for supportive measures.
3. 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.
4. Missed dose advice should be discussed at initiation: If a dose is missed the patient should take rivaroxaban immediately and continue on the following day with their once daily dose as before. The dose should not be doubled within the same day to make up for a missed dose.
5. 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

1. NICE TA256: Rivaroxaban for the prevention of stroke and systemic embolism in people with atrial fibrillation. June 2012. Accessed April 2016 via: https://www.nice.org.uk/guidance/ta256/resources/rivaroxaban-for-the-prevention-of-stroke-and-systemic-embolism-in-people-with-atrial-fibrillation-82600494885061
2. NICE CG180: Atrial fibrillation: management. July 2014. Accessed April 2016 via: https://www.nice.org.uk/guidance/cg180/resources/atrial-fibrillation-management-35109805981381
3. SPC Xarelto. Bayer. July 2015. Accessed April 2016 via: https://www.medicines.org.uk/emc/medicine/25586