

Prescribing Criteria for Rivaroxaban (Xarelto®) in Stroke Prevention in (non-valvular) AF

Rivaroxaban is licensed for prevention of stroke and systemic embolism in ADULT patients with non-valvular atrial fibrillation with one or more of the following risk factors:

- Previous stroke or transient ischemic attack
- Age ≥ 75 years
- Diabetes mellitus, congestive heart failure or hypertension

Rivaroxaban has been approved as a GREEN drug across Wiltshire

Any potential use of Rivaroxaban outside of NICE and/or license should be discussed with the Medicines Management Team.

Please note that the anticoagulation service at Salisbury district hospital recommend rivaroxaban (off-label) for the treatment of extensive superficial thrombophlebitis for patients at high risk of DVT.

NICE TA256 (published May 2012) allows Rivaroxaban to be used as an option in stroke prevention in AF as per the license above. **The CHADS2-VASc score can be used to assess a patient's stroke risk.**

Please use the following checklists in order to prescribe Rivaroxaban appropriately and safely.

*NOTE: These lists are not exhaustive and professional judgment should be used on an individual patient basis.

1. Does the patient have any of the following contra-indications * (from Summary of Product Characteristics)? (tick any that apply)

<input type="checkbox"/>	Hepatic disease associated with coagulopathy and clinically relevant bleeding risk including cirrhotic patients with Child Pugh B & C.
<input type="checkbox"/>	Active clinically significant bleeding
<input type="checkbox"/>	Pregnancy & breastfeeding
<input type="checkbox"/>	Lesion or condition at significant risk of major bleeding such as 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.
<input type="checkbox"/>	Concomitant treatment with any other anticoagulant agent e.g. unfractionated heparin (UFH), low molecular weight heparins, heparin derivatives, oral anticoagulants except under the circumstances of switching therapy to or from rivaroxaban or when UFH is given at doses necessary to maintain a patent central venous or arterial catheter.
<input type="checkbox"/>	Hypersensitivity to Rivaroxaban or to any of the excipients

If any of the contra-indications apply to your patient do not prescribe Rivaroxaban and seek advice.

2. Patient groups where specialist advice should be sought before prescribing * (tick any that apply)

<input type="checkbox"/>	Previous history of intracranial haemorrhage – <i>some AF patients especially those considered at high risk of stroke may benefit from anti-thrombotic therapy, seek the opinion of a stroke specialist.</i>
<input type="checkbox"/>	Recent major extracranial bleed within the last 6 months where the cause has not been identified or treated – <i>seek opinion of specialist</i>
<input type="checkbox"/>	Safety & efficacy of rivaroxaban has not been studied in patients with prosthetic heart valves; therefore, there are no data to support that rivaroxaban provides adequate anticoagulation in this patient population. Treatment with rivaroxaban is therefore not recommended for these patients.
<input type="checkbox"/>	Patient with recent history of recurrent falls who are at higher bleeding risk.

3. Assess your patient's bleeding risk. - The following risk factors can increase the risk of bleeding: The HAS-BLED score can be used to assess the bleeding risk of the patient (see reverse of 'Choosing the most suitable oral anticoagulant' document for further information)

<input type="checkbox"/>	Previous history bleed or predisposition to bleeding (e.g. diverticulitis)	Chronic alcohol abuse- especially if associated with binge drinking.
<input type="checkbox"/>	Congenital or acquired coagulation disorders	Uncontrolled hypertension
<input type="checkbox"/>	Recent biopsy or major trauma	Bacterial Endocarditis
<input type="checkbox"/>	Moderate & severe renal impairment	Acute hepatic impairment (e.g. bilirubin > 2xULN + LFTS > 3x ULN), chronic liver disease (e.g. cirrhosis)
<input type="checkbox"/>	Low platelet count < 80 x 10 ⁹ /L or a thrombocytopenia or anaemia of undiagnosed cause	On concomitant drugs associated with an increased bleeding risk e.g. SSRIs, oral steroids, NSAIDs, clopidogrel, methotrexate or other immune-suppressant agents
<input type="checkbox"/>	Bronchiectasis or history of pulmonary bleeding.	Vascular retinopathy

It might be worth considering co-prescription of a PPI to add gastroprotection in certain patient groups on concomitant medications which increase bleeding risk.

Dose is 20mg once daily (standard adult dose)

Renal Function – As renal function declines, drug clearance is reduced.	
Creatinine Cl (ml/min)	Recommended dose
Mild and Moderate renal impairment (30 to ≤80ml/min)	No dose adjustment for MILD renal impairment, but in MODERATE renal impairment (CrCl 30-49ml/min) the dose should be reduced to 15mg once daily .
Severe renal impairment (Cr Cl<30ml/min)	Rivaroxaban plasma levels may be significantly increased (1.6 fold on average) which may lead to an increased bleeding risk. Rivaroxaban should be used with caution in pts with a Cr Cl 15-29ml/min and the dose reduced to 15mg once daily . Use is not recommended in pts with Cr Cl <15ml/min.

There are no requirements to monitor urea & creatinine in the SPC. However U&Es must be checked if there is any clinical suspicion of renal deterioration as the dose may need adjusting.

Weight of patient
No dose adjustment is necessary.

Patients being switched from warfarin
Warfarin should be stopped & then Rivaroxaban started once INR is below 3.0, so INR monitoring is needed initially.

Other important considerations:

- A bleeding risk that would lead to a contra-indication to warfarin would also contra-indicate Rivaroxaban.
- Sub-optimal compliance with warfarin may not be improved by switching to Rivaroxaban as many of the causes of non-compliance with warfarin may also result in non-compliance with Rivaroxaban (e.g. alcoholism, chaotic lifestyle, wilful non-compliance). As Rivaroxaban has a short half-life (5-9hrs in young patients & 11-13hrs in the elderly) missing a dose could be associated with an increased risk of stroke.
- Ensure that the patient is given an alert card by the pharmacy and that the patient knows to carry it around with them.
- Rivaroxaban is stable in monitored dosage systems (e.g. dossette) (unlike warfarin and Dabigatran).
- Rivaroxaban has **no antidote** and so patients with bleeds are managed with supportive care.
- For patients with swallowing difficulties or PEG tubes etc, please contact the Medicines Management Team for specific advice.

Drug Interactions (See SPC for full details, this list is not exhaustive)	
Interacting Drug	Management
Anti-platelets (e.g. aspirin, clopidogrel)	May increase the haemorrhagic risk. Careful monitoring for bleeds and anaemia would be essential.
NSAIDs	May increase the haemorrhagic risk. Careful monitoring for bleeds and anaemia would be essential.
P-gp inhibitors: e.g. Itraconazole & Ketoconazole	Combination thought to result in increased Rivaroxaban plasma concentrations. Concomitant use not recommended.
P-gp inducers: e.g. Rifampicin, St. John's wort, Phenobarbital, Carbamazepine, or Phenytoin	Expected to result in decreased Rivaroxaban concentrations. Concomitant use should be avoided unless the patient is closely observed for signs and symptoms of thrombosis.
Dronedarone	Due to limited clinical data, concomitant use not recommended
Protease Inhibitors e.g. Ritonavir	Not recommended for concomitant treatment with Rivaroxaban