

Xarelto® 15 and 20 mg film-coated tablets (rivaroxaban) Prescribing Information

(Refer to full Summary of Product Characteristics (SmPC) before prescribing)

Presentation: 15mg/20mg rivaroxaban tablet

Indication(s): 1. Prevention of stroke & systemic embolism in adult patients with non-valvular atrial fibrillation with one or more risk factors such as congestive heart failure, hypertension, age ≥ 75 , diabetes mellitus, prior stroke or transient ischaemic attack (SPAF). 2. Treatment of deep vein thrombosis (DVT) & pulmonary embolism (PE), & prevention of recurrent DVT & PE in adults (see W&P for haemodynamically unstable PE patients).

Posology & method of administration: *Dosage 1 (SPAF):* 20 mg orally *o.d.* with food. *Dosage 2 (DVT & PE):* 15 mg *b.i.d.* for 3 weeks followed by 20 mg *o.d.* for continued treatment & prevention of recurrent DVT & PE; take with food. Refer to SmPC for full information on duration of therapy & converting to/from Vitamin K antagonists (VKA) or parenteral anticoagulants. **Renal impairment:** mild (creatinine clearance 50-80 ml/min) - no dose adjustment; moderate (creatinine clearance 30-49 ml/min) & severe (creatinine clearance 15-29 ml/min) - limited data indicate rivaroxaban plasma concentrations are significantly increased, use with caution - *SPAF:* reduce dose to 15mg *o.d.*, - *DVT & PE:* 15 mg *b.i.d.* for 3 weeks, thereafter 20mg *o.d.* Consider reduction from 20mg to 15mg *o.d.* if patient's bleeding risk outweighs risk for recurrent DVT & PE; Creatinine clearance <15 ml/min - not recommended. **Hepatic impairment:** Do not use in patients with coagulopathy & clinically relevant bleeding risk including cirrhotic patients with Child Pugh B & C patients.

Paediatrics: Not recommended. **Contra-indications:** Hypersensitivity to active substance or any excipient; active clinically significant bleeding; lesion or condition considered to confer a significant risk for major bleeding (refer to SmPC); concomitant treatment with any other anticoagulants except when switching therapy to or from rivaroxaban or when unfractionated heparin is given at doses necessary to maintain an open central venous or arterial catheter; hepatic disease associated with coagulopathy & clinically relevant bleeding risk including cirrhotic patients with Child Pugh B & C; pregnancy & breast feeding. **Warnings & precautions:** Clinical surveillance in line with anticoagulant practice is recommended throughout the treatment period. There is no need for monitoring of coagulation parameters during treatment with rivaroxaban in clinical routine, if clinically indicated rivaroxaban levels can be measured by calibrated quantitative anti-Factor Xa tests. Discontinue if severe haemorrhage occurs. In studies mucosal bleedings & anaemia were seen more frequently during long term rivaroxaban treatment compared with VKA treatment - haemoglobin/haematocrit testing may be of value to detect occult bleeding. The following sub-groups of patients are at increased risk of bleeding & should be carefully monitored after treatment initiation so use with caution: in patients with severe renal impairment or with renal impairment concomitantly receiving potent inhibitors of CYP3A4 (PK models show increased rivaroxaban concentrations); in patients treated concomitantly with

medicines affecting haemostasis. Not recommended in patients: with creatinine clearance <15 ml/min; with an increased bleeding risk (refer to SmPC); receiving concomitant systemic treatment with azole-antimycotics or HIV protease inhibitors; with prosthetic heart valves; with PE who are haemodynamically unstable or may receive thrombolysis or pulmonary embolectomy. If invasive procedures or surgical intervention are required stop Xarelto use at least 24 hours beforehand. Restart use as soon as possible provided adequate haemostasis has been established. See SmPC for full details. **Elderly population** - Increasing age may increase haemorrhagic risk. Xarelto contains lactose. **Interactions:** Concomitant use with strong inhibitors of both CYP3A4 & P-gp not recommended as clinically relevant increased rivaroxaban plasma concentrations are observed. Avoid co-administration with dronedarone. Use with caution in patients concomitantly receiving other anticoagulants, NSAIDs or platelet aggregation inhibitors due to the increased bleeding risk. Strong CYP3A4 inducers should be used concomitantly with caution as they may reduce rivaroxaban plasma concentrations. **Pregnancy & breast feeding:** Contra-indicated. **Effects on ability to drive and use machines:** Adverse reactions like syncope (uncommon) & dizziness (common). Patients experiencing these effects should not drive or use machines. **Undesirable effects:** *Common:* anaemia, dizziness, headache, eye haemorrhage, hypotension, haematoma, epistaxis, haemoptysis, gingival bleeding, GI tract haemorrhage, GI & abdominal pains, dyspepsia, nausea, constipation, diarrhoea, vomiting, pruritus, rash, ecchymosis, cutaneous & subcutaneous haemorrhage, pain in extremity, urogenital tract haemorrhage, renal impairment, fever, peripheral oedema, decreased general strength & energy, increase in transaminases, post-procedural haemorrhage, contusion, wound secretion. *Serious: cf. CI/Warnings and Precautions - in addition:* thrombocytopenia, allergic reactions, occult bleeding/haemorrhage from any tissue (e.g. cerebral & intracranial, haemarthrosis, muscle) which may lead to complications (incl. compartment syndrome, renal failure, fatal outcome), syncope, tachycardia, abnormal hepatic function, hyperbilirubinaemia, jaundice, vascular pseudoaneurysm. Prescribers should consult SmPC in relation to full side effect information. **Overdose:** No specific antidote is available. **Legal Category:** POM. **Package Quantities and Basic NHS Costs:** 15mg - 14 tablets: £29.40, 28 tablets: £58.80, 42 tablets: £88.20, 100 tablets: £210.00; 20mg - 28 tablets: £58.80, 100 tablets £210.00 **MA Number(s):** EU/1/08/472/011-21 **Further information available from:** Bayer plc, Bayer House, Strawberry Hill, Newbury, Berkshire RG14 1JA, U.K. Telephone: 01635 563000. **Date of preparation:** August 2013.

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Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Bayer plc. Tel.: 01635 563500, Fax.: 01635 563703, Email: phds@bayer.co.uk

References: 1. Data on File. Bayer HealthCare AG, Berlin, Germany. 2. IMS Health. LRx database. August 2013.