

▼ Xarelto® 2.5, 10, 15 and 20 mg film-coated tablets (rivaroxaban) Prescribing Information

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

Presentation: 2.5mg/10mg/15mg/20mg rivaroxaban tablet. **Indication(s):** 2.5mg Xarelto, co-administered with acetylsalicylic acid (ASA) alone or with ASA plus clopidogrel or ticlopidine, is indicated for the prevention of atherothrombotic events in adult patients after an acute coronary syndrome (ACS) with elevated cardiac biomarkers. 10mg Prevention of venous thromboembolism (VTE) in adult patients undergoing elective hip or knee replacement surgery. Treatment of deep vein thrombosis (DVT) & pulmonary embolism (PE), & prevention of recurrent DVT & PE in adults (see W&P for haemodynamically unstable PE patients). 15mg/20mg 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). Treatment of DVT & PE, & prevention of recurrent DVT & PE in adults (see W&P for haemodynamically unstable PE patients). **Posology & method of administration:** 2.5mg – Oral *b.i.d.* dose; patients should also take a daily dose of 75 – 100 mg ASA or a daily dose of 75 – 100 mg ASA in addition to either a daily dose of 75 mg clopidogrel or a standard daily dose of ticlopidine. Start Xarelto as soon as possible after stabilisation, including revascularisation for ACS; at the earliest 24 hours after admission & at discontinuation of parenteral anticoagulation. If dose is missed take next dose, do not double the dose. 10mg – *hip or knee replacement surgery:* Oral *o.d.* dose; initial dose taken 6 to 10 hours after surgery provided haemostasis established. *DVT & PE:* When extended prevention of recurrent DVT and PE is indicated (following completion of at least 6 months therapy for DVT or PE), the recommended dose is 10 mg *o.d.* In patients in whom the risk of recurrent DVT or PE is considered high, such as those with complicated comorbidities, or who have developed recurrent DVT or PE on extended prevention with Xarelto 10 mg *o.d.*, a dose of Xarelto 20 mg *o.d.* should be considered. 15mg/20mg – Take with food *SPAF:* 20 mg orally *o.d.* *DVT & PE:* 15 mg *b.i.d.* for 3 weeks followed by 20 mg *o.d.* for continued treatment & prevention of recurrent DVT & PE. **All strengths** - Refer to SmPC for full information on duration of therapy & converting to/from Vitamin K antagonists (VKA) or parenteral anticoagulants. **Special populations:** Patients undergoing cardioversion: Xarelto can be initiated or continued in patients who may require cardioversion. Patients with non-valvular atrial fibrillation who undergo PCI (percutaneous coronary intervention) with stent placement: There is limited experience of a reduced dose of 15 mg Xarelto once daily (or 10 mg Xarelto once daily for patients with moderate renal impairment [creatinine clearance 30 – 49 ml/min]) in addition to a P2Y12 inhibitor for a maximum of 12 months in patients with non-valvular atrial fibrillation who require oral anticoagulation & undergo PCI with stent placement. **Renal impairment:** mild (creatinine clearance 50-80 ml/min) - no dose adjustment; 2.5mg /10mg - moderate (creatinine clearance 30-49 ml/min) – no dose adjustment. Severe (creatinine clearance 15-29ml/min) - limited data indicate rivaroxaban concentrations are significantly increased, use with caution. 15mg/20mg - moderate & severe renal impairment - limited data indicate 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; **All strengths** - 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. **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 under specific circumstances of switching anticoagulant therapy 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. 2.5mg - concomitant treatment of ACS with antiplatelet therapy in patients with a prior stroke or transient ischaemic attack. **Warnings & precautions (W&P):** Clinical surveillance in line with anticoagulant practice is recommended throughout the treatment period. Discontinue if severe haemorrhage occurs. Increasing age may increase haemorrhagic risk. Xarelto should be discontinued at the first appearance of a severe skin rash, or any other sign of hypersensitivity in conjunction with mucosal lesions. **Not recommended:** in patients with an increased bleeding risk (refer to SmPC); in patients receiving concomitant systemic treatment with strong concurrent CYP3A4- & P-gp-inhibitors, i.e. azole-antimycotics or HIV

protease inhibitors; in patients with prosthetic heart valves; 2.5mg treatment in combination with antiplatelet agents other than ASA & clopidogrel/ticlopidine; 10mg/15mg/20mg in haemodynamically unstable PE patients or patients who require thrombolysis or pulmonary embolectomy. **Use with caution:** in patients with severe renal impairment or with moderate renal impairment concomitantly receiving other medicinal products which increase rivaroxaban plasma concentrations; treated concomitantly with medicines affecting haemostasis; when neuraxial anaesthesia or spinal/epidural puncture is employed; in patients at risk of ulcerative gastrointestinal disease (prophylactic treatment may be considered); 2.5mg in ACS patients > 75 years of age or with low body weight (<60kg). Patients on treatment with Xarelto & ASA or Xarelto & ASA plus clopidogrel/ticlopidine should only receive concomitant treatment with NSAIDs if the benefit outweighs the bleeding risk. **All strengths** - 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. 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 NSAIDs, ASA or platelet aggregation inhibitors due to the increased bleeding risk; use with caution in patients concomitantly receiving SSRIs/SNRIs due to a possible increased bleeding risk. Concomitant use of strong CYP3A4 inducers should be avoided unless patient is closely observed for signs & symptoms of thrombosis. **Pregnancy & breast feeding:** Contra-indicated. **Effects on ability to drive & use machines:** syncope (uncommon) & dizziness (common) were reported. 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, increase in transaminases, pruritus, rash, ecchymosis, cutaneous & subcutaneous haemorrhage, pain in extremity, urogenital tract haemorrhage (menorrhagia very common in women <55 yrs treated for DVT, PE & prevention of recurrence), renal impairment, fever, peripheral oedema, decreased general strength & energy, post-procedural haemorrhage, contusion, wound secretion. **Serious: cf. CI/Warnings & Precautions – in addition:** thrombocytosis, thrombocytopenia, Stevens-Johnson syndrome/Toxic Epidermal Necrolysis, DRESS syndrome, anaphylactic reactions including shock, angioedema & allergic oedema, 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, hepatic impairment, cholestasis & hepatitis (incl. hepatocellular injury), increases in bilirubin, blood alkaline phosphatase & GGT, increased conjugated bilirubin, jaundice, vascular pseudoaneurysm following percutaneous vascular intervention. Prescribers should consult SmPC in relation to full side effect information. **Overdose:** No specific antidote is available. **Legal Category:** POM. **Package Quantities & Basic NHS Costs:** 2.5mg - 56 tablets: £50.40. 10mg - 10 tablets: £18.00, 30 tablets: £54.00 & 100 tablets: £180.00. 15mg - 14 tablets: £25.20, 28 tablets: £50.40, 42 tablets: £75.60, 100 tablets: £180.00; 20mg - 28 tablets: £50.40, 100 tablets £180.00; Treatment Initiation pack (42 tablets of 15mg, 7 tablets of 20mg): £88.20 **MA Number(s):** 2.5mg - EU/1/08/472/025-035, 041, 046-047. 10mg - EU/1/08/472/001-10, 022, 042-045 15mg/20mg - EU/1/08/472/011-21, 023-024, 036-040, 048-049 **Further information available from:** Bayer plc, 400 South Oak Way, Reading, RG2 6AD, U.K. Telephone: 0118 206 3000. **Date of preparation:** July 2018

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Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in Google Play or Apple App Store. Adverse events should also be reported to Bayer plc. Tel.: 0118 206 3500, Fax.: 0118 206 3703, Email: pvuk@bayer.com