Xarelto® (rivaroxaban) for the management of venous thromboembolism (VTE)

This material is developed and fully funded by Bayer for UK healthcare professionals.

Prescribing Information and adverse event reporting can be found at the end of this document.

NICE 2020 guideline [NG158] recommends Xarelto for adult patients with confirmed VTE[1]

Anticoagulation treatment for confirmed DVT or PE[1]

For patients with no haemodynamic instability, renal impairment, or antiphospholipid syndrome, and with confirmed DVT or PE, offer either apixaban or rivaroxaban. If neither is suitable, offer:

- LMWH for at least 5 days followed by dabigatran or edoxaban

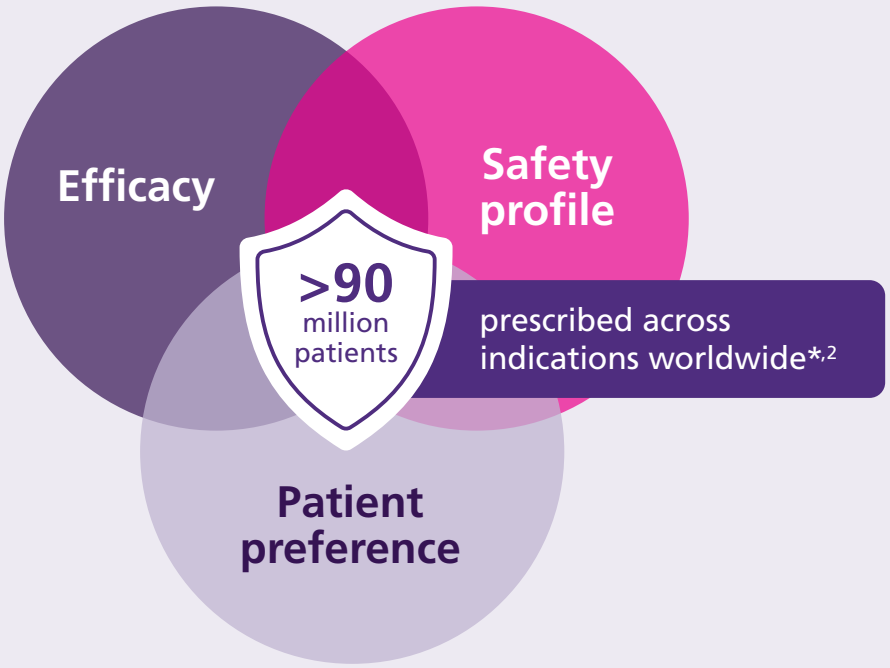
or

- LMWH and VKA for at least 5 days or until the INR is at least 2.0 in two consecutive readings, then a VKA on its own

NICE RECOMMENDED FOR VTE[1]

How can Xarelto help you and your adult patients with VTE?

Your patients with VTE need a treatment that considers efficacy, safety outcome, and their preference.



Xarelto® is indicated for PE/DVT, treatment of deep vein thrombosis and pulmonary embolism and prevention of recurrent deep vein thrombosis and pulmonary embolism in adults.[3]

PP-XAR-GB-3598, September 2023

Xarelto® rivaroxaban

Xarelto provides effective clot resolution during the 3-week, high-risk acute phase[4,5]

Your adult patients are most at risk of a VTE recurrence 3–4 weeks after an initial thrombotic event.[4] You can protect them during the high-risk acute phase of VTE with effective clot resolution.[5]

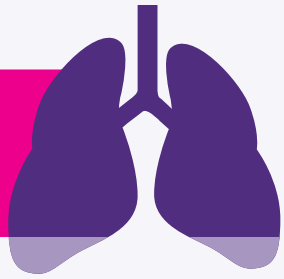
EINSTEIN PE DVT[5]

Pre-defined safety analysis

347

Clot resolution following 3 weeks of Xarelto 15 mg BID[†,5]

88% **of patients treated with Xarelto experienced complete or partial resolution** (n=180)



- **88%** complete (41%) or partial (47%) resolution
- **12%** no change
- **0%** worsening

Overall rates of clot resolution were comparable between Xarelto and enoxaparin/VKA (87.2% vs 86.8% respectively).[5]

Adapted from Van Es J, *et al.* 2013.

An acceptable safety profile, even in vulnerable patients[6,7]

Xarelto significantly reduced the risk of major bleeding vs standard of care[‡], including in frail patients and those with moderate renal impairment.[6,7]

The primary safety outcome, defined as a first major or non-major clinically relevant bleeding event, occurred in 9.4% of patients treated with Xarelto (n=4130) vs 10.0% with enoxaparin/VKA (n=4116) (HR: 0.93; 95% CI: 0.81–1.06).[6]

EINSTEIN PE DVT[6]

Safety analysis

8246

Rates of major bleeding with Xarelto across the EINSTEIN clinical programme[§,6,7]

Overall population[6]	Fragile patients[‖,6]	Patients with moderate renal impairment[¶,7]
1.0% (n=4130)	**1.3%** (n=788)	**0.9%** (n=320)
vs 1.7% with enoxaparin/VKA (n=4116)	vs 4.5% with enoxaparin/VKA (n=779)	vs 3.9% with enoxaparin/VKA (n=310)
HR: 0.54; 95% CI: 0.37–0.79	HR: 0.27; 95% CI: 0.13–0.54	HR: 0.23; 95% CI: 0.06–0.81
p=0.002	p=0.011	$p_{interaction}$=0.034

Adapted from Prins M, *et al.* 2013, and Bauersachs R, *et al.* 2014.

Choose an oral treatment your patients prefer over injections[8]

It's important to consider patient choice when prescribing a treatment.
Offer them an oral treatment they prefer.[8]

In a French national survey of 167 patients with VTE…

81.5% **of patients preferred oral treatment over injections**,[8]**

Adapted from Lanéelle D, *et al*. 2021.
Data were collected by a questionnaire sent to 1936 French vascular physicians between February and April 2019.
The study did not involve any commercial or financial relationships with Bayer.[8]

Xarelto offers an injection-free option from the start[3]

Treat and prevent a VTE recurrence with Xarelto 15 mg twice daily during the high-risk acute phase, followed by a once-daily dose of Xarelto 20 mg from day 22.[3]

DAY 1 TO 21		FROM DAY 22	AFTER MONTH 6	
Day	**Night**	**Once daily**	**Once daily**	
			 **or**	
Xarelto 15 mg	Xarelto 15 mg	Xarelto 20 mg	Xarelto 10 mg	Xarelto 20 mg
One tablet twice daily (From PE or DVT diagnosis)		**Assess individual risk**		**If high risk of VTE recurrence:** • Additional comorbidities • Recurrent PE or DVT on extended prevention
Initial high-risk treatment period[3,4]		**Continued treatment**[3]		**Extended treatment for as long as their risk persists**[3,9]

For patients in which extended prevention of recurrent DVT and PE is indicated (following the completion of 6 months' therapy for DVT or PE), the recommended dose is Xarelto 10 mg OD. 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 OD, a dose of Xarelto 20 mg OD should be considered.[3]

1408 'GRANDMA' PORTIONS

WHAT DOES PROTECTION MEAN TO YOUR PATIENTS WITH VTE?

Which of your adult patients with VTE can Xarelto help you protect?

BID, twice daily; CI, confidence interval; CrCl, creatinine clearance; CT, computerised tomography; DVT, deep vein thrombosis; HR, hazard ratio; INR, International Normalised Ratio; LMWH, low-molecular-weight heparin; NICE, National Institute for Health and Care Excellence; OD, once daily; PE, pulmonary embolism; VKA, vitamin K antagonist; VTE, venous thromboembolism.

* Total number of patients prescribed Xarelto across indications (including but not limited to VTE) since launch in >110 countries.[2,10]

† Pre-defined safety analysis of the EINSTEIN PE study involving 347 patients with scan-confirmed PE who received a follow-up CT or Q-scan after 21 days of anticoagulant therapy. Three patients with symptomatic worsening and confirmed recurrent PE were excluded from this analysis.[5]

‡ Enoxaparin followed by a VKA (either warfarin or acenocoumarol).[6,7]

§ Primary safety outcome: composite of major and clinically relevant non-major bleeding.[6]

‖ Fragile is defined as the presence of one or more of the following risk factors: >75 years old, CrCl <50 ml/min and low body weight (≤50 kg).[6]

¶ Moderate renal impairment defined as CrCl 30–49 ml/min.[7]

** 8.4% of patients preferred injections, and 10.1% had no preference for the modality of administration.[8]

1. NICE guideline [NG158]. Venous thromboembolic diseases: diagnosis, management and thrombophilia testing. 2020. Available at: https://www.nice.org.uk/guidance/ng158/chapter/Recommendations#diagnosis-and-initial-management. Accessed March 2023.
2. IQVIA MIDAS. Database Quarterly sales Q2 [Data on file]. 2021.
3. Xarelto® (rivaroxaban). Summary of Product Characteristics, as approved by the European Commission.
4. Limone BL, *et al. Thromb Res*. 2013;132:420–426.
5. Van Es J, *et al. J Thromb Haemost*. 2013;11:679–685.
6. Prins MH, *et al. Thrombosis J*. 2013;11:21–31.
7. Bauersachs R, *et al. Thrombosis J*. 2014;12:25–32.
8. Lanéelle D, *et al. Front Cardiovasc Med*. 2021;8:675969.
9. Khan F, *et al. BMJ*. 2019;366:l4363.
10. Bayer AG. Periodic Benefit-Risk Evaluation Report/Periodic Safety Update Report (BAY 59-7939) [Data on file]. 2021.

Adverse events should be reported. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk or search for MHRA Yellow Card in Google Play or Apple App Store. Adverse events should be reported to Bayer plc. Tel.: 01182063500, Fax.: 01182063703, Email: pvuk@bayer.com

BAYER

Xarelto® rivaroxaban

Xarelto® (rivaroxaban) 2.5, 10, 15 and 20 mg film-coated tablets & 1mg/ml granules for oral suspension
Prescribing Information
(Refer to full Summary of Product Characteristics (SmPC) before prescribing)

Presentation: 2.5mg/10mg/15mg/20mg rivaroxaban tablet & 1mg/ml granules for oral suspension. **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. Xarelto, co-administered with acetylsalicylic acid (ASA), is indicated for the prevention of atherothrombotic events in adult patients with coronary artery disease (CAD) or symptomatic peripheral artery disease (PAD) at high risk of ischaemic events. *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). *Paediatrics: 1mg/ml* – Treatment of VTE and prevention of VTE recurrence in term neonates, infants & toddlers, children, & adolescents aged less than 18 years after at least 5 days of initial parenteral anticoagulation treatment. Treatment of VTE & prevention of VTE recurrence in children & adolescents aged less than 18 years & weighing from 30 kg to 50 kg (for 15 mg) / above 50 kg (for 20 mg) after at least 5 days of initial parenteral anticoagulation treatment. **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, and should not be started until haemostasis is achieved in successful lower limb revascularisation for symptomatic PAD; 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:* Adults – 15 mg *b.i.d.* for 3 weeks followed by 20 mg *o.d.* for continued treatment & prevention of recurrent DVT & PE; Children & adolescents – calculate dose based on body weight: body weight <30kg refer to the SmPC for Xarelto 1mg/ml granules for oral suspension; body weight 30-50kg take 15mg *o.d.*; body weight >50kg take 20mg *o.d.*. Monitor child's weight & review regularly. Xarelto is not recommended for use in children below 18 years of age in indications other than the treatment of VTE and prevention of VTE recurrence. *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. *15mg/20mg* – adults with moderate (creatinine clearance 30-49 ml/min) & severe (creatinine clearance 15-29ml/min) – *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; children & adolescents with moderate or severe renal impairment (glomerular filtration rate <50 mL/min/1.73 m^2) – not recommended; *All strengths* – Severe impairment: limited data indicate rivaroxaban concentrations are significantly increased, use with caution. 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:*** Only for treatment of VTE & prevention of VTE recurrence. **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. Presence of malignant neoplasms at high risk of bleeding. *2.5mg* – concomitant treatment of ACS with antiplatelet therapy in patients with a prior stroke or transient ischaemic attack; concomitant treatment of CAD/PAD with ASA in patients with previous haemorrhagic or lacunar stroke, or any stroke within a month. **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. Patients with active cancer: the individual benefit of antithrombotic treatment should be weighed against the risk for bleeding. Gastrointestinal or genitourinary tract tumours have been associated with an increased risk of bleeding. Patients with CAD/PAD: after recent revascularisation procedure of the lower limb due to symptomatic PAD, if required, a dual antiplatelet therapy with clopidogrel, should be short-term, long-term dual antiplatelet therapy should be avoided. Xarelto in combination with other antiplatelets is not recommended. Xarelto should be discontinued at the first appearance of a severe skin rash, or any other sign of hypersensitivity in conjunction with mucosal lesions. 1mg/ml oral suspension - sodium benzoate may increase jaundice in newborn infants (up to 4 weeks old). *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; for patients with a history of thrombosis diagnosed with antiphospholipid syndrome; Xarelto should not be used for thromboprophylaxis in patients having recently undergone transcatheter aortic valve replacement (TAVR); *2.5mg* treatment in combination with antiplatelet agents other than ASA & clopidogrel/ticlopidine, patients after recent lower limb revascularisation procedures due to symptomatic PAD with a previous stroke or TIA receiving dual antiplatelet therapy; *10mg/15mg/20mg* in haemodynamically unstable PE patients or patients who require thrombolysis or pulmonary embolectomy; *1mg/1ml* in children less than 6 months of age who at birth had <37 weeks of gestation, a body weight of <2.6 kg, or had <10 days of oral feeding; in children ≥1 year old with moderate or severe renal impairment (glomerular filtration rate <50 mL/min/1.73 m^2); in children ≤1 year old with serum creatinine results >97.5th percentile. *Use with caution:* in patients 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 patients ≥75 years of age or with lower body weight (<60kg); in CAD patients with severe symptomatic heart failure. 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. *2.5mg/10mg* in patients with moderate renal impairment concomitantly receiving other medicinal products which increase rivaroxaban plasma concentrations; *15mg/20mg* in patients with renal impairment concomitantly receiving other medicinal products which increase rivaroxaban plasma concentrations; *1mg/ml* in children with cerebral vein & sinus thrombosis who have a CNS infection. *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 tablets 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 (in children: very common), eye haemorrhage, hypotension, haematoma, epistaxis (in children: very common), haemoptysis, gingival bleeding, GI tract haemorrhage, GI & abdominal pains, dyspepsia, nausea, constipation, diarrhoea, vomiting (in children: very common), 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, common in female adolescents after menarche), renal impairment, fever (in children: very common), peripheral oedema, decreased general strength & energy, post-procedural haemorrhage, contusion, wound secretion. *Serious: cf. CI/Warnings & Precautions – in addition:* thrombocytosis, thrombocytopenia (in children: common), 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, anticoagulant-related nephropathy or fatal outcome), syncope, tachycardia (in children: common), hepatic impairment, cholestasis & hepatitis (incl. hepatocellular injury), increases in bilirubin (in children: common), blood alkaline phosphatase & GGT, increased conjugated bilirubin, jaundice, vascular pseudoaneurysm following percutaneous vascular intervention, eosinophilic pneumonia. Prescribers should consult SmPC in relation to full side effect information. **Overdose:** In the case of an overdose, the patient should be observed carefully for bleeding complications and other adverse reactions. A specific reversal agent is available, refer to the SmPC for andexanet alfa. **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 *1mg/ml* – 100ml bottle: £9.00, 250ml bottle: £18.00 **MA Number(s):** *Great Britain: 2.5mg* – PLGB 00010/0708. *10mg* – PLGB 00010/0705. *15/20mg* – PLGB 00010/0706, 0707, 0709. *1mg/ml* – PLGB 00010/0746. *Northern Ireland: 2.5mg* – EU/1/08/472/025-035, 041, 046-047. *10mg* – EU/1/08/472/001-010, 022, 042-045 *15mg/20mg* – EU/1/08/472/011-016, 017-021, 023-024, 036-040, 048-049. *1mg/ml* – EU/1/08/472/050-051 **Further information available from:** Bayer plc, 400 South Oak Way, Reading, RG2 6AD, U.K. Telephone: 0118 206 3000. **Date of preparation:** July 2023

Xarelto® is a trademark of the Bayer Group.

Adverse events should be reported.
Reporting forms and information can be found at https://yellowcard.mhra.gov.uk or search for MHRA Yellow Card in Google Play or Apple App Store.
Adverse events should also be reported to Bayer plc.
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