Guide to the impact of non-medical switching for patients taking anticoagulants for non-valvular atrial fibrillation

Adverse events should be reported.
Reporting forms and information can be found at https://yellowcard.mhra.gov.uk/ or search 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

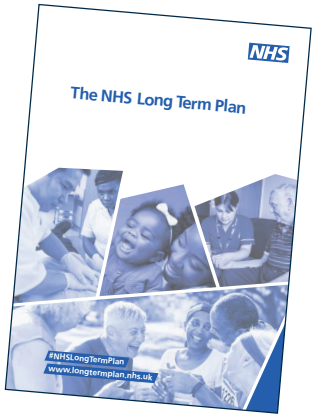
RP-XAR-GB-5239
November 2023

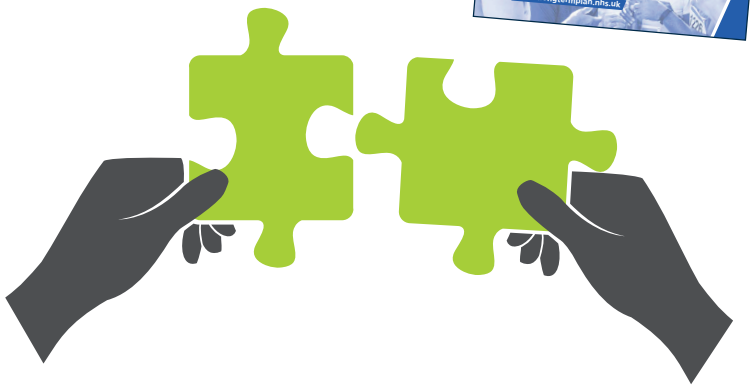
Atrial fibrillation and stroke risk management

Patients with AF carry a 5 times greater risk of stroke compared to those without this condition.[1]

The NHS Long Term Plan aims to prevent up to 150,000 heart attacks, strokes and dementia cases over a ten-year period and efforts should be focused on early detection and treatment of cardiovascular disease.[2]

The National Institute for Health and Care Excellence recommend apixaban, dabigatran, edoxaban and rivaroxaban as options for first-line management of stroke prevention in non-valvular AF.[3]





Shared decision-making between the HCP and patient is key when choosing an anticoagulant.[3,4] Patients should be informed on the risks and benefits of each drug and treatment selection should be guided by:

- Clinical risk profiles
- Patient preferences[3]

All 4 DOACs should not be considered the same. It is important to consider clinical trial populations and resultant outcomes when choosing a DOAC for a specific patient.[5-8] For example, up to 40% of patients with NVAF also had diabetes in ROCKET-AF, a phase III study evaluating rivaroxaban.[9,10] A subgroup analysis demonstrated that the relative efficacy and safety of rivaroxaban vs. warfarin was similar in patients with or without type 2 diabetes, which supports the use of rivaroxaban in T2DM patients with NVAF.[11]

DOAC dosing

Some studies have shown ≥ 80% of patients with AF prefer once-daily anticoagulant treatments over twice-daily.[12,13]

Patients may have a variety of different preferences when deciding on a drug therapy. Dosing frequency has been identified as one of the most important elements for patients when selecting a DOAC.[14,15]

Medication non-adherence has been found to be lower in patients taking once-daily therapies versus multiple-daily dose regimens in patients with chronic CVD[16] and those taking DOACs for AF[17]

Non-medical switching of medicines

Non-medical switching: changing a stable patient's medication where there is no clinical or patient-specific reason such as inadequate response, troublesome adverse effects or adherence issues.[18]

The **British Medical Association's General Practice Committee** guidance outlines that when considering switching medication, HCPs must:

- **Review all patients on an individual basis**
- **Only change medications in the patient's best interest**
- **Ensure any switching decisions are underpinned by their clinical judgement**
- **Ensure that changes are communicated to the patient**[19]

Solely financial incentives for repetitively switching medications may frustrate patients. Patients may lose confidence in their HCP and they may become non-adherent to the therapy prescribed.[19] This may have a damaging effect on the HCP-patient relationship.

Non-medical switching case study

Due to a financial incentive in one locality, patients with NVAF in a GP practice were switched from one DOAC to another.

One of these patients, Mary, a 72-year-old lady of Asian descent with concomitant CKD and type 2 diabetes was informed of the switch by her GP via telephone call. Her medication record was updated and a different DOAC was delivered to her home by her community pharmacy.

10 days later, Mary was admitted to hospital with a gastrointestinal bleed.

Fictional case study.
The picture is of a model.

Why did this happen?

PROBLEM	OUTCOME
Non-medical DOAC to DOAC switching	Unnecessary alteration of stable medication for a high risk patient with NVAF, diabetes and CKD, resulting in adverse events
Mary informed of switch via telephone call	Due to a language barrier, Mary did not fully understand the conversation regarding the DOAC switch
New DOAC prescription delivered to Mary's home	Mary had no communication with her community pharmacist who may have been able to reinforce the change in medication
Mary still had stock left of her old DOAC	Mary did not realise that her old DOAC and the newly prescribed DOAC carried out the same role and so took both medicines together
Mary was hospitalised with a gastrointestinal bleed	This error resulted in an unnecessary hospital admission causing harm to the patient and a further burden on healthcare services
Mary is now worried about taking her DOAC	This may cause adherence issues and Mary may lose trust in her GP practice

Key learning outcomes:

- The British Medical Association's GPC guidance on drug switching must be considered when changing medications[19]
- HCPs must use their clinical judgement when making a switch.[19] Language barriers may increase the risk of adverse events to patients.[20] In this case study, better communication may have reduced the risk of adverse outcomes[21]
- Medication changes should be made in the patient's best interests.[19] In this case study, Mary was stable on her existing DOAC and any switching was undertaken purely for financial reasons
- Each individual patient must be carefully reviewed when considering changing therapies. For some patients like Mary, continuity in prescribing may be safer and will improve compliance[19]

The impact of non-medical switching on patients

A survey by the American Society of Preventive Cardiology revealed the negative impact of non-medical switching of blood-thinning medication by health insurers on patient lives'.[22]

96% of the survey respondents placed a high value on having the right blood thinner,[22] which highlights the importance of patient inclusion and choice in decision-making around therapies.

Respondents were vetted to ensure they had all been taking anticoagulants which were then non-medically switched by payers. 254 survey respondents and 21 focus group members were considered.[23]

> "I didn't feel comfortable switching from something that I know worked well."[22]

Impact of non-medical switching on patient health

Patient responses from the survey by the American Society for Preventive Cardiology:[22]

28% reported side-effects

20% stopped taking their blood thinner altogether

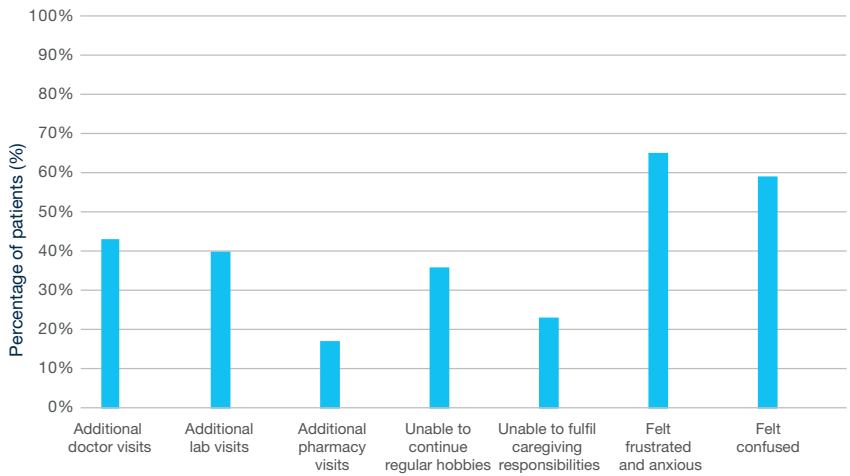
4% suffered a stroke

7% suffered heart attacks

5% required hospitalisation

> "We get these arbitrary decisions out of nowhere and you're stuck with it."

Impact of non-medical switching on patient daily lives and mental health



Treatment decisions must lie with the prescribing HCP and the patient. The one-size fits-all approach is not applicable for patients requiring anticoagulant therapies who often have complex medical histories.[22]

Results from market research undertaken by PM Healthcare on behalf of Bayer around implementation of the national procurement for DOACs and HCP attitudes regarding DOAC to DOAC switching revealed a variety of considerations when contemplating changing DOAC therapies:[24]

Patient considerations

> "It is important to be open, honest and upfront with the patients. Make the reviews about what matters to the patient rather than about the change." ***~ UK HCP***

- Each DOAC has a different safety and efficacy profile so DOAC prescriptions should be tailored to the patient, considering factors such as renal clearance, interactions with other medications and once or twice daily dosing
- Switching DOACs may confuse patients and there is significant risk of patients taking two anticoagulants at the same time
- Mass switching may result in DOAC supply issues
- Patients may be reluctant to a switch, especially based on cost alone if they are already stable on their DOAC therapy
- Engaging patients and empowering them to make an informed choice on whether to switch therapies is important. This may be difficult for elderly patient groups who may not have the capacity to make a decision
- Repeated switching can be inconvenient for patients and may affect adherence
- Switching may be beneficial for patients who are on twice daily DOAC therapies who are forgetting to take their medication as prescribed or who would like to reduce their pill burden
- Following the NHSE guidance on DOAC procurement[25] could be useful for anticoagulant naïve patients
- Switching DOAC therapy provides an ideal opportunity to review patients

Financial considerations

- With DOACs coming off patent in the coming years, switching therapies now may be futile, especially as many areas have recently undertaken warfarin to DOAC switches
- Primary care incentive to switch DOACs may be diminished with changes to the Investment and Impact Fund indicators for 2023/2024

HCP workforce considerations

- There may be lack of capacity and HCP resource to support with switching DOACs
- HCPs involved in switching must have the appropriate clinical knowledge, expertise and support from more experienced HCP colleagues where appropriate to confidently undertake a switch
- Switching DOACs constitutes a time-consuming, complex patient review process and time pressures may increase the risk of an error being made
- Further HCP time and resource would be required to revert switches for patients unhappy on a new DOAC

> "People look at the cost of the drug but not at the time taken up with the clinician appointment, the time taken to counsel the patient, the patient confusion, liaising with community pharmacy, considering implications if patients miss or double dose, so cost should not be the only consideration for things like this. This can be really frustrating for HCPs." ***~ UK HCP***

Multidisciplinary team considerations

- Important to consider the view of secondary care HCPs when considering switching DOACs for patients under specialist care
- Effective communication across the primary/secondary care interface is key to inform other multidisciplinary team members on changes to DOACs for patients under specialist care or those recently discharged
- For patients initiated on anticoagulant therapy by secondary care, clarity is needed on whether primary or secondary care are responsible for continued management
- Anticoagulant management of high risk, complex patients under renal or haematology specialities should be left to the respective team

When considering switching DOAC therapies, the patient's best interests and HCP clinical judgement must be taken into consideration, as advised by the BMA.[19] Shared-decision making between HCPs and patients is important[4] and patients should be allowed to make informed decisions when choosing an anticoagulant.[3] Disregarding patient preferences regarding anticoagulant therapy may increase the risk of non-adherence and AF-related stroke.[22]

Abbreviations: AF, atrial fibrillation; BMA, British Medical Association; CKD, chronic kidney disease; CVD, cardiovascular disease; DOAC, direct-oral anticoagulant; GP, general practitioner; GPC, General Practice Committee; HCP, healthcare professional; NHS, National Health Service; NHSE, National Health Service England; NVAF, non-valvular atrial fibrillation; T2DM, type 2 diabetes mellitus; UK, United Kingdom.

References

1 Stroke Association. Atrial Fibrillation: information and resources. Available at: https://www.stroke.org.uk/professionals/atrial-fibrillation-information-and-resources. Accessed November 2023.

2 NHS England. The NHS Long Term Plan. 2019; published online Jan. Available at: https://www.longtermplan.nhs.uk/wp-content/uploads/2019/08/nhs-long-term-plan-version-1.2.pdf. Accessed November 2023.

3 NICE. Atrial fibrillation: diagnosis and management (NG196). 2021. Available at: www.nice.org.uk/guidance/ng196. Accessed November 2023.

4 NICE. Medicines adherence: involving patients in decisions about prescribed medicines and supporting adherence (CG76). 2009. Available at: https://www.nice.org.uk/guidance/cg76. Accessed November 2023.

5 Apixaban UK SmPC.

6 Dabigatran UK SmPC.

7 Edoxaban UK SmPC.

8 Rivaroxaban UK SmPC.

9 Patel MR, Mahaffey KW, Garg J, *et al*. Rivaroxaban versus Warfarin in Nonvalvular Atrial Fibrillation. *N Engl J Med* 2011; **365**: 883–91.

10 Camm AJ, Sabbour H, Schnell O, Summaria F, Verma A. Managing thrombotic risk in patients with diabetes. *Cardiovasc Diabetol* 2022; **21**: 160.

11 Bansilal S, Bloomgarden Z, Halperin JL, *et al*. Efficacy and safety of rivaroxaban in patients with diabetes and nonvalvular atrial fibrillation: The Rivaroxaban Once-daily, Oral, Direct Factor Xa Inhibition Compared with Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation (ROCKET AF Trial). *American Heart Journal* 2015; **170**: 675-682.e8.

12 Bakhai A, Sandberg A, Mittendorf T, *et al*. Patient perspective on the management of atrial fibrillation in five European countries. *BMC Cardiovasc Disord* 2013; **13**: 1–10.

13 Gavín O, Grandes J, García MA, *et al*. Treatment preferences as basis for decision making in patients using direct oral anticoagulants in Spain. *J Thromb Thrombolysis* 2021; **51**: 475–84.

14 Losi S, Berra CCF, Fornengo R, Pitocco D, Biricolti G, Orsini Federici M. The role of patient preferences in adherence to treatment in chronic disease: a narrative review. *Drug Target Insights* 2021; **15**: 13–20.

15 Mueller S, Meinecke A-K, Buchwald S, Eriksson D, Wilke T. Patient preferences for non-vitamin K antagonist oral anticoagulants in stroke prevention: a multi-country discrete choice experiment. 2019.

16 Caldeira D, Vaz-Carneiro A, Costa J. The impact of dosing frequency on medication adherence in chronic cardiovascular disease: Systematic review and meta-analysis. *Revista Portuguesa de Cardiologia (English Edition)* 2014; **33**: 431–7.

17 Yeh Y, Wang R, Marston X, Zimmermann L, Ye X, Gao X. Improved adherence to anticoagulant therapy with once-daily regimen: a real-world study in patients with atrial fibrillation in Germany. ESC 2020.

18 Costa OS, Salam T, Duhig A, *et al*. Specialist physician perspectives on non-medical switching of prescription medications. *Journal of Market Access & Health Policy* 2020; **8**: 1–9.

19 BMA. Prescribing in general practice. 2018; published online April. Available at: https://www.bma.org.uk/media/1563/bma-prescribing-in-general-practice-april-2018.pdf. Accessed November 2023.

20 Al Shamsi, et al. Oman Med J 2020;35:e122.

21 Tiwary A, et al. Wellcome Open Res 2019;4:7.

22 The American Society for Preventive Cardiology. The Impact of Non-Medical Switching on Patients Taking a Blood Thinner. 2022; published online Aug.

23 Baum SJ. Am J Prev Cardiol 2023;13:100470.

24 Bayer Data on file [REF-XAR-GB-4841].

25 NHS. Operational note: Commissioning recommendations for national procurement for DOACs. January 2022. Available at: https://www.england.nhs.uk/wp-content/uploads/2022/01/B1279-national-procurement-for-DOACs-commissioning-recommendations-v1.pdf. Accessed November 2023.

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.
Tel.: 0118 206 3500, Fax.: 0118 206 3703,
Email: pvuk@bayer.com