ELIQUIS® (apixaban) prescriber checklist for switching from warfarin

This checklist applies to the ELIQUIS indication for the prevention of stroke / systemic embolism in adult patients with NVAF. It is not to be used in relation to other ELIQUIS indications or until the prescribing decision has been made to consider the patient for ELIQUIS. This checklist is intended for healthcare professional use only and should not be used by or given to patients.

Patient name:

MRN number:

Date of birth:

Signed by healthcare professional:

Print name:

Date:

Signed by patient / carer:

Print name:

Date:

Assessing your patient's risk

NICE guidance NG196 recommends that anticoagulation is reassessed for warfarin patients with poor anticoagulation control, shown by any of the following:[1]

- 2 INR values higher than 5 or 1 INR value higher than 8 within the past 6 months
- 2 INR values less than 1.5 within the past 6 months
- TTR less than 65%

Patients at risk may include those suffering from drug interactions, adherence issues, or lifestyle factors that make it difficult to keep their INR within therapeutic range. By identifying these patients, you can optimise their anticoagulation therapy.

ELIQUIS (apixaban): an oral, direct factor Xa inhibitor indicated for prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation (NVAF) with one or more risk factors, such as prior stroke or transient ischaemic attack (TIA); age ≥75 years; hypertension; diabetes mellitus; symptomatic heart failure (NYHA Class ≥II).[2]

INR = International Normalised Ratio NVAF = Non-Valvular Atrial Fibrillation NYHA = New York Heart Association TTR = Time in Therapeutic Range

Prescribing Information and Adverse Event reporting information can be found at the end of this document. This promotional checklist has been produced by the BMS / Pfizer Alliance.

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ELIQUIS® (apixaban) prescriber checklist*

This checklist is to support prescribers switching patients from warfarin to ELIQUIS, and is intended for healthcare professionals only. It should not be given to patients.

Please ensure that your patient is eligible for ELIQUIS prior to prescribing. The table below provides an example checklist that may be used to assess a patient's suitability prior to initiating treatment with ELIQUIS, but these questions do not form an exhaustive list. Please refer to the SmPC for full prescribing information.[2]

Have you assessed the following in this patient?

Diagnosis and risk assessment	**Assessed**
Individual risk of stroke (e.g. CHA_2DS_2-VASc or $CHADS_2$)	☐
Individual risk of bleeding (e.g. by HAS-BLED or ORBIT)	☐
Renal function	
Prior to initiating ELIQUIS, renal function testing should be performed. ELIQUIS is **NOT** recommended in patients with CrCl <15 ml/min or in patients undergoing dialysis. Please see renal function results on the next page for more information.	☐
Hepatic function	
ELIQUIS is contraindicated in patients with hepatic disease associated with coagulopathy and clinically relevant bleeding risk. ELIQUIS is **NOT** recommended in patients with severe hepatic impairment. It should be used with caution in patients with mild or moderate hepatic impairment (Child Pugh A or B). Patients with elevated liver enzymes alanine aminotransferase (ALT) / aspartate aminotransferase (AST) >2 x ULN or total bilirubin ≥ 1.5 x ULN were excluded in clinical trials. Therefore ELIQUIS should be used with caution in this population. Prior to initiating ELIQUIS, liver function testing should be performed.	☐
Active clinically significant bleeding, lesion or condition if considered a significant risk factor for major bleeding, as per the SmPC	
This may include: current / 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. **ELIQUIS is contraindicated in these patients.**	☐
Hereditary conditions which may contraindicate ELIQUIS	
ELIQUIS contains lactose – patients with rare hereditary problems of galactose intolerance, total lactase deficiency, or glucose-galactose malabsorption should **NOT** take ELIQUIS	☐
Prosthetic heart valves	
ELIQUIS is **NOT** recommended in patients with prosthetic heart valves; the safety and efficacy of ELIQUIS have not been studied in this setting	☐
Pregnant or breastfeeding	
Avoid use of ELIQUIS during pregnancy or when breastfeeding	☐
Antiphospholipid syndrome	
ELIQUIS is **NOT** recommended for patients with a history of thrombosis who are diagnosed with antiphospholipid syndrome	☐
Concomitant medications	
Please see medications to assess on the next page	☐

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ELIQUIS® (apixaban) prescriber checklist*

Prior to prescribing, the following values should be calculated and recorded:

Prior to prescribing, the following values should be calculated and recorded:

Renal function	**Assessed**
ELIQUIS is **NOT** recommended in patients with CrCl <15 ml/min or in patients undergoing dialysis. **Serum creatinine:** _____ µmol/l **Baseline CrCl:** _____ ml/min *CrCl should be calculated using the Cockcroft and Gault formula:[3] Estimated CrCl in ml/min = [(140 – age) x (weight in kg) x (constant: 1.23 for men; 1.04 for women)] / serum creatinine (µmol/L)*	☐
Liver function	
ELIQUIS is **NOT** recommended in patients with severe hepatic impairment. AST: _____ ALT: _____ Alk phos: _____ Bilirubin: _____ Gamma gt: _____	☐
Full blood count	☐
Baseline clotting tests (as appropriate)	
Prothrombin time (PT): _____ Activated Partial Thromboplastin Time (aPTT): _____ International Normalised Ratio (INR): _____	☐
Body mass index (BMI) BMI = weight in kg / [height in m]^2: _____	☐
Is your patient on any other medicinal products known to affect haemostasis? If yes to any of these products, please see the SmPC for further information prior to prescribing ELIQUIS.	
Other anticoagulants	
Concomitant use with any other anticoagulant agent is contraindicated, except under specific circumstances of switching anticoagulant therapy, when UFH is given at doses necessary to maintain an open central venous or arterial catheter, or when UFH is given during catheter ablation for AF	☐
Strong inhibitors of both CYP3A4 and P-gp	
ELIQUIS is **NOT** recommended in patients receiving concomitant systemic treatment with strong inhibitors of both CYP3A4 and P-gp, such as azole-antimycotics (ketoconazole, itraconazole, voriconazole and posaconazole) and HIV protease inhibitors (e.g. ritonavir)	☐
Strong inducers of both CYP3A4 and P-gp	
ELIQUIS should be **used with caution** in patients receiving concomitant systemic treatment with strong inducers of both CYP3A4 and P-gp, such as rifampicin, phenytoin, carbamazepine, phenobarbital or St. John's Wort	☐
SSRIs, SNRIs, NSAIDs, aspirin and / or $P2Y_{12}$ inhibitors ELIQUIS should be **used with caution** due to increased bleeding risk	☐
Platelet aggregation inhibitors	
ELIQUIS is **NOT** recommended with other platelet aggregation inhibitors or thrombolytic agents due to increased risk of bleeding (refer to SmPC for further information)	☐
Choosing the right dose of ELIQUIS for your patient If your patient does not meet the dose reduction criteria as outlined below, prescribe ELIQUIS 5 mg BD	
If your patient meets 2 or more of the criteria below, prescribe ELIQUIS 2.5 mg BD	
Age ≥80 years: _____ Body weight ≤60 kg: _____ Serum creatinine ≥1.5 mg/dl (133 µmol/l): _____	☐
If your patient has severe renal impairment, prescribe ELIQUIS 2.5 mg BD	
Severe renal impairment = CrCl 15–29 ml/min	☐
Switching your patient from warfarin to ELIQUIS This table is provided for you to record baseline measurements, any monitoring required during the switching process and the dose of ELIQUIS that you have prescribed	
If INR is >2, stop warfarin – once INR is <2, ELIQUIS can be initiated.	
Baseline INR / date: _____ / _____ 2nd INR / date: _____ / _____ 3rd INR / date: _____ / _____	☐
Other baseline measurements:	☐
Monitoring undertaken:	☐
Dose of ELIQUIS prescribed:	☐

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Patient follow-up checklist*

Guidelines from NICE and EHRA recommend that patients taking an anticoagulant should be reviewed at least annually to assess their need for anticoagulation and the quality of anticoagulation.[1,3,4] Some patients may need to be followed up more frequently at 6-month or more frequently.[3] Please refer to the SmPC before prescribing.[2]

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Have you assessed the following in this patient?

Renal function test	Assessed
6 month reviews are recommended for patients with declining renal function as per HSE anticoagulation prescribing tips[3]	
– Repeat every 6 months or more frequently if the patient has renal dysfunction/impairment or if patient is 75 years of age or older, or is frail	☐
– Follow up at 12 months	☐
6-month review	
– Enquire about the presence of any adverse effects such as bleeding	☐
– Assess other side effects	☐
– Assess compliance with treatment and reinforce advice regarding the importance of a regular dosing schedule	☐
– Assess for the presence of thromboembolic events (e.g. symptoms of stroke, or breathlessness – may suggest a pulmonary embolism)	☐
– Assess concomitant and over-the-counter medicines	☐
– Assess modifiable risk factors (e.g. obesity, hypertension, diabetes mellitus, obstructive sleep apnoea, alcohol consumption, smoking and exercise)	☐
– Determine the need for blood sampling	☐
– Assess optimal and correct dosing	☐
12-month review	
– Assess benefits and risks of on-going therapy (CHA_2DS_2-VASc / HAS-BLED or ORBIT score)	☐
– Repeat renal and hepatic function tests, and full blood count	☐
– Enquire about the presence of any adverse effects such as bleeding	☐
– Assess side effects	☐
– Assess compliance with treatment and reinforce advice regarding the importance of a regular dosing schedule	☐
– Assess for the presence of thromboembolic events (e.g. symptoms of stroke, or breathlessness – may suggest a pulmonary embolism)	☐
– Assess concomitant and over-the-counter medicines	☐
– Assess modifiable risk factors	☐
– Determine the need for blood sampling	☐
– Assess optimal and correct dosing	☐

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Patient discussion checklist*

The table below provides an example of a checklist that may be used to guide a discussion with patients starting on ELIQUIS and to support the switch process. Please note that this is a sample of potential assessment questions that could be used and is not an exhaustive list. Please refer to the SmPC before prescribing.[2]

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Please ensure you have discussed the following points with your patient

Rationale for switch from warfarin	**Discussed**
– Understand the differences between ELIQUIS and warfarin, such as efficacy, safety, convenience and monitoring	☐
– Provide an explanation for the patient regarding the choice of ELIQUIS and its benefits	☐
– Understand the difference between ELIQUIS dosing and warfarin dosing and why they differ	☐
– Common side effects which were associated with warfarin which may also be associated with ELIQUIS (e.g. bruising)	☐
Dose of ELIQUIS prescribed	
– Advise patient on the dose of ELIQUIS they are receiving and the reasons for the choice of dose	☐
How and when to take ELIQUIS	
– One tablet twice a day with or without food	☐
– At roughly the same times each day and 12 hours apart	☐
What to do if a dose is missed?	
– If a dose is missed, take ELIQUIS immediately and then continue with twice-daily intake as before	☐
What to do if an extra dose is taken accidentally?	
– Contact pharmacist, doctor or nurse	☐
How long to take ELIQUIS for	
– Continue until told by doctor to stop	☐
– May have to take for rest of life	☐
– Discuss ways of remembering to take twice daily	☐
– Ensure patient knows how to order repeat prescription	☐
Anticoagulation monitoring – patients being switched from warfarin	
– Advise patients who are accustomed to INR monitoring that no INR monitoring is required with ELIQUIS	☐
Food interactions	
– Advise patients that ELIQUIS should be swallowed with water, with or without food	☐
Informing healthcare professionals – as with all anticoagulants	
– **Doctor** – inform before any additional medication is required	☐
– **Dentist** – needs to be informed because there is an increased risk of bleeding if dental treatment is needed	☐
– **Pharmacist** – so they can advise about medicines suitable to take with anticoagulants	☐
– **All HCPs** – ensure patient has a patient alert card and emphasise the importance of carrying at all times and producing when seeing a healthcare professional	☐
Surgery	
– Inform surgeon that you are taking ELIQUIS	☐
Drug interactions	
– Check if the patient is taking any drugs other than those recorded in their notes, e.g. OTC preparations	☐
– Advise patients to consult pharmacist and Patient Information Leaflet before using OTC preparations	☐
– Please refer to SmPC for full list of interactions[2]	☐
Side effects	
– Most relate to bruising and bleeding	☐
– Discuss actions in case of minor and major bleeding episodes. In case of a bleeding event that does not stop on its own, seek medical attention immediately	☐
– Please refer to SmPC for full list of side effects[2]	☐

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Patient support*

ELIQUIS patient support

– Provide with ELIQUIS patient information and advise to also read the Patient Information Leaflet contained within their box of ELIQUIS and complete the patient alert card

Contact numbers

– Contact the healthcare team if there are any concerns. Check that the patient has appropriate contact numbers – please see the SmPC for contact numbers to the pharmaceutical company

Alert card

– Emphasise the importance of carrying this at all times and producing when seeing a healthcare professional

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References

1NICE NG196. Atrial fibrillation: diagnosis and management. Available at: www.nice.org.uk/guidance/ng196
2 ELIQUIS® (apixaban) Summary of Product Characteristics. Available at: www.medicines.ie.
3 HSE anticoagulation Prescribing tips. Available at: www.hse.ie/eng/services/publications/clinical-strategy-and-programmes/noac-prescribing-tips-for-noacs.pdf
4 Steffel J et al. Europace 2021; 00, 1–65

Notes

ELIQUIS® (apixaban) PRESCRIBING INFORMATION
Ireland

Consult Summary of Product Characteristics (SmPC) before prescribing

PRESENTATION: Film-coated tablets; 5 mg and 2.5 mg apixaban.
INDICATION (SPC section 4.1): Prevention of stroke and systemic embolism in adults with non-valvular atrial fibrillation (NVAF) with one or more risk factors, such as prior stroke or transient ischaemic attack (TIA), age ≥ 75 years, hypertension, diabetes mellitus or symptomatic heart failure (NYHA Class ≥ II). Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults (see Special warnings and precautions for information on haemodynamically unstable PE patients). Prevention of venous thromboembolic events (VTE) in adults who have undergone elective hip or knee replacement surgery (2.5 mg only).
DOSAGE AND ADMINISTRATION (SPC section 4.2): Oral. Taken with water, with or without food. *Prevention of stroke and systemic embolism in patients with NVAF:* The recommended dose is 5 mg twice a day. In patients who meet at least two of the following criteria: serum creatinine ≥ 1.5 mg/dL (133 micromole/L), age ≥ 80 years, or body weight ≤ 60 kg the recommended dose is Eliquis, 2.5 mg twice daily. Patients with severe renal impairment (creatinine clearance 15-29 ml/min) should receive Eliquis 2.5 mg twice daily. Therapy should be continued long term. *Treatment of DVT, treatment of PE and prevention of recurrent DVT and PE (VTEt):* The recommended dose for the treatment of acute DVT and treatment of PE is 10 mg twice daily for the first 7 days followed by 5 mg twice daily. As per available medical guidelines, short duration of treatment (at least 3 months) should be based on transient risk factors (e.g. recent surgery, trauma, immobilisation). The recommended dose for the prevention of recurrent DVT and PE is 2.5 mg twice daily. When prevention of recurrent DVT and PE is indicated, the 2.5 mg twice daily dose should be initiated following completion of 6 months of treatment with Eliquis 5 mg twice daily or with another anticoagulant. The duration of overall therapy should be individualised after careful assessment of the treatment benefit against the risk for bleeding. *Prevention of VTE (VTEp): elective hip or knee replacement surgery:* The recommended dose is 2.5 mg twice a day. The initial dose should be taken 12 to 24 hours after surgery. Hip replacement surgery, the recommended duration of treatment is 32 to 38 days. Knee replacement surgery, the recommended duration of treatment is 10 to 14 days. *Missed Dose for All Indications*: If a dose is missed, Eliquis should be taken immediately and then continue with twice daily dose as before. *Switching:* Switching treatment from parenteral anticoagulants to Eliquis (and vice versa) can be done at the next scheduled dose. These medicinal products should not be administered simultaneously. *Switching treatment from VKA therapy to Eliquis*: Warfarin or other VKA therapy should be discontinued and Eliquis started when the international normalized ratio (INR) is < 2. *Switching treatment from Eliquis to VKA therapy*: Administration of Eliquis should be continued for at least 2 days after beginning VKA therapy. After 2 days of co- administration of Eliquis with VKA therapy, an INR should be obtained prior to next scheduled dose of Eliquis. Co-administration of Eliquis and VKA therapy should be continued until the INR is ≥2. *Renal Impairment - mild or moderate renal impairment*: For the prevention of VTE in elective hip or knee replacement surgery (VTEp), for the treatment of DVT, treatment of PE and prevention of recurrent DVT and PE (VTEt), no dose adjustment is necessary. For the prevention of stroke and systemic embolism in patients with NVAF and serum creatinine ≥ 1.5 mg/dL (133 micromole/L) associated with age ≥ 80 years or body weight ≤ 60 kg, a dose reduction is necessary. In the absence of other criteria for dose reduction (age, body weight), no dose adjustment is necessary. *Severe renal impairment (creatinine clearance 15-29 mL/min):* For the prevention of VTE in elective hip or knee replacement surgery (VTEp), for the treatment of DVT, treatment of PE and prevention of recurrent DVT and PE (VTEt), Eliquis is to be used with caution. For the prevention of stroke and systemic embolism in patients with NVAF, patients should receive the lower dose of Eliquis 2.5mg twice daily. In patients with creatinine clearance < 15 mL/min, or in patients undergoing dialysis, there is no clinical experience therefore Eliquis is not recommended. See SmPC for further details. *Hepatic impairment:* Contraindicated in patients with hepatic disease associated with coagulopathy and clinically relevant bleeding risk. Not recommended in patients with severe hepatic impairment. Use with caution in patients with mild or moderate hepatic impairment (Child Pugh A or B). No dose adjustment is required in patients with mild or moderate hepatic impairment. Use with caution in patients with elevated liver enzymes (ALT/AST >2 x ULN) or total bilirubin ≥ 1.5 x ULN. Prior to initiating Eliquis, liver function testing should be performed. *Catheter ablation (NVAF)*: Patients can continue Eliquis use while undergoing catheter ablation. *Cardioversion (NVAF)*: Eliquis can be initiated or continued in NVAF patients who may require cardioversion. See SmPC for further details. *Patients with NVAF and acute coronary syndrome (ACS) and/or percutaneous coronary intervention (PCI)*: There is limited experience of treatment with apixaban at the recommended dose for NVAF patients when used in combination with antiplatelet agents in patients with ACS and/or undergoing PCI after haemostasis is achieved. See SmPC for further details. *Paediatric population*: Eliquis is not recommended in children and adolescents below the age of 18.
CONTRAINDICATIONS (SPC section 4.3): Hypersensitivity to active substance or to excipients, active clinically significant bleeding, hepatic disease associated with coagulopathy and clinically relevant bleeding risk, lesion or condition if considered a significant risk factor for major bleeding, see SmPC for further details. Concomitant treatment with any other anticoagulant agent except under specific circumstances of switching anticoagulant therapy or when unfractionated heparin (UFH) is given at doses necessary to maintain an open central venous or arterial catheter or when UFH is given during catheter ablation for atrial fibrillation, see SmPC for further details.
WARNINGS AND PRECAUTIONS (SPC section 4.4): *Haemorrhage risk:* Carefully observe for signs of bleeding. Use with caution in conditions with increased risk of haemorrhage. Discontinue administration if severe haemorrhage occurs. An agent to reverse the anti-factor Xa activity of apixaban is available. For information on reversal and managing bleeding, see SmPC for further details. *Interaction with other medicinal products affecting haemostasis*: Concomitant treatment with any other anticoagulant is contraindicated (see contraindications). Concomitant use of Eliquis with antiplatelet agents increases the risk of bleeding. Care with concomitant SSRIs, SNRIs or NSAIDs, including acetylsalicylic acid. Following surgery, other platelet aggregation inhibitors are not recommended concomitantly with Eliquis. In patients with atrial fibrillation and conditions that warrant mono or dual antiplatelet therapy, a careful assessment of the potential benefits against the potential risks should be made before combining this therapy with Eliquis. A clinical trial enrolled patients with atrial fibrillation with ACS and/or undergoing PCI and a planned treatment period with a P2Y12 inhibitor, with or without ASA, and oral anticoagulant (either apixaban or VKA) for 6 months. Concomitant use of ASA increased the risk of ISTH (International Society on Thrombosis and Hemostasis) major or CRNM (Clinically Relevant Non-Major) bleeding in apixaban-treated subjects. See SmPC for further details. *Use of thrombolytic agents for the treatment of acute ischemic stroke:* Limited experience. *Patients with prosthetic heart valves*: safety and efficacy of Eliquis have not been studied in patients with prosthetic heart valves, with or without atrial fibrillation. Therefore, the use of Eliquis is not recommended in this setting. *Patients with antiphospholipid syndrome:* Direct acting Oral Anticoagulants (DOACs), including Eliquis, are not recommended for patients with a history of thrombosis who are diagnosed with antiphospholipid syndrome (see SmPC for further details). *Surgery and invasive procedures*: Discontinue at least 48 hours prior to elective surgery or invasive procedures with a moderate or high risk of bleeding. Discontinue at least 24 hours prior to elective surgery or invasive procedures with a low risk of bleeding. If surgery or invasive procedures cannot be delayed, appropriate caution should be exercised, taking into consideration an increased risk of bleeding. Eliquis should be restarted after the invasive procedure or surgical intervention as soon as possible provided the clinical situation allows and adequate haemostasis has been established. For patients undergoing catheter ablation for atrial fibrillation, Eliquis treatment does not need to be interrupted. *Temporary discontinuation*: Discontinuing anticoagulants, including Eliquis, for active bleeding, elective surgery, or invasive procedures places patients at an increased risk of thrombosis. Lapses in therapy should be avoided and if anticoagulation with Eliquis must be temporarily discontinued for any reason, therapy should be restarted as soon as possible. *Spinal/epidural anaesthesia or puncture*: Patients treated with antithrombotic agents for prevention of thromboembolic complications are at risk of developing an epidural or spinal haematoma which can result in long- term or permanent paralysis. The risk of these events may be increased by the post- operative use of indwelling epidural catheters or the concomitant use of medicinal products affecting haemostasis. Indwelling epidural or intrathecal catheters must be removed at least 5 hours prior to the first dose of Eliquis. The risk may also be increased by traumatic or repeated epidural or spinal puncture. Patients are to be frequently monitored for signs and symptoms of neurological impairment (e.g., numbness or weakness of the legs, bowel or bladder dysfunction). If neurological compromise is noted, urgent diagnosis and treatment is necessary. Prior to neuraxial intervention the physician should consider the potential benefit versus the risk in anticoagulated patients or in patients to be anticoagulated for thromboprophylaxis. There is no clinical experience with the use of Eliquis with indwelling intrathecal or epidural catheters. See SmPC for further details. *Haemodynamically unstable PE patients or patients who require thrombolysis or pulmonary embolectomy*: Eliquis is not recommended as an alternative to unfractionated heparin in patients with pulmonary embolism who are haemodynamically unstable or may receive thrombolysis or pulmonary embolectomy since the safety and efficacy of Eliquis have not been established. *Patients with active cancer*: Patients with active cancer can be at high risk of both venous thromboembolism and bleeding events. When apixaban is considered for DVT or PE treatment in cancer patients, a careful assessment of the benefits against the risks should be made. *Renal impairment*: see dosage and administration section. *Elderly patients*: Increasing age may increase haemorrhagic risk. Also, the co-administration of Eliquis with ASA in elderly patients should be used cautiously because of a potentially higher bleeding risk. *Body weight*: Low body weight (< 60 kg) may increase haemorrhagic risk. *Hepatic impairment*: see dosage and administration section. *Interaction with Inhibitors of CYP3A4 and P-gp*: Not recommended with strong inhibitors of both CYP3A4 and P-gp. These medicinal products may increase Eliquis exposure by 2-fold or greater in the presence of additional factors that increase Eliquis exposure (e.g. severe renal impairment) see SmPC for further details. *Interaction with Inducers of CYP3A4 and P-gp*: Eliquis should not be used for the treatment of DVT and PE in patients receiving concomitant systemic treatment with strong inducers of both CYP3A4 and P-gp since efficacy may be compromised. Concomitant systemic treatment with strong inducers of both CYP3A4 and P-gp, Eliquis should be used with caution for the prevention of VTE in elective hip or knee replacement surgery, for the prevention of stroke and systemic embolism in patients with NVAF and for the prevention of recurrent DVT and PE, though no dose adjustment for Eliquis is required during concomitant therapy with such medicinal products. *Hip fracture surgery*: Eliquis has not been studied in clinical trials in patients undergoing hip fracture surgery. Therefore, it is not recommended in these patients. *Laboratory parameters*: Clotting tests (PT, INR, and aPTT) are affected by the mechanism of action of apixaban. Changes observed at the expected therapeutic dose are small and subject to a high degree of variability, see SmPC for further details. *Information about excipients*: Eliquis contains lactose. Patients with galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take Eliquis.
DRUG INTERACTIONS (SPC Section 4.5): Eliquis should be used with caution when co-administered with SSRIs/SNRIs, NSAIDs, ASA and/or P2Y12 inhibitors because these medicinal products typically increase the bleeding risk. There is limited experience of co-administration with other platelet aggregation inhibitors (such as GPIIb/IIIa receptor antagonists, dipyridamole, dextran or sulfinpyrazone) or thrombolytic agents. As such agents increase the bleeding risk, co-administration of these products with Eliquis is not recommended. See SmPC for further details.Due to an increased bleeding risk, concomitant treatment with any other anticoagulants is contraindicated, except under specific circumstances of switching anticoagulant therapy, when UFH is given at doses necessary to maintain an open central venous or arterial catheter or when UFH is given during catheter ablation for atrial fibrillation. Administration of activated charcoal reduces Eliquis exposure. Also see contraindications and special warnings and

precautions section; Consult SmPC (contraindications, special warnings and precautions and drug interactions) for full details on interactions.

PREGNANCY AND LACTATION (SPC section 4.6): *Pregnancy:* As a precautionary measure, it is preferable to avoid the use of apixaban during pregnancy. *Breastfeeding:* A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from apixaban therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

UNDESIRABLE EFFECTS (SPC section 4.8): Increased risk of occult or overt bleeding from any tissue or organ, which may result in post haemorrhagic anaemia. The signs, symptoms, and severity will vary according to the location and degree or extent of the bleeding. Frequencies: common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100); rare (≥ 1/10,000 to < 1/1,000); very rare (< 1/10,000); not known (cannot be estimated from the available data). **Prevention of VTE in adult patients who have undergone elective hip or knee replacement surgery (VTEp):** *Common*: anaemia; haemorrhage*; haematoma*; nausea; contusion. *Uncommon*: thrombocytopenia*; epistaxis*; haematochezia*; liver function test abnormal (including blood bilirubin increased*); haematuria*; specific haemorrhage such as gastrointestinal*, abnormal vaginal*, urogenital*, post procedural*, wound secretion*, incision site*, operative*. *Rare*: hypersensitivity*; anaphylaxis*; haemoptysis*; gingival bleeding*; specific haemorrhage such as eye (including conjunctival)*, rectal*, muscle*. *Not known*: angioedema*; specific haemorrhage such as brain (encompassing intracranial, intraspinal)*, intra-abdominal*, respiratory tract*, haemorrhoidal*, mouth*, retroperitoneal*, traumatic*, erythema multiforme*. **Prevention of stroke and systemic embolism in adult patients with NVAF, with one or more risk factors (NVAF):** *Common*: anaemia; haemorrhage*; haematoma*; hypotension (including procedural hypotension); epistaxis*; nausea; gingival bleeding*; gamma-glutamyltransferase increased; haematuria*; contusion; specific haemorrhage such as eye (including conjunctival)*, gastrointestinal*, rectal*. *Uncommon*: thrombocytopenia*; hypersensitivity*; anaphylaxis*; haemoptysis*; haematochezia*; liver function test abnormal (including blood bilirubin increased*); specific haemorrhage such as brain (encompassing intracranial, intraspinal)*, intra-abdominal*, haemorrhoidal*, mouth*, abnormal vaginal*, urogenital*, post procedural*, wound secretion*, incision site*, operative*, traumatic*. *Rare*: specific haemorrhage such as respiratory tract*, retroperitoneal*, muscle*. *Very Rare*: erythema multiforme*. *Not known:* angioedema*.

Treatment of DVT and PE, and prevention of recurrent DVT and PE (VTEt): *Common*: anaemia; thrombocytopenia*; haemorrhage*; haematoma*; epistaxis*; nausea; gingival bleeding*; gamma-glutamyltransferase increased; alanine aminotransferase increased; skin rash; haematuria*; contusion; specific haemorrhage such as gastrointestinal*, mouth*, rectal*, abnormal vaginal*, urogenital*. *Uncommon*: hypersensitivity*; anaphylaxis*; haemoptysis*; haematochezia*; liver function test abnormal (including blood bilirubin increased*); specific haemorrhage such as eye (including conjunctival)*, haemorrhoidal*, muscle*, post procedural*, wound secretion*, incision site*, operative*, traumatic*. *Rare*: specific haemorrhage such as brain (encompassing intracranial, intraspinal)*, respiratory tract*. *Not Known*: angioedema*; specific haemorrhage such as intra-abdominal* and retroperitoneal*, erythema multiforme*.

*Denotes serious adverse reaction

Refer to SmPC for all other adverse events

LEGAL CATEGORY: POM.

MARKETING AUTHORISATION NUMBER (SPC section 8):
EU/1/11/691/002-3, EU/1/11/691/008, EU/1/11/691/014

PACKAGE QUANTITIES: Carton of 20 film-coated tablets 2.5 mg, 60 film-coated tablets 2.5 mg, 56 film-coated tablets 5 mg, 28 film- coated tablets 5 mg.

MARKETING AUTHORISATION HOLDER (SPC section 7): Bristol-Myers Squibb/Pfizer EEIG, Plaza 254, Blanchardstown Corporate Park 2, Dublin 15, D15 T867, Ireland

FOR FURTHER INFORMATION CONTACT: medical.information@bms.com or 1 800 749 749 (Ireland)

DATE OF PREPARATION: April 2021

ADDITIONAL INFORMATION AVAILABLE ON REQUEST

Approval Code: 432-IE-2100041

Adverse events should be reported. Reporting forms and information can be found at:
Ireland - via HPRA Pharmacovigilance at www.hpra.ie
Adverse events should also be reported to Bristol-Myers Squibb via medical.information@bms.com or 1 800 749 749 (Ireland)

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