ELIQUIS® (apixaban) 2.5 mg & 5 mg

Film-coated Tablets Prescribing Information

Consult summary of product characteristics (SmPC) prior to prescribing

PRESENTATION: Film-coated tablets; 5 mg and 2.5 mg apixaban.
INDICATION: 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 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 adult patients who have undergone elective hip or knee replacement surgery (2.5 mg only).
DOSAGE: 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: No dose adjustment in mild or moderate renal impairment. Eliquis is to be used with caution in severe renal impairment (creatinine clearance 15-29 mL/min) as there may be an increased risk of bleeding. For the prevention of stroke and systemic embolism in patients with NVAF and severe renal impairment, patients should receive the lower dose of Eliquis 2.5 mg twice daily. Patients with NVAF and serum creatinine ≥ 1.5 mg/dL (133 micromole/L) associated with age ≥ 80 years or body weight ≤ 60 kg should also receive the lower dose of Eliquis 2.5 mg twice daily for stroke/systemic embolism prevention. In patients with creatinine clearance < 15 mL/min, or in patients undergoing dialysis, there is no clinical experience therefore Eliquis is not recommended.
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.
Paediatric population: Eliquis is not recommended in children and adolescents below the age of 18.
CONTRAINDICATIONS: 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 (refer to SmPC). 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 (refer to SmPC).
WARNINGS AND PRECAUTIONS: *Haemorrhage risk:* Carefully observe for signs of bleeding. Use with caution in conditions with increased risk of haemorrhage. Discontinue administration if severe haemorrhage occurs.
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.
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. For information on reversal and managing bleeding, see SmPC for further details.
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. (refer to SmPC)
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:* efficacy and safety of Eliquis in the treatment of DVT, treatment of PE and prevention of recurrent DVT and PE (VTEt) in patients with active cancer have not been established.
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) (refer to SmPC).*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).
Information about excipients: Eliquis contains lactose. Patients with galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption should not take Eliquis.
DRUG INTERACTIONS: Medicinal products associated with serious bleeding are not recommended concomitantly with Eliquis, such as: thrombolytic agents, GPIIb/IIIa receptor antagonists, thienopyridines (e.g.clopidogrel), dipyridamole, dextran and sulfinpyrazone.
Eliquis should be used with caution when co-administered with SSRIs/SNRIs or NSAIDs (including acetylsalicylic acid) because these medicinal products typically increase the bleeding risk. 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: *Pregnancy:* Not recommended.

Breastfeeding: Discontinue breastfeeding or discontinue Eliquis therapy.
UNDESIRABLE EFFECTS: 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; Hypotension (including procedural hypotension); specific haemorrhage such as gastrointestinal, epistaxis, abnormal vaginal, urogenital, post procedural, incision site, operative; haematochezia. Liver function test abnormal Rare :hypersensitivity, allergic oedema and anaphylaxis; specific haemorrhage such as eye (including conjunctival), gingival, rectal, muscle; haemoptysis.
Prevention of stroke and systemic embolism in adult patients with NVAF, with one or more risk factors (NVAF): Common: anaemia, nausea, specific haemorrhage such as eye (including conjunctival), gastrointestinal, rectal; haemorrhage, haematoma, epistaxis, gingival bleeding, haematuria, contusion, hypotension (including procedural hypotension); Gamma-glutamyltransferase increased. Uncommon: hypersensitivity, allergic oedema and anaphylaxis; specific haemorrhage such as brain, intracranial, intraspinal, intra-abdominal, abnormal vaginal, urogenital, mouth, haemorrhoidal, traumatic, post procedural, incision site; haemoptysis, haematochezia, thrombocytopenia, Liver function test abnormal. Rare: specific haemorrhage such as respiratory tract, retroperitoneal.
Treatment of DVT and PE, and prevention of recurrent DVT and PE (VTEt): Common: anaemia, nausea, skin rash, haemorrhage, haematoma, epistaxis; specific haemorrhage such as mouth, gastrointestinal, rectal; gingival bleeding, haematuria, abnormal vaginal, urogenital, contusion, gamma-glutamyltransferase increased, alanine aminotransferase increased; thrombocytopenia. Uncommon: Hypersensitivity, allergic oedema and Anaphylaxis, specific haemorrhage such as eye (including conjunctival), haemorrhoidal, traumatic, post procedural, incision site; haemoptysis, muscle, haematochezia, Liver function test abnormal. Rare: specific haemorrhage such as brain, intracranial, intraspinal, respiratory tract.
Please refer to the SmPC for further details of adverse reactions including other types of haemorrhage.
LEGAL CATEGORY: POM.
MARKETING AUTHORISATION NUMBER:
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: Bristol-Myers Squibb/Pfizer EEIG.
LOCAL REPRESENTATIVE IN IRELAND:
Bristol-Myers Squibb Pharmaceuticals uc, Plaza 254, Blanchardstown Corporate, Park 2, Ballycoolin, Dublin, D15 T867, Ireland. Tel: 01 483 3625
DATE OF LAST REVISION: July 2019
ADDITIONAL INFORMATION AVAILABLE ON REQUEST
Mercury Internal Ref. no: 432IE1904861-01

Adverse events should be reported. Reporting forms and information can be found at:
Ireland - Freepost HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517.
Website: www.hpra.ie; Email: medsafety@hpra.ie
Adverse events should also be reported to Bristol-Myers Squibb via medical.information@bms.com or 1 800 749 749 (Ireland).