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.

**INDICATIONS:** Prevention of stroke and system 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 2.5 mg twice a day. Patients with severe renal impairment (creatinine clearance 12-29 ml/min) should be treated with 2.5 mg once daily. The recommended dose in patients with atrial fibrillation undergoing catheter ablation for atrial fibrillation (AFib) (refer to SmPC) is 2.5 mg twice a day.
- **Treatment of DVT, treatment of PE and prevention of recurrent DVT and PE (VTE):** 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 the 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 another anticoagulant. The duration of therapy should be individualised after careful assessment of the treatment benefit versus the risk for the against the risk for the benefit.
- **Temporary discontinuation of VTE:** Patient is to be treated with a low molecular weight heparin for 5-10 days, and then continue with twice daily dose as before.
- **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 normalised ratio (INR) is < 2.
- **Switching treatment from Eliquis to VKA therapy:** administration of Eliquis should be discontinued for at least 5 days before switching to VKA therapy. After 2 days of 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 adult 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 micromol/L), associated with age ≥ 80 years or body weight ≤ 80 kg received a dose of 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:** Apixaban is indicated 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). Dose adjustment for Eliquis 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 tests 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:** use not recommended in children and adolescents below the age of 18.

**CONTRAINDICATIONS:** Hypersensitivity to active substance or to excipients, active or clinically relevant 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 except agent 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:** Haemorrhagic risk: Carefully observe for signs of bleeding. Use with caution in conditions with increased risk of haemorrhage. Discontinue administration if severe haemorrhage occurs. Interactions with other medicinal products associated with haemostasis. Concomitant treatment with any other anticoagulant is contraindicated (see contraindications). Concomitant use of Eliquis with antiplatelet agents increases the risk of bleeding.

Care should be taken if Eliquis is used in combination with SSRIs/SNRIs or NSAIDs (including acetylsalicylic acid) because these medicinal products typically increase the risk of bleeding. Due to limited data on haemostasis in patients receiving concomitant systemic therapy 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 should be avoided. 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. Eliquis should not be used for the treatment of DVT and PE in patients with active cancer. Patients with active cancer have not been established.

**Drug Interactions:** Medicinal products associated with serious bleeding are not recommended concomitantly with Eliquis, such as: thrombolytic agents, GPIIb/IIIa receptor antagonists, thiopurinylines (e.g. clopidogrel), dipryidamole, dextrin and suflanilamine.

**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).**

**Interactions with Inducers of CYP3A4 and P-gp:** Not recommended 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. Eliquis has not been studied in clinical trials in patients undergoing hip fracture surgery. Therefore, it is not recommended in these patients.

**Hepatic impairment:** see dosage and administration section.

**Elderly patients:** increasing age may increase haemorrhagic risk. Also, the coadministration of Eliquis with ASA in elderly patients should be used cautiously because of a potentially higher bleeding risk.

**Body weight:** low body weight is associated with increased haemorrhagic risk.

**Hepatic impairment:** see dosage and administration section.

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**Hypertension:** see Special warnings and precautions for information on haemodynamically unstable PE patients.**

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**Eliquis should be used with caution when co-administered with SSRIs/SNRIs or NSAIDs (including acetylsalicylic acid) because these medicinal products typically increase the risk of bleeding. Due to limited data on haemostasis in patients receiving concomitant systemic therapy 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 should be avoided. 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. Eliquis should not be used for the treatment of DVT and PE in patients with active cancer. Patients with active cancer have not been established.

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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, confusion. 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; confusion, 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 and BASIC NHS PRICE:
EU/1/11/691/001-3, EU/1/11/691/008, EU/1/11/691/014
Carton of 10 film-coated tablets 2.5mg £9.30, 20 film-coated tablets 2.5mg £19.00, 60 film-coated tablets 2.5mg £57.00, 56 film-coated tablets 5mg £53.20, 28 film-coated tablets 5mg £26.60.

MARKETING AUTHORISATION HOLDER: Bristol-Myers Squibb/Pfizer EEIG.
LOCAL REPRESENTATIVE IN UK:
Bristol-Myers Squibb/Pfizer EEIG, BMS House, Uxbridge Business Park, Sanderson Road, Uxbridge, Middlesex, UB8 1DH. Telephone: 0800-731-1736.

DATE OF LAST REVISION: July 2019

ADDITIONAL INFORMATION AVAILABLE ON REQUEST
Mercury Internal Ref. no; GCMA code. 432UK190074-01; PP-ELI-GBR-5510

Adverse events should be reported. Reporting forms and information can be found at:
UK - www.mhra.gov.uk/yellowcard, or search for MHRA Yellow Card in the Google Play or Apple App Store
Adverse events should also be reported to Bristol-Myers Squibb via medical.information@bms.com or 0800 731 1736 (UK)