**Presentation**: Film-coated tablets; 5 mg and 2.5 mg apixaban.

**Indications**: 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/or 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**: Oral. Taken with water, with or without food. Prevention of stroke and systemic embolism in adults 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 (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 transient risk factors (e.g. recent trauma, immobility).

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. For patients with coagulopathy and/or anticoagulant (e.g. warfarin) therapy, the duration of overall therapy should be individualised after careful assessment of the treatment benefit against the risk for bleeding.

Prevention of VTE in 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 39 to 54 days.

All indications included in 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 satisfied.

**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 adults with NVAF the recommended dose is Eliquis, 2.5 mg twice daily. Patients with severe renal impairment 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 receive the lower dose of 1.5 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. No dose adjustment is recommended in patients with mild or moderate hepatic impairment. Use with caution in patients with elevated liver enzymes (ALT/AST >2x ULN) or total bilirubin ≥ 1.5 x ULN. Prior to initiating Eliquis, liver function testing should be performed.

Catheter ablation: 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 coronary artery disease: Eliquis is indicated for the prevention of stroke and systemic embolism in patients with NVAF and one or more of the following risk factors: age ≥ 75 years, hypertension, diabetes mellitus, or symptomatic heart failure (NYHA Class ≥ II). Treatment of deep vein thrombosis (DVT) and/or 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 VTE in elective hip or knee replacement surgery: The recommended dose is 2.5 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 trauma, immobility).

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. For patients with coagulopathy and/or anticoagulant (e.g. warfarin) therapy, the duration of overall therapy should be individualised after careful assessment of the treatment benefit against the risk for bleeding.

**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, 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 or intracranial catheter or when UFH is given during catheter ablation for atrial fibrillation, see SmPC for further details.

**Warnings and Precautions**: Haemorrhage risk: Carefully observe for signs and symptoms suggestive of bleeding and caution in patients with increasing risk of haemorrhage. Discontinue administration if severe haemorrhage occurs. An agent is reserved to reverse the anti-factor Xa activity of apixaban is available. For information on reversal and managing bleeding, see SmPC for further details.

**Drug Interactions**: Eliquis is 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: 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, post procedural; haematochezia. Liver function test abnormal · Gamma-glutamyltransferase increased.

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), 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 (VTEp): 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.

Refer to SmPC for all other adverse events, 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 £9.50, 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 Pharmaceuticals Ltd, Uxbridge Business Park, Sanderson Road, Uxbridge, Middlesex UB8 1DH, UK. Tel: 01895 523000

DATE OF LAST REVISION: March 2020
ADDITIONAL INFORMATION AVAILABLE ON REQUEST

Mercury Internal Ref. no; GCMA code 432UK2000283-01; PP-ELI-GBR-6502

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)