

LIXIANA ▼ (edoxaban) 60mg/30mg/15mg film coated tablets

See summary of product characteristics prior to prescribing for full list of adverse events

Presentation: 60 mg (yellow) / 30 mg (pink)/ 15mg (orange) edoxaban film coated tablets (as tosilate). **Indications:** Prevention of stroke and systemic embolism in adult patients with nonvalvular atrial fibrillation (NVAF) with one or more risk factors, such as congestive heart failure, hypertension, age \geq 75 years, diabetes mellitus, prior stroke or transient ischaemic attack (TIA) and treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults. **Posology and method of administration:** *NVAF* -The recommended dose is 60 mg edoxaban once daily with or without food. Therapy with edoxaban in NVAF patients should be continued long term. *VTE* - The recommended dose is 60 mg edoxaban once daily following initial use of parenteral anticoagulant for at least 5 days with or without food. Duration of therapy (at least 3 months) should be based on risk profile of the patient. For NVAF and VTE the recommended dose is 30 mg edoxaban once daily in patients with one or more of the following clinical factors: moderate or severe renal impairment (creatinine clearance (CrCL) 15 - 50 mL/min), low body weight \leq 60 kg and / or concomitant use of the following P-glycoprotein (P-gp) inhibitors: ciclosporin, dronedarone, erythromycin, or ketoconazole. The 15mg dose of edoxaban is not indicated as monotherapy, and should only be used during a switch from edoxaban to VKA (see SmPC for full details). If a dose of edoxaban is missed, the dose should be taken immediately and then continued once daily on the following day. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients; clinically significant active bleeding. Hepatic disease associated with coagulopathy and clinically relevant bleeding risk. Lesion or condition, if considered to be a significant risk for major bleeding. This may include current or recent gastrointestinal (GI) 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. Uncontrolled severe hypertension. Concomitant treatment with any other anticoagulants e.g. UFH, low molecular weight heparins, heparin derivatives (fondaparinux, etc.), VKA or NOACs except under specific circumstances of switching oral anticoagulant therapy or when UFH is given at doses necessary to maintain an open central venous or arterial catheter. Pregnancy and breast-feeding. **Special warnings and precautions for use:** Haemorrhagic risk: Use with caution in patients with increased risk of bleeding such as elderly on ASA and should be discontinued if severe haemorrhage occurs. The anticoagulant effect of edoxaban cannot be reliably monitored with standard laboratory testing. A specific anticoagulant reversal agent for edoxaban is not available. Haemodialysis does not significantly clear edoxaban. **Renal impairment:** Renal function should be assessed prior to initiation of edoxaban and afterwards when clinically indicated. Not recommended in patients with end stage renal disease or on dialysis. **Renal function and NVAF:** A trend towards decreasing efficacy with increasing creatinine clearance was observed for edoxaban compared to well-managed warfarin. Edoxaban should only be used in patients with NVAF and high creatinine clearance after a careful benefit risk evaluation. **Hepatic impairment:** Not recommended in patients with severe hepatic impairment and should be used with caution in patients with mild or moderate hepatic impairment. Edoxaban should be used with caution in

patients with elevated liver enzymes (ALT/AST $>$ 2 x ULN) or total bilirubin \geq 1.5 x ULN. *Surgery or other interventions:* discontinue edoxaban at least 24 hours before the procedure. If the procedure cannot be delayed, the increased risk of bleeding should be weighed against the urgency of the procedure. Edoxaban should be restarted as soon as haemostasis is achieved. *Prosthetic heart valves and moderate to severe mitral stenosis:* Not recommended. *Haemodynamically unstable PE patients or patients who require thrombolysis or pulmonary embolectomy:* Not recommended. *Patients with active cancer:* Not recommended. **Drug interactions:** The *P-gp inhibitors* ciclosporin, dronedarone, erythromycin, or ketoconazole result in increased concentration of edoxaban and a dose reduction of 30mg is required. Edoxaban should be used with caution with concomitant *P-gp inducers* (e.g. phenytoin, carbamazepine, phenobarbital or St John's Wort). Concomitant high dose ASA (325mg) or chronic NSAIDs is not recommended. There is very limited experience with dual antiplatelet therapy or fibrinolytic agents. **Pregnancy:** Not recommended. *Breastfeeding:* discontinue breast feeding or edoxaban therapy. **Undesirable effects:** Common: anaemia, epistaxis, lower GI haemorrhage, upper GI haemorrhage, oral/pharyngeal haemorrhage, nausea, blood bilirubin increased, gamma GT increased, cutaneous soft tissue haemorrhage, rash, pruritus, macroscopic haematuria/urethral haemorrhage, vaginal haemorrhage, puncture site haemorrhage, liver function test abnormal. Uncommon: hypersensitivity, intracranial haemorrhage (ICH), intraocular haemorrhage, other haemorrhage, haemoptysis, surgical site haemorrhage. Rare: anaphylactic reaction, allergic oedema, subarachnoid haemorrhage, pericardial haemorrhage, retroperitoneal haemorrhage, intramuscular haemorrhage (no compartment syndrome), intra-articular haemorrhage, subdural haemorrhage, procedural haemorrhage.

Legal category: POM **Package quantities and basic NHS costs:** 60mg / 30mg – 28 tablets £51.80 15mg – 10 tablets £18.50 **Marketing Authorisation (MA) number:** EU/1/15/993/001-16

MA holder: Daiichi Sankyo Europe GmbH, Zielstattstrasse 48, 81379 Munich, Germany

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Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Daiichi Sankyo UK Medical Information on 0800 028 5122, medinfo@daiichi-sankyo.co.uk