

Prescribing EDOXABAN for the acute treatment and secondary prevention of Venous Thromboembolism (VTE) (Pulmonary Embolism (PE) or Deep Vein Thrombosis (DVT))

*Note: Edoxaban is also licensed for the prevention of stroke in patients with non-valvular atrial fibrillation.
Guidance for use for this indication can be found at: [SEL APC CVD Guidelines](#)*

Edoxaban ▼ (Lixiana®) is a direct oral anticoagulant (DOAC) licensed for the acute treatment of VTE (PE or DVT) and for the secondary prevention of VTE in patients at risk of recurrent events. The National Institute for Health and Care Excellence (NICE) has approved the use of edoxaban as an option for the acute management and secondary prevention of VTE.

In South London, edoxaban may be considered as an option for any patient experiencing a provoked or unprovoked DVT or PE, except those patients in whom there is an underlying malignancy or those who are pregnant or breast-feeding where a low molecular weight heparin (LMWH) is preferred, or patients with renal impairment (creatinine clearance (CrCl) < 30ml/min) in whom warfarin is preferred (edoxaban is contra-indicated when CrCl < 15ml/min).

- Patients with provoked VTE events (e.g. caused by surgery, trauma, long distance travel, immobility, pregnancy or hormone replacement therapy) usually require 3 - 6 months of edoxaban therapy.
- Patients with unprovoked events or where there are on-going risk factors for recurrence may require a longer duration, as advised by the initiating clinician.

Additional resources have been developed to support implementation including:

- [Overview summary of VTE treatment](#)
- [Screening checklist and Notification of initiation of a DOAC for the treatment of VTE](#) This document **must be completed and sent to the General Practitioner (GP) on initiation.**
- [Transfer of prescribing responsibility to primary care for DOACs.](#) This document **must be completed and sent to the GP when transferring the prescribing responsibility** in accordance to South London guidelines.

Edoxaban for VTE should only be initiated by clinicians with expertise in managing anticoagulant therapy. The initiating clinician / organisation is responsible for ensuring patient follow up and providing a supply of edoxaban for the first three months of treatment. During this time, efforts should be made to reinforce adherence and address any adverse effects.

Transfer of Prescribing Responsibility to Patient's Own GP

Following the initial 3 month period, patients requiring longer term anticoagulant therapy may be considered for transfer back to the patient's own GP, provided the agreed transfer of care guidance is followed. If edoxaban is prescribed for unlicensed / non-approved indications prescribing responsibility will remain with the initiating clinician/organisation.

Contraindications (for full details – see BNF or SPC)	Cautions (for full details – see BNF or SPC)
<ul style="list-style-type: none"> • Hypersensitivity to the active substance or to any of the excipients • Clinically significant active bleeding • Any lesion or condition considered a significant risk factor for major bleeding e.g. current or 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 • Prosthetic heart valves requiring anticoagulant treatment or mitral stenosis - the effect of edoxaban has not been studied in this patient group • Uncontrolled severe hypertension • Severe hepatic impairment or hepatic disease associated with coagulopathy and clinically relevant bleeding risk • Established renal failure (CrCl <15 ml/min*) • Pregnancy and/ or breast feeding • For contra-indications for use with other medicines see overleaf 	<ul style="list-style-type: none"> • Conditions which carry a haemorrhagic risk e.g. bacterial endocarditis, thrombocytopenia, congenital or acquired coagulation disorders • Active cancer- efficacy and safety of edoxaban in the treatment and/or prevention of VTE in patients with active cancer have not been established. • Haemodynamically unstable PE patients or patients who require thrombolysis or pulmonary embolectomy- not recommended since the safety and efficacy of edoxaban have not been established in these clinical situations • Low body weight ≤ 60kg • Mild or moderate hepatic impairment (Child Pugh score A or B) or elevated liver enzymes > twice the upper limit of normal (ULN), bilirubin >1.5x ULN (these patients were excluded from trials) • Moderate to severe renal impairment (CrCl 15-49 ml/min*) • For cautions for use with other medication see overleaf

Note: BNF=British National Formulary; SPC=Summary of Product Characteristics

*** Estimated Glomerular Filtration Rate (eGFR) should NOT be used to guide dosing decisions. Creatinine clearance must be estimated using the [Cockcroft-Gault equation calculator](#) or refer to the South London creatinine clearance informationsheet.**

This guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

Approved: June 2016

Review date: June 2018

South East London Area Prescribing Committee. A partnership between NHS organisations in South East London: Bexley/ Bromley/ Greenwich/ Lambeth/ Lewisham & Southwark Clinical Commissioning Groups (CCGs) & GSTFT/KCH/SLAM/Oxleas NHS Foundation Trusts & Lewisham & Greenwich NHS Trust

Not to be used for commercial or marketing purposes. Strictly for use within the NHS

Dosing

The recommended dose of edoxaban is 60mg ONCE daily with or without food following initial treatment with a parenteral anticoagulant for at least 5 days (this will be supplied by the initiating organisation).

- Reduce dose to 30mg ONCE daily with or without food in patients with one of the following characteristics:
 - Low body weight \leq 60kg
 - Moderate to severe renal impairment (CrCl 15-49 ml/min), or
 - Concomitant treatment with ciclosporin, dronedarone, erythromycin, ketoconazole.
- Patients with provoked VTE events (e.g. caused by surgery, trauma, long distance travel, immobility, pregnancy or hormone replacement therapy) usually require 3 - 6 months of edoxaban therapy.
- Patients with unprovoked events or where there are on-going risk factors for recurrence may require a longer duration, as advised by the initiating clinician.
- Treatment must only be started when parenteral anticoagulation therapy (LMWH / unfractionated heparin (UFH)) is discontinued. Edoxaban must not be administered concomitantly with any additional anticoagulation.
 - For patients on LMWH – the first dose of edoxaban must be given when the next dose of LMWH is due.
 - For patients on continuous infusions of UFH – stop the heparin infusion and give the first dose of edoxaban 4 hours later.

For patients identified as at risk of upper GI bleeding the co-prescription of a proton pump inhibitor (e.g. lansoprazole/omeprazole) may be considered.

Monitoring

International normalised ratio (INR) monitoring is not required for patients taking edoxaban. However, clinical surveillance is recommended throughout the treatment period in line with good anticoagulation practice.

- All patients prescribed edoxaban should be reviewed **at least annually** to assess benefits and risks of on-going therapy weighing the risk for thrombotic events against the bleeding risks.
- Patients should be monitored for signs of bleeding or anaemia; treatment should be stopped if severe bleeding occurs.
- A baseline renal function test is required and consequent re-testing should take place at least annually (frequency determined by the patient's baseline renal function as guided by the initiating clinician).
- For patients on long-term therapy clinicians will need to monitor patients and make any other dose adjustments necessary based on body weight, renal function and concomitant medication (see dosage section above).

Side effects (for full details see the BNF or SPC)

- As with any other form of anticoagulation, there is a risk of bleeding during treatment with edoxaban, and patients should be monitored for signs of bleeding or anaemia. Patients should be advised to seek medical advice if they experience persistent or frequent episodes of bleeding. Patients experiencing major or life threatening bleeding should seek urgent medical attention.
- Other common side effects include: nausea, rash, pruritus, abnormal liver function tests (raised bilirubin and gamma-glutamyl transferase (GGT)).

Edoxaban is a black triangle drug - any adverse effect must be reported to the MHRA using the yellow card system and via the local incident reporting system

Drug interactions (for full details on drug interactions – see BNF or SPC)

Drug / Drug class	Recommendation
Other anticoagulant agents (e.g. UFH or heparin derivatives, LMWHs, oral anticoagulants)	Concomitant use is contraindicated due to increased risk of bleeding, except where switching therapy to or from edoxaban or when UFH is given at doses necessary to maintain a patent catheter
Use of fibrinolytic agents for the treatment of acute ischaemic stroke	May be considered by hyper-acute stroke units if the clinician can be certain that there is no anticoagulant effect present based on laboratory testing of clotting
Aspirin and other antiplatelet agents	Increased risk of bleeding – use with caution; should be stopped if clinically appropriate (seek advice from cardiologist); if required to continue close monitoring required and gastro-protection is advised
Non-steroidal anti-inflammatory drugs (NSAIDs)	Increased risk of bleeding if used long-term. Avoid where possible; if required use at the lowest dose and for the shortest duration possible; close monitoring required and gastro-protection is advised
Any other medicinal products affecting haemostasis	May increase the risk of bleeding when used concomitantly, close monitoring required
P-glycoprotein inducers - such as St. John's wort (<i>Hypericum perforatum</i>), rifampicin, phenobarbital, carbamazepine or phenytoin	Concomitant use will result in decreased edoxaban plasma concentrations. No dose adjustment to edoxaban is required, however it should be used with caution. The co-administration of edoxaban with any of these agents should only be considered under specialist haematology supervision

Approved: June 2016

Review date: June 2018

South East London Area Prescribing Committee. A partnership between NHS organisations in South East London: Bexley/ Bromley/ Greenwich/ Lambeth/ Lewisham & Southwark Clinical Commissioning Groups (CCGs) & GSTFT/KCH/SLAM/Oxleas NHS Foundation Trusts & Lewisham & Greenwich NHS Trust

Not to be used for commercial or marketing purposes. Strictly for use within the NHS

Systemic ketoconazole, ciclosporin, dronedarone or erythromycin	Concomitant administration increases plasma edoxaban level. Maximum edoxaban dose of 30mg once daily when prescribed concurrently
Protease inhibitors	Not recommended for concomitant treatment
Amiodarone, quinidine, verapamil	No dose adjustment necessary

Roles and responsibilities

Initiating clinician / organisation	Patient's own GP
<ul style="list-style-type: none"> To initiate / guide the initiation of edoxaban in line with NICE and local guidance To supply edoxaban for the first 3 months of treatment To provide counselling to improve adherence and address any early adverse effects If treatment is required for longer than three months; to transfer care to the GP in line with local transfer of care guidance If treatment is required for longer than three months; to give the GP clear guidance about intended duration of treatment or further follow-up required For patients requiring long-term treatment; to arrange a follow-up at 12 months to review ongoing need for therapy 	<ul style="list-style-type: none"> To ensure use of edoxaban is in line with the NICE / local guidance To agree to take over prescribing responsibility when the patient is stable on therapy (at least 3 months after initiation and in line with the transfer of care guidance) To agree to take over prescribing earlier in patients with complex medication supply issues e.g. patients using medication compliance aids (MCA) or housebound patients To emphasise the importance of adherence to edoxaban therapy and address any patient concerns To ensure monitoring of renal and hepatic function is undertaken as directed by the initiating clinician and at least annually. If results fall outside normal range then refer to contraindication, caution and dosing sections in the prescribing guidelines and/or seek specialist advice as appropriate To monitor ongoing risk of bleed and if appropriate, seek specialist advice

Additional information

1. Patients taking edoxaban should be encouraged to carry an anticoagulation card (available from initiating clinician / anticoagulation clinics) at all times or to wear a medic-alert bracelet.
2. There is no specific reversal agent should a patient experience a bleed on edoxaban. In the event of a significant bleed, the patient should be referred to accident and emergency for supportive measures.
3. Other healthcare professionals should be made aware that edoxaban is prescribed for any patients who are to undergo invasive treatments, including elective surgery and dental treatment.
4. Missed dose advice should be discussed at initiation: If a dose of edoxaban is missed, the dose should be taken immediately and then be continued the following day with the once-daily intake as recommended. The dose should not be doubled within the same day to make up for a missed dose.
5. If a patient has been assessed as being appropriate for a multi-compartment compliance aid (MCA), often known as a dosette box, consideration can be given to including edoxaban tablets as they do not have any special storage requirements.

References

1. NICE TA354. Edoxaban for the treatment and secondary prevention of deep vein thrombosis and/or pulmonary embolism. Aug 2015. Accessed April 2016 at <https://www.nice.org.uk/guidance/ta354/resources/edoxaban-for-treating-and-for-preventing-deep-vein-thrombosis-and-pulmonary-embolism-82602668308165>
2. SPC Lixiana. Daiichi Sankyo UK Limited. July 2015. Accessed April 2016 at <http://www.medicines.org.uk/emc/medicine/30506>
3. The Hokusai-VTE Investigators. Edoxaban versus Warfarin for the Treatment of Symptomatic Venous Thromboembolism. N Engl J Med 2013;369:1406-15

Approved: June 2016

Review date: June 2018

South East London Area Prescribing Committee. A partnership between NHS organisations in South East London: Bexley/ Bromley/ Greenwich/ Lambeth/ Lewisham & Southwark Clinical Commissioning Groups (CCGs) & GSTFT/KCH/SLAM/Oxleas NHS Foundation Trusts & Lewisham & Greenwich NHS Trust

Not to be used for commercial or marketing purposes. Strictly for use within the NHS