NICE RECOMMENDED AND SMC ACCEPTED IN NVAF AND VTE[1-4]

PRACTICAL GUIDE

LIXIANA® (edoxaban)

For clinical data and prescriber resources please visit **www.lixiana.co.uk**

Prescribing information and adverse event reporting information can be found on the back cover.

Daiichi-Sankyo

Lixiana® edoxaban

OVERVIEW

THIS GUIDE IS SPECIFICALLY FOR PRESCRIBERS IN RELATION TO THE USE OF LIXIANA® (EDOXABAN)

It includes information on the following:

- Indications
- Summary of efficacy and safety
- Dosing recommendations and dose reduction
- Information on switching patients to or from LIXIANA®
- Contraindications
- Special patient populations
- Temporary discontinuation
- Perioperative management
- Overdose
- Management of bleeding complications
- Coagulation testing
- Patient alert card

Please consult the Summary of Product Characteristics (SmPC) for full prescribing information.

ONCE-DAILY LIXIANA® FOR YOUR ELIGIBLE PATIENTS WITH NVAF OR VTE

INDICATIONS[5]

LIXIANA® is indicated for:

- 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 ≥75 years, diabetes mellitus, prior stroke or transient ischaemic attack (TIA)
- Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults

SIMPLE AND CONVENIENT FOR PATIENTS AND PRESCRIBERS[5]

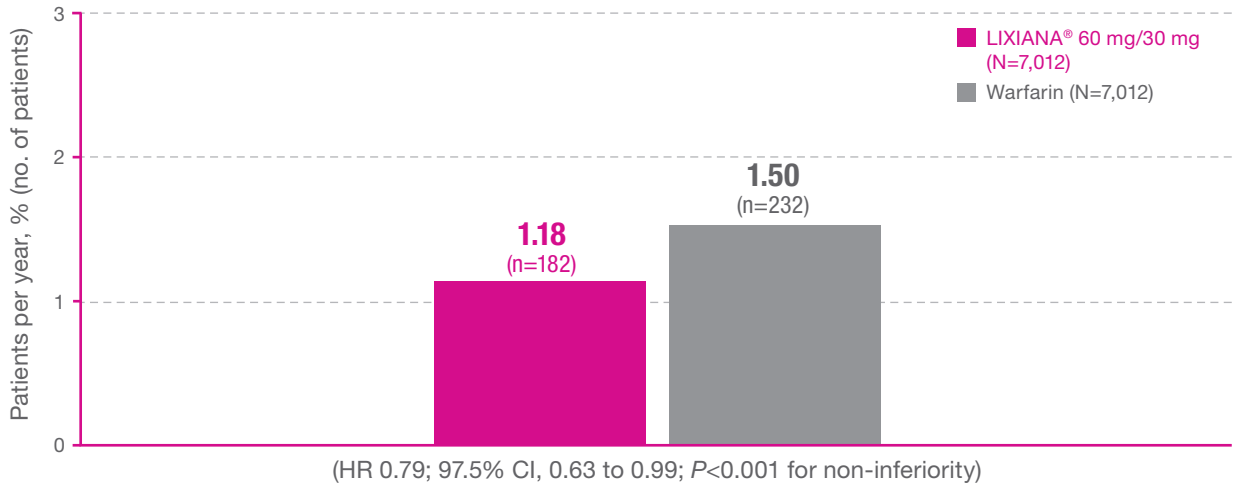
- Once-daily dosing, with or without food
- Consistent dosing regimen across both NVAF and VTE indications (following initial use of heparin for at least 5 days in VTE)

EFFICACY AND SAFETY IN NVAF

PROVEN EFFICACY IN PREVENTING STROKE AND SYSTEMIC EMBOLIC EVENTS IN NVAF PATIENTS – COMPARABLE TO WELL-MANAGED WARFARIN

- LIXIANA® 60 mg/30 mg was comparable to well-managed warfarin in the prevention of stroke and SEE in the modified intention-to-treat population (primary efficacy endpoint)[6]
- In NVAF patients with high creatinine clearance, there is a trend towards decreasing efficacy with increasing creatinine clearance for edoxaban vs well-managed warfarin, therefore careful evaluation of thromboembolic and bleeding risk is necessary before initiation

STROKE/SYSTEMIC EMBOLIC EVENTS IN THE MODIFIED INTENTION-TO-TREAT POPULATION DURING THE TREATMENT PERIOD[6]



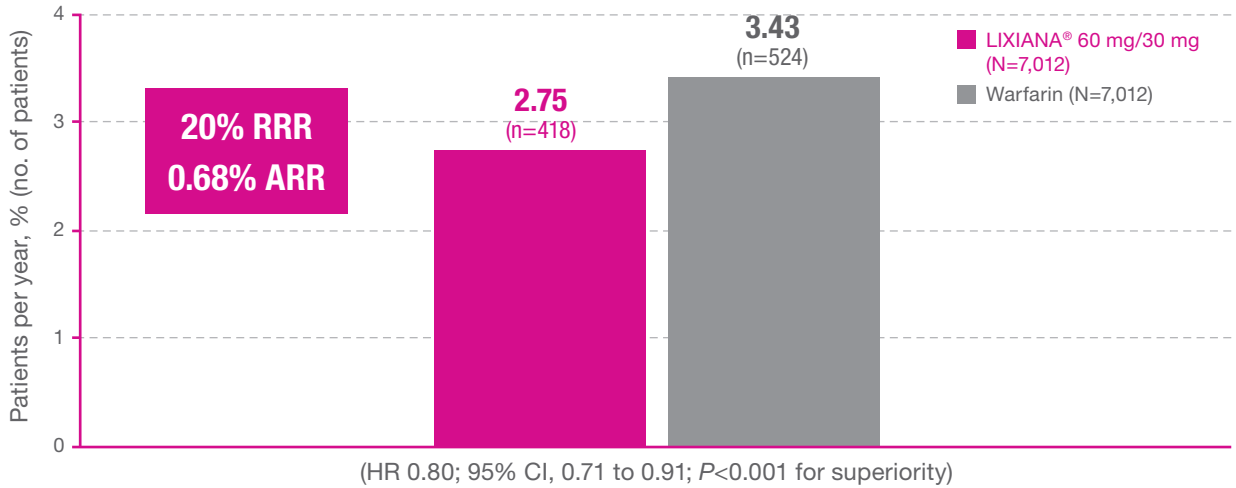
(HR 0.79; 97.5% CI, 0.63 to 0.99; *P*<0.001 for non-inferiority)

- Patients on the 30 mg reduced dose achieved efficacy consistent with overall trial results[7]

SEE, systemic embolic events; HR, hazard ratio; CI, confidence interval

SUPERIOR REDUCTION IN MAJOR BLEEDING IN NVAF PATIENTS VS. WELL-MANAGED WARFARIN

ANNUAL RATE OF MAJOR BLEEDING EVENTS (PRIMARY SAFETY ENDPOINT) IN THE SAFETY ON-TREATMENT POPULATION[6]



- Patients on the 30 mg reduced dose achieved a reduction in major bleeding consistent with overall trial results[7]

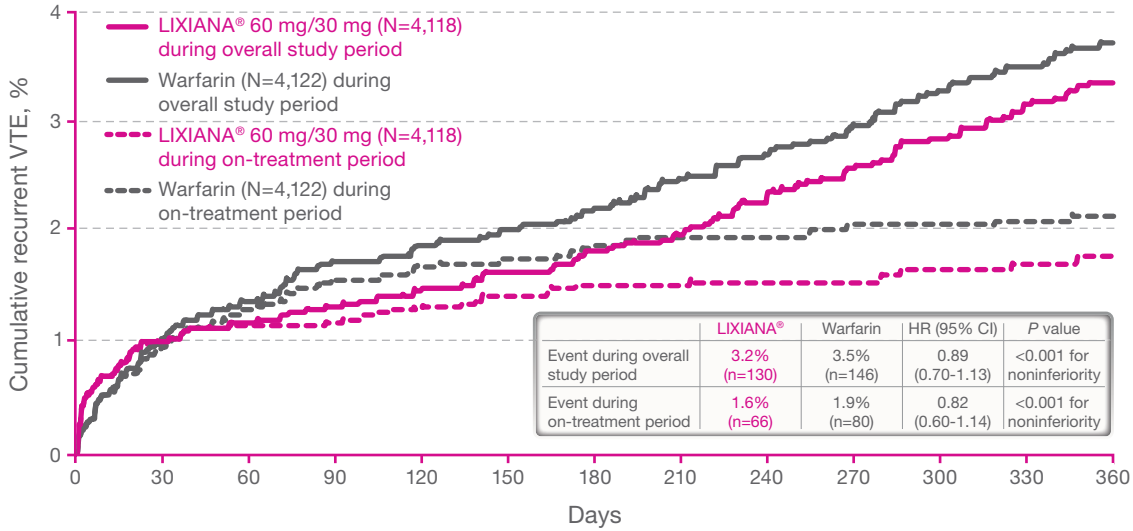
The primary safety endpoint was the incidence of adjudicated major bleeding,[6] defined by the International Society on Thrombosis and Haemostasis (ISTH) as (i) fatal bleeding; and/or (ii) symptomatic bleeding in critical area or organ, such as intracranial, intraspinal, intraocular, retroperitoneal, intraarticular, pericardial, or intramuscular with compartment syndrome, and/or (iii) bleeding causing a fall in haemoglobin level of 2.0 g/dL or more, or leading to transfusion of two or more units of whole blood or red cells.[6]

RRR, relative risk reduction; ARR, absolute risk reduction

EFFICACY AND SAFETY IN DVT AND PE

PROVEN EFFICACY IN THE TREATMENT AND PREVENTION OF RECURRENT VTE – COMPARABLE TO WELL-MANAGED WARFARIN

FIRST RECURRENT VTE EVENTS (PRIMARY EFFICACY ENDPOINT) DURING OVERALL STUDY AND ON-TREATMENT PERIODS[9,10]*



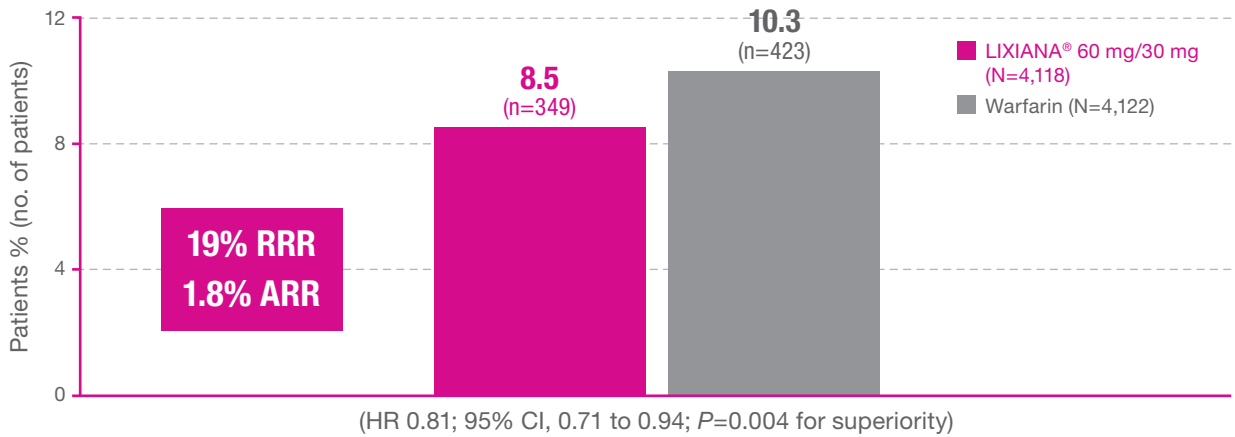
	LIXIANA®	Warfarin	HR (95% CI)	*P* value
Event during overall study period	3.2% (n=130)	3.5% (n=146)	0.89 (0.70-1.13)	<0.001 for noninferiority
Event during on-treatment period	1.6% (n=66)	1.9% (n=80)	0.82 (0.60-1.14)	<0.001 for noninferiority

- Patients on the 30 mg reduced dose achieved efficacy consistent with overall trial results[9]
- In NVAF patients with high creatinine clearance, there is a trend towards decreasing efficacy with increasing creatinine clearance for edoxaban vs well-managed warfarin, therefore careful evaluation of thromboembolic and bleeding risk is necessary before initiation

* The overall study period included the period of randomisation through to the end of 12 months or study closure[9]

SUPERIOR REDUCTION IN CLINICALLY RELEVANT BLEEDING IN VTE PATIENTS VS. WELL-MANAGED WARFARIN

COMPOSITE OF MAJOR AND CLINICALLY RELEVANT NONMAJOR BLEEDING EVENTS (PRIMARY SAFETY ENDPOINT) DURING ON-TREATMENT PERIOD[9]



- Patients on the 30 mg reduced dose achieved a reduction in clinically relevant bleeding consistent with overall trial results[9]

The primary safety endpoint was a composite of major and clinically relevant nonmajor bleeding,[9] as defined by the International Society on Thrombosis and Haemostasis (ISTH). Major bleeding was defined as overt bleeding associated with a decrease in haemoglobin of 2.0 g/L or more, or requiring a transfusion of 2 or more units of blood, occurring in a critical site or contributing to death.[8] Clinically relevant non major bleeding was defined as overt bleeding not meeting the criteria for major bleeding but associated with medical intervention, unscheduled contact (visit or telephone call) with a physician, (temporary) cessation of study treatment, or associated with other discomfort such as pain, or impairment of daily life activities.[11]

DOSING

THE RECOMMENDED DOSE OF LIXIANA® IS **60 MG IN A ONCE-DAILY TABLET**[5]

It can be taken with water, with or without food. To aid compliance, patients should be encouraged to take their dose at the same time every day.

Treatment with LIXIANA® in patients with NVAF should be continued long term.

The duration of treatment for VTE and prevention of recurrent VTE should be individualised after assessment of the treatment benefit against the risk for bleeding. Short duration of therapy (at least 3 months) should be based on transient risk factors (e.g. recent surgery, trauma, immobilisation) and longer durations should be based on permanent risk factors or idiopathic DVT or PE.

RECOMMENDED DOSE

60 mg

Tablet actual size

INITIATING TREATMENT[5]

For the treatment of VTE, patients should receive an initial course of heparin for at least 5 days prior to treatment with LIXIANA®. This is not required for the initiation of LIXIANA® in patients with NVAF for the prevention of stroke and systemic embolism.

Renal function (CrCl) and liver function should be assessed in all patients prior to LIXIANA® initiation. In NVAF patients with high creatinine clearance, there is a trend towards decreasing efficacy with increasing creatinine clearance for edoxaban vs well-managed warfarin, therefore careful evaluation of thromboembolic and bleeding risk is necessary before initiation.

Information on switching patients to LIXIANA® from other treatments can be found on pages 10 to 13.

DOSE REDUCTION[5]

A dose of 30 mg once daily is required for certain patients who fall into one or more of the following subgroups.

These are:

MODERATE OR SEVERE RENAL IMPAIRMENT (CREATININE CLEARANCE [CRCL] 15–50 ML/MIN)

BODY WEIGHT ≤60 KG

CONCOMITANT USE OF THE P-GP INHIBITORS DRONEDARONE, CICLOSPORIN, ERYTHROMYCIN, KETOCONAZOLE

30 mg

Tablet actual size

In this case, patients should take one 30 mg tablet at the same time every day, with or without food.

MISSED DOSE[5]

If a patient misses a dose of LIXIANA® he/she should take it immediately and then continue the following day with the once-daily intake as recommended.

The patient should not take double the prescribed dose on the same day to make up for a missed dose.

SWITCHING TO AND FROM LIXIANA®

Switching patients to or from treatment with LIXIANA® is the same for both the VTE and NVAF indications. It should be noted that once a patient is switched to treatment with LIXIANA®, International Normalised Ratio (INR), prothrombin time (PT), or activated partial thromboplastin time (aPTT) are not useful measurements for anticoagulation effect.[5]

FROM NON-VKA ORAL ANTICOAGULANTS (NOAC) TO LIXIANA®[5]

Discontinue the NOAC and start LIXIANA® at the time of the next non-VKA dose.

FROM LIXIANA® TO NOAC[5]

Discontinue LIXIANA® and start the NOAC at the time of the next scheduled dose of LIXIANA®.

FROM VKA THERAPY TO LIXIANA®[5]

When converting patients from VKA therapy to LIXIANA®, discontinue warfarin or other VKA therapy and start LIXIANA® treatment when the INR is ≤2.5.

VKA, vitamin K antagonist

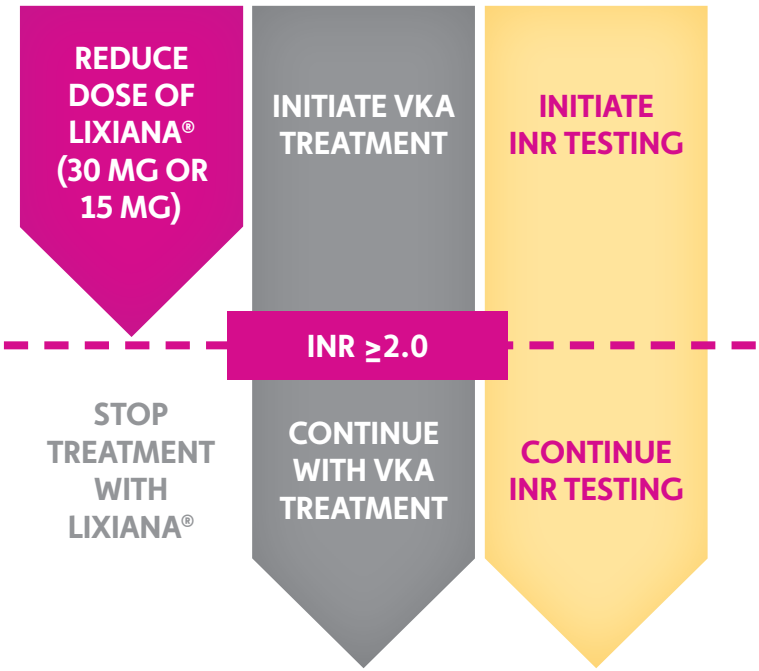
FROM LIXIANA® TO VKA THERAPY[5]

ORAL OPTION

For patients currently on a 60 mg dose, administer a LIXIANA® dose of 30 mg once daily together with an appropriate VKA dose. For patients currently on a 30 mg dose, administer a LIXIANA® dose of 15 mg once daily together with an appropriate VKA dose.

Patients should not take a loading dose of VKA in order to promptly achieve a stable INR between 2 and 3. It is recommended to take into account the maintenance dose of VKA and if the patient was previously taking a VKA or to use valid INR driven VKA treatment algorithm, in accordance with local practice.

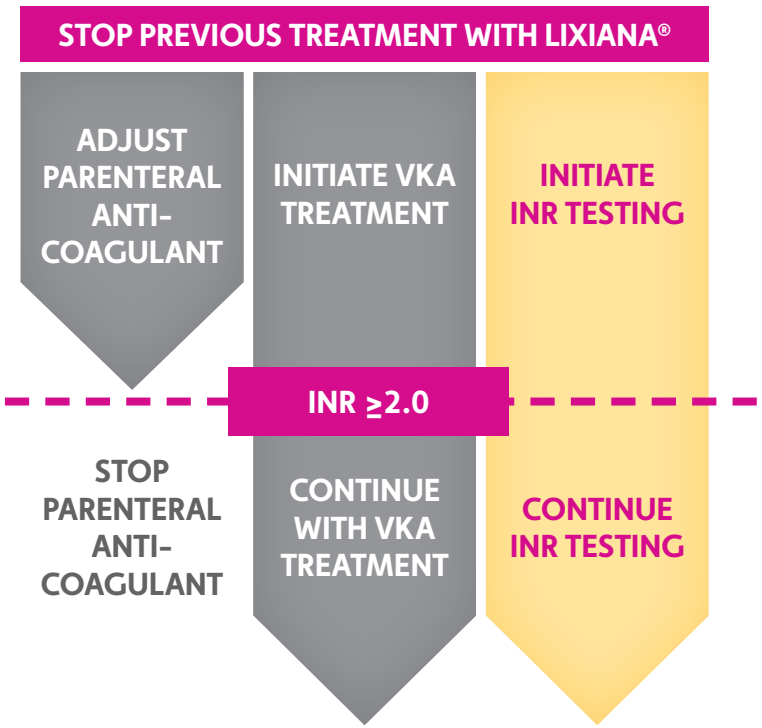
Once an INR ≥2.0 is achieved, LIXIANA® should be discontinued. Most patients (85%) should be able to achieve an INR ≥2.0 within 14 days of concomitant administration of LIXIANA® and VKA. After 14 days it is recommended that LIXIANA® is discontinued and the VKA continued to be titrated to achieve an INR between 2 and 3.



There is a potential for inadequate anticoagulation during the transition from LIXIANA® to VKA. Continuous adequate anticoagulation should be ensured during any transition to an alternate anticoagulant.

PARENTERAL ROUTE[5]

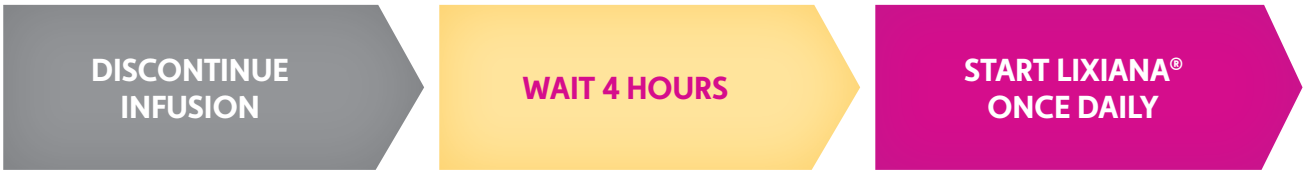
Discontinue LIXIANA® treatment and administer a parenteral anticoagulant and VKA treatment at the time of the next scheduled LIXIANA® dose. Once a stable INR of ≥2.0 is achieved, the parenteral anticoagulant should be discontinued and the VKA continued.



FROM PARENTERAL ANTICOAGULANT TO LIXIANA®[5]

LIXIANA® should not be administered simultaneously with a parenteral anticoagulant.

Patients on continuously administered parenteral drug such as intravenous (IV) unfractionated heparin:



Patients on subcutaneous anticoagulant (low molecular weight heparin (LMWH), e.g. fondaparinux):

FROM LIXIANA® TO PARENTERAL ANTICOAGULANT[5]

LIXIANA® should not be administered simultaneously with a parenteral anticoagulant.

Discontinue LIXIANA® and start the parenteral anticoagulant at the time of the next scheduled dose of LIXIANA®.

CONTRAINDICATIONS

As an anticoagulant, LIXIANA® may increase the risk of bleeding. Therefore, patients prescribed LIXIANA® should be carefully observed for signs of bleeding.[5]

LIXIANA® is contraindicated in the following patients:[5]
• Those with hypersensitivity to the active substance or to any of the excipients
• Those with clinically significant active bleeding
• Those with a lesion or condition at significant risk of major bleeding such as: – Current or recent gastrointestinal (GI) ulceration – Malignant neoplasms at high risk of bleeding – Recent brain or spinal injury or surgery – Recent ophthalmic surgery – Recent intracranial haemorrhage – Suspected or diagnosed oesophageal varices, arteriovenous malformations, vascular aneurysms or major intraspinal or intracerebral vascular abnormalities
• Those with hepatic disease associated with coagulopathy and clinically relevant bleeding risk
• Those on concomitant treatment with any other anticoagulants e.g. unfractionated heparin (UFH), low molecular weight heparin (enoxaparin, dalteparin, etc.), heparin derivatives (fondaparinux, etc.), oral anticoagulants (warfarin, dabigatran etexilate, rivaroxaban, apixaban, etc.) except under the circumstances of switching therapy to or from LIXIANA® or when UFH is given at doses necessary to maintain an open central venous or arterial catheter
• LIXIANA® is contraindicated during pregnancy and women of child-bearing potential should avoid becoming pregnant during treatment. As LIXIANA® is also contraindicated during breastfeeding, it should be decided whether to cease therapy or to discontinue breastfeeding
• Those with uncontrolled severe hypertension

SPECIAL PATIENT POPULATIONS

Several groups of patients are at increased risk of bleeding and should be carefully monitored for signs and symptoms of bleeding complications. Any treatment decision must be based on careful assessment of the treatment benefit against risk of bleeding.[5]

Prior to initiation of LIXIANA® and when clinically indicated, renal function testing (CrCl) should be performed

Patients with renal impairment[5]	
End stage renal disease: dialysis, renal failure (CrCl <15 ml/min)	Not recommended
Moderate or severe renal impairment (CrCl 15–50 ml/min)	Dose reduction to 30 mg once daily (OD) (see Dose reduction section on page 9)
Mild renal impairment (CrCl >50–80 ml/min)	No dose reduction required – 60 mg OD

Renal function in NVAF	
Patients with NVAF and high creatinine clearance	There is a trend towards decreasing efficacy with increasing creatinine clearance for edoxaban vs well-managed warfarin, therefore careful evaluation of thromboembolic and bleeding risk is necessary before initiation

Patients with hepatic impairment[5]	
Hepatic disease associated with coagulopathy and clinically relevant bleeding	Contraindicated
Mild or moderate hepatic impairment	No dose reduction required – 60 mg OD; use with caution
Severe hepatic impairment	Not recommended
Elevated liver enzymes ALT/AST >2x ULN or total bilirubin ≥1.5x ULN	Use with caution

Prior to initiation and during long term treatment (>1 year) with LIXIANA®, liver function testing should be performed.

Patients receiving concomitant treatment[5]	
P-gp inhibitors: dronedarone, ciclosporin, erythromycin, ketoconazole	Dose reduction to 30 mg OD (see Dose reduction section page 9)
Amiodarone, quinidine, or verapamil	No dose reduction required – 60 mg OD
P-gp inducers (e.g. rifampicin, phenytoin, carbamazepine, phenobarbitol or St Johns Wort)	Use with caution
P-gp substrates (digoxin)	No dose modification – 60 mg OD
Medication affecting haemostasis such as NSAIDs, aspirin/acetylsalicylic acid (ASA), or platelet aggregation inhibitors	Not recommended. LIXIANA® can be coadministered with low dose ASA (≤100 mg/day)
Chronic use of NSAIDs	Not recommended
Selective serotonin reuptake inhibitors (SSRIs)/Serotonin and norepinephrine reuptake inhibitors (SNRIs)	Possibility of increased risk of bleeding

TEMPORARY DISCONTINUATION[5]

Breaks in therapy should be avoided wherever possible. However, in an instance where a temporary discontinuation is unavoidable (e.g. before a surgical intervention or invasive procedure), LIXIANA® should be restarted as soon as possible.

PERIOPERATIVE MANAGEMENT[5]

In situations where a patient requires a surgical intervention or invasive procedure (including tooth extraction), **LIXIANA® should be stopped as soon as possible and preferably at least 24 hours beforehand**, and appropriate caution exercised due to the increased risk of thrombosis. The half-life of LIXIANA® is 10–14 hours. As LIXIANA® is a reversible Factor Xa inhibitor, its anticoagulant activity should lessen within 24–48 hours of the last administered dose.

In deciding whether a procedure should be delayed until 24 hours after the last dose of LIXIANA®, the increased risk of bleeding should be weighed against the urgency of the intervention. LIXIANA® should be restarted after the surgical or other procedures as soon as adequate haemostasis has been established, noting that the time to onset of the LIXIANA® anticoagulant therapeutic effect is 1–2 hours. If oral medicinal products cannot be taken during or after surgical intervention, consider administering a parenteral anticoagulant and then switch to oral once-daily LIXIANA®.

OVERDOSE[5]

Overdose with LIXIANA® may lead to haemorrhage. A specific antidote antagonising the pharmacodynamic effect of LIXIANA® is not available. Early administration of activated charcoal may be considered in case of LIXIANA® overdose to reduce absorption. This recommendation is based on standard treatment of drug overdose and data available with similar compounds, as the use of activated charcoal to reduce absorption of LIXIANA® has not been specifically studied in the LIXIANA® clinical programme.

MANAGEMENT OF BLEEDING COMPLICATIONS[5]

If bleeding complications are experienced, treatment should be delayed or discontinued, taking the half-life of LIXIANA® (10–14 hours) into account.

Management should be individualised according to the severity and location of the haemorrhage:

- Symptomatic treatment, such as mechanical compression, surgical intervention, fluid replacement and haemodynamic support, blood product or component transfusion
- For life-threatening bleeding that cannot be controlled with measures such as transfusion or haemostasis, the administration of a 4-factor prothrombin complex concentrate (PCC) at 50 IU/kg has been shown to reverse the effects of LIXIANA® 30 minutes after completing the infusion

Recombinant factor VIIa (r-FVIIa) can also be considered. However, there is limited clinical experience with the use of this product in individuals receiving LIXIANA®.

Haemodialysis does not significantly contribute to LIXIANA® clearance.

ROUTINE COAGULATION TESTING[5]

Treatment with LIXIANA® does not require routine clinical coagulation monitoring. As a result of Factor Xa inhibition, LIXIANA® prolongs standard clotting tests such as INR, prothrombin time (PT), or activated partial thromboplastin time (aPTT). Changes observed in these clotting tests at the expected therapeutic dose are small and subject to a high degree of variability. These tests are therefore not recommended to assess the pharmacodynamic effects of LIXIANA®.

There are no specific blood tests or assays available for LIXIANA®.

PATIENT ALERT CARD

EVERY PATIENT PRESCRIBED LIXIANA® WILL RECEIVE A PATIENT ALERT CARD IN THE PACK WITH THEIR TABLETS.

This will inform doctors, dentists, pharmacists and other healthcare professionals about the patient's anticoagulation treatment, along with emergency contact details. Encourage patients to carry this card with them at all times and to show it to healthcare professionals prior to any consultation or procedure.

Patients should be reminded of the importance of compliance to their treatment regimen, the need to watch for signs and symptoms of bleeding and when to seek medical advice.

Patient alert cards are available from
Medinfo@daiichi-sankyo.co.uk
or by calling 0800 028 5122

PRESCRIBING INFORMATION

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

Refer to the Lixiana Summary of Product Characteristics (SmPC) prior to prescribing

Presentation: 60 mg (yellow) / 30 mg (pink) / 15 mg (orange) edoxaban (as tosilate) film-coated tablets. **Indications:** Prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation (NVAF) with one or more risk factors, such as congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, prior stroke or transient ischaemic attack (TIA). 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:* Recommended dose is 60 mg edoxaban once daily with or without food. Continue therapy long term. *VTE:* Recommended dose is 60 mg edoxaban once daily with or without food following initial use of parenteral anticoagulant for at least 5 days. 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: moderate or severe renal impairment (creatinine clearance (CrCL) 15 - 50 mL/min); low body weight ≤ 60 kg; concomitant use of the P-glycoprotein (P-gp) inhibitors, ciclosporin, dronedarone, erythromycin, or ketoconazole. The 15 mg dose of edoxaban is not indicated as monotherapy, and should only be used during a switch from edoxaban to VKA in certain patients (see SmPC for full details). Edoxaban can be initiated or continued in patients who may require cardioversion. For transoesophageal echocardiogram guided cardioversion in patients not previously treated with anticoagulants, edoxaban should be started at least 2 hours before cardioversion to ensure adequate anticoagulation. Cardioversion should be performed no later than 12 hours after the dose of edoxaban on the day of the procedure. Confirm prior to cardioversion that the patient has taken edoxaban as prescribed. 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 including 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 DOACs 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:* Caution in patients with increased risk of bleeding such as elderly on ASA. Discontinue 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:* CrCl should be monitored at the 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 CrCl was observed for edoxaban compared to well-managed warfarin. Edoxaban should only be used in patients with NVAF and high CrCl after a careful benefit risk evaluation. *Hepatic impairment:* Not recommended in severe hepatic impairment. Caution in mild or moderate hepatic impairment. Caution in patients with elevated liver enzymes (ALT/AST > 2 x ULN) or total bilirubin ≥ 1.5 x ULN. Perform liver function testing prior to initiation and then periodically monitor for treatment beyond 1 year. *Surgery or other interventions:* discontinue edoxaban as soon as possible and preferably at least 24 hours before the procedure. If procedure cannot be delayed, the increased risk of bleeding should be weighed against urgency of the procedure. Restart edoxaban as soon as haemostasis 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 in treatment and/or prevention of VTE. *Patients with a history of thrombosis diagnosed with antiphospholipid syndrome:* DOACs including edoxaban are not recommended. **Drug interactions:** Concomitant use of the *P-gp inhibitors* ciclosporin, dronedarone, erythromycin, or ketoconazole requires edoxaban dose reduction to 30 mg. Edoxaban should be used with caution with concomitant *P-gp inducers* (e.g. rifampicin, phenytoin, carbamazepine, phenobarbital, St John's Wort). Concomitant high dose ASA (325 mg) or chronic NSAIDs is not recommended. Concomitant ASA at doses > 100 mg and < 325 mg should be under medical supervision only. Very limited experience with dual antiplatelet therapy or fibrinolytics. Possibility of increased bleeding risk with concomitant SSRIs or SNRIs. **Adverse reactions:** *Common:* anaemia, dizziness, headache, epistaxis, abdominal pain, 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. *Serious uncommon:* thrombocytopaenia, hypersensitivity, intracranial haemorrhage (ICH), intraocular haemorrhage, other haemorrhage, haemoptysis, surgical site haemorrhage. *Serious rare:* anaphylactic reaction, allergic oedema, subarachnoid haemorrhage, pericardial haemorrhage, retroperitoneal haemorrhage, intramuscular haemorrhage (no compartment syndrome), intra-articular haemorrhage, subdural haemorrhage, procedural haemorrhage. **Legal classification:** POM. **Package quantities, marketing authorisation (MA) numbers and basic NHS costs:** 60 mg – 28 tablets – EU/1/15/993/018 - £49.00. 30 mg – 28 tablets – EU/1/15/993/005 - £49.00. 15 mg – 10 tablets - EU/1/15/993/001 - £17.50. **MA holder:** Daiichi Sankyo Europe GmbH, Zielstattstrasse 48, 81379 Munich, Germany.

Date of preparation of Prescribing Information: May 2019 EDX/19/0141

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 Pharmacovigilance on 0800 028 5122, pharmacovigilance@daiichi-sankyo.co.uk

References:

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Date of preparation: August 2019.
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Lixiana® edoxaban