

LIXIANA FILM-COATED TABLETS

Edoxaban (15, 30 and 60 mg)

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1. What Lixiana is used for

Lixiana is used in adults to:

- prevent blood clots in the brain (stroke) and other blood vessels in the body if you have a form of irregular heart rhythm called nonvalvular atrial fibrillation and at least one additional risk factor such as congestive heart failure, high blood pressure; treat blood clots in the veins of the legs (deep vein thrombosis) and in the blood vessels in the lungs (pulmonary embolism), and to prevent blood clots from re-occurring in the blood vessels in the legs and/or lungs.

2. How Lixiana works

Lixiana contains the active substance edoxaban and belongs to a group of medicines called anticoagulants. This medicine helps to prevent blood clots from forming. It works by blocking the activity of factor Xa, which is an important component of blood clotting.

3. Before you use Lixiana

- When you must not use it

- if you are allergic to edoxaban or any of the other ingredients of this medicine. (listed in section Ingredients);
- if you are actively bleeding
- if you have a disease or condition that increases the risk of serious bleeding (e.g. stomach ulcer, injury or bleeding in the brain, or recent surgery of the brain or eyes)
- if you are taking other medicines to prevent blood clotting (e.g. warfarin, dabigatran, rivaroxaban, apixaban or heparin), except when

changing anticoagulant treatment or while getting heparin through a venous or arterial line to keep it open

- if you have a liver disease which leads to an increased risk of bleeding
- if you have uncontrolled high blood pressure
- if you are pregnant or breast feeding

- Before you start to use it

Talk to your doctor or pharmacist before taking Lixiana,

- if you have an increased risk of bleeding, as could be the case if you have any of the following conditions:
 - endstage kidney disease or if you are on dialysis
 - severe liver disease
 - bleeding disorders
 - a problem with the blood vessels in the back of your eyes (retinopathy)
 - recent bleeding in your brain (intracranial or intracerebral bleeding)
 - problems with the blood vessels in your brain or spinal column
- if you have a mechanical heart valve

Lixiana 15 mg is only to be used when changing from Lixiana 30 mg to a vitamin K antagonist (e.g. warfarin) (see section 4. How to take Lixiana).

Take special care with Lixiana

- if you know that you have a disease called antiphospholipid syndrome (a disorder of the immune system that causes an increased risk of blood clots), tell your doctor who will decide if the treatment may need to be changed.

If you need to have an operation

- it is very important to take Lixiana before and after the operation exactly at the times you have been told by your

doctor. If possible, Lixiana should be stopped at least 24 hours before an operation. Your doctor will determine when to restart Lixiana.

In emergency situations your physician will help determine the appropriate actions regarding Lixiana.

- Taking other medicines

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

If you are taking any of the following:

- some medicines for fungal infections (e.g. ketoconazole)
- medicines to treat abnormal heart beat (e.g. dronedarone, quinidine, verapamil)
- other medicines to reduce blood clotting (e.g. heparin, clopidogrel or vitamin K antagonists such as warfarin, acenocoumarol, phenprocoumon or dabigatran, rivaroxaban, apixaban)
- antibiotic medicines (e.g. erythromycin, clarithromycin)
- medicines to prevent organ rejection after transplantation (e.g. ciclosporin)
- anti-inflammatory and pain-relieving medicines (e.g. naproxen or acetylsalicylic acid)
- antidepressant medicines called selective serotonin reuptake inhibitors or serotonin-norepinephrine reuptake inhibitors

If any of the above apply to you, tell your doctor before taking Lixiana, because these medicines may increase the effects of Lixiana and the chance of unwanted bleeding. Your doctor will decide, if you should be treated with Lixiana and if you should be kept under observation.

If you are taking any of the following:

- some medicines for treatment of epilepsy (e.g. phenytoin, carbamazepine, phenobarbital)

- St John's Wort, a herbal product used for anxiety and mild depression
- rifampicin, an antibiotic medicine.

If any of the above apply to you, tell your doctor before taking Lixiana, because the effect of Lixiana may be reduced. Your doctor will decide if you should be treated with Lixiana and if you should be kept under observation.

4. How to use Lixiana

- How much to use

The recommended dose is one **60 mg** tablet once daily. Swallow the tablet, preferably with water.

Lixiana can be taken with or without food.

If you have difficulty swallowing the tablet whole, talk to your doctor about other ways to take Lixiana. The tablet may be crushed and mixed with water or apple puree immediately before you take it. If necessary, your doctor may also give you the crushed Lixiana tablet through a stomach tube.

- If you have impaired kidney function, the dose may be reduced to one 30 mg tablet once daily by your doctor.

- If your body weight is 60 kg or lower, the recommended dose is one 30 mg tablet once daily.

- If your doctor has prescribed medicines known as P-gp inhibitors: ciclosporin, dronedarone, erythromycin, or ketoconazole, the recommended dose is one 30 mg tablet once daily.

- When to use it

Your doctor may change your anticoagulant treatment as follows:

Changing from vitamin K antagonists (e.g. warfarin) to Lixiana

Stop taking the vitamin K antagonist (e.g. warfarin). Your doctor will need to do blood measurements and will instruct you when to start taking Lixiana.

Changing from non-VKA oral anticoagulants (dabigatran, rivaroxaban, or apixaban) to Lixiana

Stop taking the previous medicines (e.g. dabigatran, rivaroxaban, or

apixaban) and start Lixiana at the time of the next scheduled dose.

Changing from parenteral anticoagulants (e.g. heparin) to Lixiana

Stop taking the anticoagulant (e.g. heparin) and start Lixiana at the time of the next scheduled anticoagulant dose.

Changing from Lixiana to vitamin K antagonists (e.g. warfarin)

If you currently take 60 mg Lixiana: Your doctor will tell you to reduce your dose of Lixiana to a 30 mg tablet once daily and to take it together with a vitamin K antagonist (e.g. warfarin). Your doctor will need to do blood measurements and will instruct you when to stop taking Lixiana.

If you currently take 30 mg (dose reduced) Lixiana:

Your doctor will tell you to reduce your dose of Lixiana to a 15 mg tablet once daily and to take it together with a vitamin K antagonist (e.g. warfarin). Your doctor will need to do blood measurements and will instruct you when to stop taking Lixiana.

Changing from Lixiana to non VKA oral anticoagulants (dabigatran, rivaroxaban, or apixaban)

Stop taking Lixiana and start the non VKA anticoagulant (e.g. dabigatran, rivaroxaban, or apixaban) at the time of the next scheduled dose of Lixiana.

Changing from Lixiana to parenteral anticoagulants (e.g. heparin)

Stop taking Lixiana and start the parenteral anticoagulant (e.g. heparin) at the time of the next scheduled dose of Lixiana.

Patients undergoing cardioversion: If your abnormal heartbeat needs to be restored to normal by a procedure called cardioversion, take Lixiana at the times your doctor tells you to prevent blood clots in the brain and other blood vessels in your body.

- How long to use it

Continue taking Lixiana for as long as your doctor recommends. If you have any further questions

on the use of this medicine, ask your doctor or pharmacist.

- If you forget to use it

You should take the tablet immediately and then continue the following day with the once daily tablet as usual. Do not take a double dose on the same day to make up for a forgotten dose.

-If you use too much (overdose)

Tell your doctor immediately if you have taken too many Lixiana tablets. If you take more Lixiana than recommended, you may have an increased risk of bleeding.

5. While you are using it

-Things you must do

Always take this medicine exactly as your doctor or pharmacist has told you.

-Things you must not do

Do not stop taking Lixiana without talking to your doctor first, because Lixiana treats and prevents serious conditions.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist

-Things to be careful of Children and adolescents

Lixiana is not recommended in children and adolescents under 18 years of age. There is no information on its use in children and adolescents.

Pregnancy and breast-feeding

Do not take Lixiana if you are pregnant or breast-feeding. If there is a chance that you could become pregnant, use a reliable contraceptive while you are taking Lixiana. If you become pregnant while you are taking Lixiana, immediately tell your doctor, who will decide how you should be treated.

Driving and using machines

Lixiana has no or negligible effects on your ability to drive or use machines.

6. Side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Like other similar medicines (medicines to reduce blood clotting), Lixiana may

cause bleeding which may potentially be life-threatening. In some cases the bleeding may not be obvious.

If you experience any bleeding event that does not stop by itself or if you experience signs of excessive bleeding (exceptional weakness, tiredness, paleness, dizziness, headache or unexplained swelling) consult your doctor immediately.

Your doctor may decide to keep you under closer observation or change your medicine.

Overall list of possible side effects:

Common (may affect up to 1 in 10 people):

- stomach ache;
- abnormal liver blood tests;
- bleeding from the skin or under the skin;
- anaemia (low levels of red blood cells);
- bleeding from the nose;
- bleeding from the vagina;
- rash;
- bleeding in the bowel;
- bleeding from the mouth and/or throat;
- blood found in your urine;
- bleeding following an injury (puncture);
- bleeding in the stomach;
- dizziness;
- feeling sick;
- headache;
- itching.

Uncommon (may affect up to 1 in 100 people):

- bleeding in the eyes;
- bleeding from a surgical wound following an operation;
- blood in the spit when coughing;
- bleeding in the brain;
- other types of bleeding;
- reduced number of platelets in your blood (which can affect clotting);
- allergic reaction;
- hives.

Rare (may affect up to 1 in 1,000 people):

- bleeding in the muscles;
- bleeding in joints;
- bleeding in the abdomen;
- bleeding in the heart;
- bleeding inside the skull;

- bleeding following; a surgical procedure;
- allergic shock;
- swelling of any part of the body due to allergic reaction.

You may report any side effects or adverse drug reactions directly to the National Centre for Adverse Drug Reaction Monitoring by visiting the website npra.gov.my [Consumers → Reporting Side Effects to Medicines (ConSERF) or Vaccines (AEFI)].

7. Storage and Disposal of Lixiana

-Storage

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and on each blister after EXP. The expiry date refers to the last day of that month.

This medicine does not require any special storage conditions.

-Disposal

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

8. Product Description

- What it looks like

Lixiana 15 mg film-coated tablets are orange, round-shaped (6.7 mm diameter) and debossed with "DSC L15" on one side. They come in PVC/Aluminium blisters of 14 film-coated tablets. Each carton contains 28 film-coated tablets.

Lixiana 30 mg film-coated tablets are pink, round-shaped (8.5 mm diameter) and debossed with "DSC L30" on one side. They come in PVC/Aluminium blisters of 14 film-coated tablets. Each carton contains 28 film-coated tablets.

Lixiana 60 mg film-coated tablets are yellow, round-shaped (10.5 mm diameter) and debossed with "DSC L60" on one side. They come in PVC/Aluminium blisters of 14 film-coated tablets. Each carton contains 28 film-coated tablets.

-Ingredients

-Active ingredient(s)
-The active substance is edoxaban (as tosilate).

Lixiana 15 mg film-coated tablets

Each tablet contains 15 mg edoxaban (as tosilate).

Lixiana 30 mg film-coated tablets

Each tablet contains 30 mg edoxaban (as tosilate).

Lixiana 60 mg film-coated tablets

Each tablet contains 60 mg edoxaban (as tosilate).

-Inactive ingredients

Lixiana 15 mg film-coated tablets

Tablet core: mannitol (E421), pregelatinised starch, croscopovidone (E1202), hydroxypropyl cellulose (E463), magnesium stearate (E470b).

Film coat: hypromellose (E464), macrogol (8000), titanium dioxide (E171), talc (E553b), carnauba wax, iron oxide red (E172), iron oxide yellow (E172).

Lixiana 30 mg film-coated tablets

Tablet core: mannitol (E421), pregelatinised starch, croscopovidone (E1202), hydroxypropyl cellulose (E463), magnesium stearate (E470b).

Film coat: hypromellose (E464), macrogol (8000), titanium dioxide (E171), talc (E553b), carnauba wax, iron oxide red (E172).

Lixiana 60 mg film-coated tablets:

Tablet core: mannitol (E421), pregelatinised starch, croscopovidone (E1202), hydroxypropyl cellulose (E463), magnesium stearate (E470b).

Film coat: hypromellose (E464), macrogol (8000), titanium dioxide (E171), talc (E553b), carnauba wax, iron oxide yellow (E172).

- MAL number:

Lixiana 15 mg film-coated tablets
MAL21026001ARZ

Lixiana 30 mg film-coated tablets
MAL21026002ARZ

Lixiana 60 mg film-coated tablets
MAL21026003ARZ

9. Manufacturer

Daiichi Sankyo Europe GmbH
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Product Registration Holder

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10.Date of revision

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