PATIENT INFORMATION LEAFLET

WARNING: (A) PREMATURE DISCONTINUATION OF IXAROLA INCREASES THE RISK OF THROMBOTIC EVENTS, (B) SPINAL/EPIDURAL HAEMATOMA

A. Premature discontinuation of IXAROLA increases the risk of thrombotic events:
Premature discontinuation of any oral anticoagulant, including IXAROLA, increases the risk of thrombotic events. If anticoagulation with IXAROLA is discontinued for a reason other than pathological bleeding or completion of a course of therapy, consider coverage with another anticoagulant.

B. Spinal/epidural haematoma:
Epidural or spinal haematomas have occurred in patients treated with IXAROLA who are receiving neuraxial anaesthesia or undergoing spinal puncture. These haematomas may result in long-term or permanent paralysis.
Consider these risks when scheduling patients for spinal procedures.
Factors that can increase the risk of developing epidural or spinal haematomas in these patients include:
• Use of indwelling epidural catheters
• Concomitant use of other drugs that affect haemostasis, such as nonsteroidal anti-inflammatory drugs (NSAIDs), platelet inhibitors, other anticoagulants
• History of traumatic or repeated epidural or spinal punctures
• History of spinal deformity or spinal surgery
• Optimal timing between the administration of IXAROLA and neuraxial procedures is not known
Monitor patients frequently for signs and symptoms of neurological impairment. If neurological compromise is noted, urgent treatment is necessary.
Consider the benefits and risks before neuraxial intervention in patients anticoagulated or to be anticoagulated for thromboprophylaxis.

SCHEDULING STATUS: S4

IXAROLA® 10 Film-coated tablets
Rivaroxaban
Contains sugar (lactose)

Read all of this leaflet carefully because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist, nurse or other health care provider.
- IXAROLA 10 has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. WHAT IXAROLA 10 IS AND WHAT IT IS USED FOR

IXAROLA 10 is used to prevent blood clots in your veins after a major operation on your legs. For example this could be an operation on your hip or knee. Your doctor has prescribed IXAROLA 10 for you because after an operation you are at an increased risk of getting blood clots.

IXAROLA 10 treat blood clots in the veins of your legs (deep vein thrombosis) and in the blood vessels of your lungs (pulmonary embolism), and to prevent blood clots from re-occurring in the blood vessels of your legs and/or lungs.

The active substance rivaroxaban belongs to a group of medicines called antithrombotic agents. It works by blocking a blood clotting factor (factor Xa) and thus reducing the tendency of the blood to form clots.

2. WHAT YOU NEED TO KNOW BEFORE YOU USE IXAROLA 10

Do not take IXAROLA 10

- **if you are allergic** to rivaroxaban or any of the other ingredients of this medicine (listed in section 6)
- **if you are bleeding excessively**
- **if you have a disease or condition in an organ of the body that increases the risk of serious bleeding (e.g. stomach ulcer, injury or bleeding in the brain, recent surgery of the brain or eyes)**
- if you are taking medicines to prevent blood clotting (e.g. warfarin, dabigatran, 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 are pregnant or breast-feeding**

Do not take IXAROLA 10 and tell your doctor if any of these apply to you.

Warnings and precautions

Talk to your doctor or pharmacist before taking IXAROLA 10.

IXAROLA 10 should not be used in combination with certain other medicines which reduce blood clotting such as prasugrel or ticagrelor other than acetylsalicylic acid and clopidogrel/ticlopidine.

Take special care with IXAROLA

- if you have an increased risk of bleeding, as could be the case in situations such as:

- moderate or severe kidney disease, since your kidney function may affect the amount of medicine that works in your body
- if you are taking other medicines to prevent blood clotting (e.g. warfarin, dabigatran, apixaban or heparin), when changing anticoagulant treatment or while getting heparin through a venous or arterial line to keep it open (see section "Other medicines and IXAROLA")
- bleeding disorders
- very high blood pressure, not controlled by medical treatment
- diseases of your stomach or bowel that might result in bleeding, e.g. inflammation of the bowels or stomach, or inflammation of the oesophagus (gullet), e.g. due to gastroesophageal reflux disease (disease where stomach acid goes upwards into the oesophagus)
- a problem with the blood vessels in the back of your eyes (retinopathy)
- a lung disease where your bronchi are widened and filled with pus (bronchiectasis), or previous bleeding from your lung

- if you have a prosthetic heart valve
- 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 your doctor determines that your blood pressure is unstable or another treatment or surgical procedure to remove the blood clot from your lungs is planned.

If any of the above apply to you, tell your doctor before you take IXAROLA. Your doctor will decide, if you should be treated with this medicine and if you should be kept under closer observation.

If you need to have an operation

- it is very important to take IXAROLA before and after the operation exactly at the times you have been told by your doctor.
- if your operation involves a catheter or injection into your spinal column (e.g. for epidural or spinal anaesthesia or pain reduction):
  - it is very important to take IXAROLA exactly at the times you have been told by your doctor
  - tell your doctor immediately if you get numbness or weakness of your legs or problems with your bowel or bladder after the end of anaesthesia, because urgent care is necessary.

Children and adolescents
IXAROLA 10 is **not recommended for people under 18 years of age.** There is not enough information on its use in children and adolescents.

Other medicines and IXAROLA 10
Always tell your health care provider if you are taking any other medicines. This includes complementary or traditional medicines.

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription.

- **If you are taking**
  - some medicines for fungal infections (e.g. fluconazole, itraconazole, voriconazole, posaconazole), unless they are only applied to the skin
  - ketoconazole tablets (used to treat Cushing's syndrome - when the body produces an excess of cortisol)
  - some medicines for bacterial infections (e.g. clarithromycin, erythromycin)
  - some anti-viral medicines for HIV / AIDS (e.g. ritonavir)
  - other medicines to reduce blood clotting (e.g. enoxaparin, clopidogrel or vitamin K antagonists such as warfarin and acenocoumarol)
  - anti-inflammatory and pain relieving medicines (e.g. naproxen or acetylsalicylic acid)
  - dronedarone, a medicine to treat abnormal heart beat
  - some medicines to treat depression (selective serotonin reuptake inhibitors (SSRIs) or serotonin norepinephrine reuptake inhibitors (SNRIs))

If any of the above apply to you, tell your doctor before taking IXAROLA, because the effect of IXAROLA may be increased. Your doctor will decide, if you should be treated with this medicine and if you should be kept under closer observation.
If your doctor thinks that you are at increased risk of developing stomach or bowel ulcers, he may also use a preventative ulcer treatment.

- **If you are taking**
- some medicines for treatment of epilepsy (phenytoin, carbamazepine, phenobarbital)
- St John's Wort (*Hypericum perforatum*), a herbal product used for depression
- rifampicin, an antibiotic

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

Pregnancy and Breastfeeding

Do not take IXAROLA 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 IXAROLA. If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other healthcare provider for advice before taking this medicine.

Driving and using machines
IXAROLA may cause side effects such as dizziness or fainting (see "Possible side effects"). You should not drive or use machines if you are affected by these symptoms.

Information about some of the ingredients
Patients with rare hereditary conditions of lactose/fructose or galactose intolerance should not take IXAROLA.
IXAROLA tablets contains less than 1 mmol (23 mg) sodium per dose, that is to say essentially 'sodium-free'.

3. How to take IXAROLA 10
Do not share medicines prescribed for you with others.
Always take IXAROLA 10 exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

How much to take
The usual dose is one IXAROLA 10 tablet (10 mg) once a day.
Swallow the tablet preferably with water.
IXAROLA 10 tablet can be taken with or without food.

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

When to take IXAROLA 10
Take the first tablet 6 - 10 hours after your operation.
Then take a tablet every day until your doctor tells you to stop.
Try to take the tablet at the same time every day to help you to remember it.
If you have had a major hip operation you will usually take the tablets for 5 weeks.
If you have had a major knee operation you will usually take the tablets for 2 weeks.

Children and adolescents up to 18 years of age
Don't give IXAROLA 10 tablets to people under 18 years of age. There is not enough information on its use in children and adolescents.

If you take more IXAROLA 10 than you should
Contact your doctor immediately if you have taken too many IXAROLA 10 tablets. Taking too much IXAROLA 10 increases the risk of bleeding.
Please consult your doctor or pharmacist in the case of accidental overdose. If neither is available, rush the patient to the nearest hospital or poison control center.

If you forget to take IXAROLA 10
If you have missed a dose, take it as soon as you remember. Take the next tablet on the following day and then carry on taking a tablet once a day as normal.
Do not take a double dose to make up for a forgotten tablet.

If you stop taking IXAROLA 10
Don't stop taking IXAROLA 10 without talking to your doctor first, because IXAROLA 10 prevents the development of a serious condition.
If you have any further questions on the use of IXAROLA 10, ask your doctor or pharmacist.

4. POSSIBLE SIDE-EFFECTS
IXAROLA 10 can have side effects.

Not all side-effects reported for IXAROLA 10 are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking IXAROLA 10, please consult your doctor, pharmacist or other healthcare professional for advice.

Like other similar medicines (antithrombotic agents), IXAROLA 10 may cause bleedings which may potentially be life threatening. Excessive bleeding may lead to a sudden drop in blood pressure (shock). In some cases these bleedings may not be obvious.

Tell your doctor, if you experience any of the following side-effects**:**

- **long or excessive bleeding**
- **exceptional weakness, tiredness, paleness, dizziness, headache, unexplained swelling, breathlessness, chest pain or angina pectoris, which may be signs of bleeding.**

Your doctor may decide to keep you under closer observation or change how you should be treated.

Possible side effects which may be a sign of severe allergic reactions

Tell your doctor immediately if you experience any of the following side effects:
- long or excessive bleeding
- exceptional weakness, tiredness, paleness, dizziness, headache, unexplained swelling, breathlessness, unexplained shock and chest pain (angina pectoris)

The following side-effects have been reported for IXAROLA 10:

Frequent
- bleeding in the stomach or bowel, blood in the urine (urogenital bleeding), heavy periods (menstrual bleeding), nose bleeds, bleeding of the gum
- bleeding in the eye (including bleeding from the whites of the eyes)
- bleeding in tissue (bruising) or deep in (a cavity of) the body (hematoma)-
- bleeding following an operation
- swelling in the limbs
- pain in the limbs
- increase in body temperature (fever)
- pale skin, weakness and breathlessness due to a reduction in red blood cells (anaemia)
- stomach ache, indigestion, feeling or being sick, constipation, diarrhoea
- impaired function of the kidneys (may be seen in tests performed by your doctor)
- low blood pressure (symptoms may be feeling dizzy or fainting when standing up (hypotension))
- weakness, tiredness, headache, dizziness
- rash, itchy skin
- blood tests may show an increase in some liver enzymes
- coughing up blood

Less frequent

- bleeding in the brain or inside the skull
- bleeding in a joint causing pain and swelling
- oozing of blood or fluid from surgical wound
- feeling unwell
- dry mouth
- allergic reactions, including allergic skin reactions
- itchy, raised rash (hives)
- impaired function of the liver (may be seen in tests performed by your doctor)
- blood tests may show an increase in bilirubin, some pancreatic or liver enzymes or in the number of platelets
- raised heartbeat
- fainting
- bleeding in the muscle
- collection of blood (hematoma) following complication in a cardiac procedure where a catheter is inserted to treat narrowed coronary arteries (pseudoaneurysm)

- swelling in a particular area
- yellowing of the skin and eyes (jaundice)

Not known: frequency cannot be estimated from the available data

- increased pressure within muscles of the legs or arms after a bleeding, which leads to pain, swelling, altered sensation, numbness or paralysis (compartment syndrome)
- decrease in urine, swelling in limbs, shortness of breath and fatigue after a severe bleeding (kidney failure)

The following side effects have been reported since authorisation:

- allergic reaction causing swelling of the face, lips, mouth, tongue or throat (angioedema and allergic oedema)
- diarrhoea, trapped gas, stomach cramp, weight loss caused by blocked bile flow (cholestasis), swollen or tender in right side of abdomen, inflamed liver including liver injury (hepatitis)
- low number of platelets, which are cells that help blood to clot (thrombocytopenia)

Reporting of side effects
If you get side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects to SAHPRA via the "6.04 Adverse Drug Reaction Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of IXAROLA 10.

5. HOW TO STORE IXAROLA 10

Store at or below 30 °C. Keep blister strips in the original carton until use.
Do not use IXAROLA 10 after the expiry date which is stated on the carton and on each blister.
Return all unused medicine to your pharmacist.
Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).
Store all medicines out of the reach of children.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What IXAROLA 10 contains
The active substance is rivaroxaban. Each tablet contains 10 mg of rivaroxaban. Contains lactose.
The other ingredients are:
Tablet core: cellulose microcrystalline, croscarmellose sodium, hydroxypropylmethylcellulose 2910, lactose monohydrate, magnesium stearate, sodium laurylsulfate,
Film coat: ferric oxide red, hydroxypropylmethylcellulose 2910, polyethylene glycol, titanium dioxide.

What IXAROLA 10 looks like and contents of the pack
IXAROLA 10 film-coated tablets are light red, round, biconvex tablets, 6 mm in diameter, debossed with "Triangle 10" on the top side and the BAYER-cross on the bottom side of the tablet.

IXAROLA 10 film-coated tablets are packed in colourless, transparent PP (polypropylene)/aluminium blister strips or colourless, transparent PVC/PVDC/aluminium blister strips containing 5 or 10 tablets per blister. Pack sizes: 5 tablets (1 x 5's blister), 10 tablets (1 x 10's blister), 30 tablets (3 x 10's blister) or 100 tablets (10 x 10's blister).
Not all pack sizes may be marketed.

Holder of certificate of registration

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