1.3.2 PATIENT INFORMATION LEAFLET

Scheduling status

S4

NEBIVOPEN 10, film-coated tablets

Rivaroxaban

Contains sugar: 95,6 mg lactose monohydrate per tablet

Read all of this leaflet carefully before you start taking NEBIVOPEN 10

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- NEBIVOPEN 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 NEBIVOPEN 10 is and what it is used for

The active substance is rivaroxaban. It belongs to a group of medicines called antithrombotic medicines. It works by inhibiting blood clotting Factor Xa and thus reducing the tendency of the blood to form clots.

After an operation you are at an increased risk of getting blood clots. NEBIVOPEN 10 may be given to you to prevent blood clots in the veins after an operation on your lower limbs (such as a hip or knee replacement operation).

NEBIVOPEN 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.

2. What you need to know before you take NEBIVOPEN 10

Do not take NEBIVOPEN 10:

- if you are hypersensitive (allergic) to rivaroxaban or any of the other ingredients of NEBIVOPEN 10 (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 (such as stomach ulcer, injury or bleeding in the brain, recent surgery of the brain or eyes)
- if you are taking medicines to prevent blood clotting (some examples are warfarin, dabigatran, apixaban or heparin), except when changing anticoagulant treatment or while getting heparin through a venous or arterial line to keep it open (see Taking other medicines with NEBIVOPEN)
- if you have a liver disease which leads to an increased risk of bleeding
- if you are pregnant or breastfeeding your baby (see Pregnancy and breastfeeding).

Warnings and precautions

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

A. Premature discontinuation of NEBIVOPEN increase the risk of thrombotic events:

Premature discontinuation of any oral anticoagulant, including NEBIVOPEN, increases the risk of thrombotic events. If anticoagulation with NEBIVOPEN 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 hematomas have occurred in patients treated with NEBIVOPEN 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 medicines 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 NEBIVOPEN 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.

Talk to your doctor or pharmacist before taking NEBIVOPEN 10.

NEBIVOPEN 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 NEBIVOPEN 10:

- if you have an increased risk of bleeding, such as:
  - bleeding disorders
  - very high blood pressure, not controlled by medical treatment
  - active ulcer or recent ulcer of your stomach or bowel
  - 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
  - recent bleeding in your brain (intracranial or intracerebral bleeding)
  - recent operation on your brain, spinal column or eye
- 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 Taking other medicines with NEBIVOPEN 10)
- 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)

- 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 NEBIVOPEN. Your doctor will decide, if you should be treated with NEBIVOPEN and if you should be kept under closer observation.

If you need to have an operation:

- it is very important to take NEBIVOPEN 10 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 NEBIVOPEN 10 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

NEBIVOPEN 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 NEBIVOPEN 10

Always tell your health care provider if you are taking any other medicine (this includes complementary or traditional medicines).

The following medicines may increase the effect of NEBIVOPEN 10:

- some medicines for fungal infections (e.g. fluconazole, ketoconazole, itraconazole, voriconazole, posaconazole), unless they are only applied to the skin
- 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 heartbeat
- some medicines to treat depression (selective serotonin reuptake inhibitors (SSRIs) or serotonin norepinephrine reuptake inhibitors (SNRIs)).

Tell your doctor before taking NEBIVOPEN 10, if you take the following, because the effect of NEBIVOPEN 10 may be reduced:

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

NEBIVOPEN 10 with food and drink

NEBIVOPEN 10 must be taken with food.

Pregnancy and breastfeeding

Do not take NEBIVOPEN 10 if you are pregnant or breastfeeding. If there is a chance that you could become pregnant, use a reliable contraceptive while you are taking NEBIVOPEN 10. If you become pregnant while you are taking NEBIVOPEN 10, tell your doctor immediately. He/she will then decide how you should be treated.

If you are pregnant or breastfeeding your baby please consult your doctor, pharmacist or other health care provider for advice before taking NEBIVOPEN 10.

Driving and using machines

NEBIVOPEN may cause dizziness or fainting (see POSSIBLE SIDE EFFECTS). You should not drive or use machines if you are affected by these symptoms, as it could interfere with your ability to drive safely.

Important information about some of the ingredients of NEBIVOPEN 10

NEBIVOPEN 10 contains lactose monohydrate. If you have been told by your doctor that you have intolerance to some sugars contact your doctor before taking NEBIVOPEN 10.

3. How to take NEBIVOPEN 10

Do not share medicines prescribed for you with any other person.

Always take NEBIVOPEN 10 exactly as your doctor has instructed you. Check with your doctor or pharmacist if you are unsure.

The usual dose is one NEBIVOPEN 10 tablet (10 mg) once a day.

Swallow the tablet preferably with water.

Try to take the tablet at the same time every day until your doctor tells you to stop.

NEBIVOPEN 10 may be taken with or without food.

Talk to your doctor about other ways to take NEBIVOPEN if you have difficulty swallowing the tablet whole. 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 NEBIVOPEN tablet through a stomach tube.

When to take NEBIVOPEN

Take the first tablet 6 - 10 hours after your operation.

Your doctor will tell you how long your treatment with NEBIVOPEN 10 will last.

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.

If you have the impression that the effect of NEBIVOPEN 10 is too strong or too weak, tell your doctor or pharmacist.

If you take more NEBIVOPEN 10 than you should

In the event of over-dosage, consult your doctor or pharmacist immediately. If neither is available, contact the nearest hospital or poison control centre.

Taking too much NEBIVOPEN 10 increases the risk of bleeding.

If you forget to take NEBIVOPEN 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 NEBIVOPEN 10

Do not stop taking NEBIVOPEN 10 without talking to your doctor first, because NEBIVOPEN 10 prevents the development of a serious condition.

4. Possible side effects

NEBIVOPEN 10 can have side effects.

Not all side effects reported for NEBIVOPEN 10 are included in this leaflet. Should your general health worsen while taking NEBIVOPEN 10, please consult your doctor, pharmacist or other health care provider for advice.

If any of the following happens, stop taking NEBIVOPEN 10 and tell your doctor immediately or go to the casualty department at your nearest hospital:

- Swelling of the hands, feet, ankles, face, eyes, mouth, lips or throat which may cause difficulty in swallowing or breathing

- Shortness of breath or wheezing
- Rash or itching.

These are very serious side effects. If you have them, you may have had a serious allergic reaction to NEBIVOPEN 10. You may need urgent medical attention or hospitalisation.

Like other similar medicines (antithrombotic agents), NEBIVOPEN 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 immediately or go to the casualty department at your nearest hospital if you notice any of the following:

- long and excessive bleedings (some signs are exceptional weakness, tiredness, paleness, dizziness, headache, unexplained swelling, breathlessness, chest pain or angina pectoris)
- skin reactions such as spreading intense skin rash, hives, blisters or mucosal lesions, e.g. in the mouth or eyes (Stevens-Johnson syndrome/toxic epidermal necrolysis)
- nausea with yellowing of the skin and eyes (jaundice)
- less urine than is normal for you (renal failure)

These are all very serious side effects. You may need urgent medical attention or hospitalisation.

Tell your doctor if you notice any of the following:

Frequently occurring side effects:

- anaemia (reduction in red blood cells which may make the skin pale and cause weakness or breathlessness)
- bleeding following an operation
- swelling in the limbs
- bleeding into the eye (including bleeding from the whites of the eyes)

- bleeding into tissue or a cavity of the body (haematoma, bruising)
- low blood pressure (symptoms may be feeling dizzy or fainting when standing up)
- coughing up blood
- gastrointestinal tract bleeding, stomach ache, indigestion, nausea and vomiting (feeling sick or being sick), constipation, diarrhoea
- blood in the urine and heavy menstrual bleeding, nose bleed, bleeding in the gum
- rash, itchy skin
- bleeding from the skin or under the skin
- pain in the limbs
- impaired function of the kidneys (may be seen in tests performed by your doctor)
- fever
- decreased general strength and energy (weakness, tiredness), headache, dizziness
- blood test may show an increase in some liver enzymes

Less frequently occurring side effects:

- thrombocytopenia (low number of platelets, which are cells that help blood to clot)
- allergic reactions, including allergic skin reactions, swelling in the deep layers of the skin, hives (raised rash), severe, potentially life-threatening allergic reaction
- bleeding into the brain or inside the skull
- fast heartbeat (tachycardia)
- dry mouth
- impaired function of the liver (may be seen in tests performed by your doctor), jaundice
- blood tests may show an increase in bilirubin, some pancreatic or liver enzymes or in the number of platelets
- bleeding into a joint causing pain and swelling
- oozing of blood or fluid from surgical wound
- bleeding into a muscle

- feeling unwell
- localised swelling
- collection of blood (haematoma) in the groin as a complication of the cardiac procedure where a catheter is inserted in your leg artery (pseudoaneurysm).

Frequency unknown:

- increased pressure within muscles of the legs or arms after a bleeding, which leads to pain, swelling, altered sensation, numbness or paralysis (compartment syndrome after a bleeding)
- kidney failure after a severe bleeding.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

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 (choloestasis), 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, pharmacist or nurse. You can also report side effects to SAHPRA via the "6.04 Adverse Drug Reaction Reporting Form", found online under SAHPRA's publications: http://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of NEBIVOPEN 10.

5. How to store NEBIVOPEN 10

Store all medicines out of reach of children.

Store at or below 30 °C, in the original package. Keep blisters in the carton until required for use.

Do not store in a bathroom.

Do not use NEBIVOPEN 10 after the expiry date which is stated on the carton after EXP. The expiry date refers to the last day of that month.

Medicines should not be disposed of via wastewater or household waste.

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What NEBIVOPEN 10 contains

The active substance is rivaroxaban. Each film-coated tablet contains 10 mg rivaroxaban.

The other ingredients are hypromellose, microcrystalline cellulose, sodium lauryl sulphate, lactose, croscarmellose sodium, magnesium stearate, hypromellose, titanium dioxide (E171), macrogol, iron oxide red (E172).

What NEBIVOPEN 10 looks like and contents of the pack

A pink, round, biconvex film-coated tablet, engraved with “10” on one side, plain on the other.

The film-coated tablets are packed in PVC/aluminium blisters.

The blister strips are packed in cartons containing 10, 14, 28, 30, 42, 98, or 100 tablets. Not all packing sizes may be marketed at one time.

Holder of certificate of registration

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Access to the corresponding Professional Information

SAHPRA Repository of Professional Information and Patient Information Leaflets:

https://www.sahpra.org.za/pi-pil-repository/

Aspen Pharmacare:

E-mail: Medinfo@aspenpharma.com

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