1.3.2 PATIENT INFORMATION LEAFLET

Scheduling status

S4

NEBIVOPEN 15, film-coated tablets

NEBIVOPEN 20, film-coated tablets

Rivaroxaban

Contains sugar:

NEBIVOPEN 15 contains 16,32 mg lactose monohydrate

NEBIVOPEN 20 contains 21,76 mg lactose monohydrate

Read all of this leaflet carefully before you start taking NEBIVOPEN

- 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 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 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 blocking a blood clotting factor (Factor Xa) and thus reduces the tendency of the blood to clot.

NEBIVOPEN is used to:

- prevent blood clots in brain (stroke) and other blood vessels in your body if you have a form of irregular heart rhythm called non-valvular atrial fibrillation
- 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

Do not take NEBIVOPEN

- if you are hypersensitive (allergic) to rivaroxaban or any of the other ingredients of NEBIVOPEN
- 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, aneurism, 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 an inherited bleeding disorder
- 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

Take special care with NEBIVOPEN

- 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)
  - recent bleeding in your brain (intracranial or intracerebral bleeding)
  - recent operation on your brain, spinal column or eye
  - a lung disease where your bronchi are widened and filled with pus (bronchiectasis), or previous bleeding from your lung
- 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**
- 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 you need to have an operation

- it is very important to take NEBIVOPEN 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 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 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

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

The following medicines may increase the effect of NEBIVOPEN:

- some medicines for fungal infections (e.g. fluconazole, ketoconazole, itraconazole, voriconazole, posaconazole), unless they are only applied to the skin
- some anti-viral medicines for HIV / AIDS (e.g. ritonavir)
- some medicines for bacterial infections (e.g. clarithromycin, erythromycin)
- 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, if you take the following, because the effect of NEBIVOPEN 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 with food and drink

NEBIVOPEN should be taken with food.

Pregnancy and breastfeeding

Do not take NEBIVOPEN 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. If you become pregnant while you are taking NEBIVOPEN, 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 healthcare professional for advice before taking NEBIVOPEN.

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

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

monohydrate may have an effect on the control of your blood sugar if you have diabetes mellitus.

3. How to take NEBIVOPEN

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

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

Swallow the tablet(s) preferably with water.

Take NEBIVOPEN together with a meal.

How much to take

- **To prevent blood clots in brain (stroke) and other blood vessels in your body:**

  The recommended dose is one tablet NEBIVOPEN 20 mg once a day.

  If you have kidney problems, the dose may be reduced to one tablet NEBIVOPEN 15 mg once a day.

- **to treat blood clots in the veins of your legs and blood clots in the blood vessels of your lungs, and for preventing blood clots from re-occurring:**

  The recommended dose is one tablet NEBIVOPEN 15 mg twice a day for the first 3 weeks.

  For treatment after 3 weeks, the recommended dose is one tablet NEBIVOPEN 20 mg once a day.

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

When to take NEBIVOPEN

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

Try to take the tablet(s) at the same time every day to help you to remember it.

If you take more NEBIVOPEN 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 increases the risk of bleeding.

If you forgot to take NEBIVOPEN

- If you are taking one 20 mg tablet or one 15 mg tablet once a day and have missed a dose, take it as soon as you remember. Do not take more than one tablet in a single day to make up for a forgotten dose. Take the next tablet on the following day and then carry on taking one tablet once a day.
- If you are taking one 15 mg tablet twice a day and have missed a dose, take it as soon as you remember. Do not take more than two 15 mg tablets in a single day. If you forget to take a dose you can take two 15 mg tablets at the same time to get a total of two tablets (30 mg) on one day. On the following day you should carry on taking one 15 mg tablet twice a day.

If you stop taking NEBIVOPEN

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

4. Possible side effects

NEBIVOPEN can have side effects.

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

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

- Swelling of the hands, feet, ankles, mouth, face, lips eyes and 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. You may need urgent medical attention or hospitalisation.

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. If you have them, you may have had a serious reaction to NEBIVOPEN. 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)
- fast heartbeat (tachycardia)
- 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, allergic reactions, including allergic skin reactions
- 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
- oozing of blood or fluid from surgical wound

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, severe, potentially life-threatening allergic reaction
- bleeding into the brain or inside the skull
- faster 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
- 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.

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.

5. How to store NEBIVOPEN

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 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 contains

The active substance is rivaroxaban. Each film-coated tablet contains 15 mg or 20 mg rivaroxaban.

The other ingredients are:

NEBIVOPEN 15: Hypromellose, microcrystalline cellulose, sodium lauryl sulphate, lactose monohydrate, croscarmellose sodium, magnesium stearate, hypromellose, titanium dioxide (E171), macrogol, iron oxide red (E172). Contains 16,32 mg lactose monohydrate per tablet.

NEBIVOPEN 20: Hypromellose, microcrystalline cellulose, sodium lauryl sulphate, lactose monohydrate, croscarmellose sodium, magnesium stearate, hypromellose, titanium dioxide (E171), macrogol, iron oxide red (E172). Contains 21,76 mg lactose monohydrate per tablet.

What NEBIVOPEN looks like and contents of the pack

NEBIVOPEN 15: A red, round, biconvex film-coated tablet, engraved with “15” on one side, plain on the other.

NEBIVOPEN 20: A brown-red, round, biconvex film-coated tablet, engraved with “20” on one side, plain on the other.

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

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

Holder of certificate of registration

PHARMACARE LIMITED

Healthcare Park

Woodlands drive

Woodmead

2191

Hotline: 0800 122 912

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Registration numbers

NEBIVOPEN 15: 53/8.2/0624

NEBIVOPEN 20: 53/8.2/0625

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

Tel: 0800 118 088

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