

### 1.3.2 PATIENT INFORMATION LEAFLET

#### Scheduling status

S4

#### **NEBIVOPEN 2,5**, film-coated tablets

Rivaroxaban

Contains sugar: 23,9 mg lactose monohydrate per tablet

#### **Read all of this leaflet carefully before you start taking NEBIVOPEN 2,5**

- 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 2,5 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 2,5 is and what it is used for
2. What you need to know before you take NEBIVOPEN 2,5
3. How to take NEBIVOPEN 2,5
4. Possible side effects
5. How to store NEBIVOPEN 2,5
6. Contents of the pack and other information

#### **1. What NEBIVOPEN 2,5 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.

You have been given NEBIVOPEN 2.5 because

- you have been diagnosed with an acute coronary syndrome (a group of conditions that includes heart attack and unstable angina, a severe type of chest pain) and have been shown to have had an increase in certain cardiac blood tests.

NEBIVOPEN 2.5 reduces the risk in adults of having another heart attack or reduces the risk of dying from a disease related to your heart or your blood vessels.

NEBIVOPEN 2.5 will not be given to you on its own. Your doctor will also tell you to take either:

- aspirin or
- aspirin plus clopidogrel or ticlopidine.

or

- you have been diagnosed with a high risk of getting a blood clot due to a coronary artery disease or peripheral artery disease which causes symptoms. NEBIVOPEN 2.5 reduces the risk in adults of getting blot clots (atherothrombotic events).

NEBIVOPEN 2.5 will not be given to you on its own. Your doctor will also tell you to take aspirin.

## **2. What you need to know before you take NEBIVOPEN 2,5**

### **Do not take NEBIVOPEN 2,5:**

- if you are hypersensitive (allergic) to rivaroxaban or any of the other ingredients of NEBIVOPEN 2,5 (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 an acute coronary syndrome and previously had a bleeding or a blood clot in your brain (stroke)
- if you have coronary artery disease or peripheral artery disease and previously had a bleeding in your brain (stroke) or where there was a blockage of the small arteries providing blood to the brain's deep tissues (lacunar stroke) or if you had a blood clot in your brain (ischaemic, non-lacunar stroke) in the previous month
- 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 2,5.

NEBIVOPEN 2,5 should not be used in combination with certain other medicines which reduce blood clotting such as prasugrel or ticagrelor other than aspirin and clopidogrel/ticlopidine.

**Take special care with NEBIVOPEN 2,5:**

- if you have an increased risk of bleeding, such as:

- 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
- you are older than 75 years
- you weigh 60 kg or less
- you have a coronary artery disease with severe symptomatic heart failure
- 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 2,5)
- 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).

Also take care if you have an active cancer – this may also mean you have an increased risk of bleeding. An active cancer means that in the last 6 months you:

- have been diagnosed with cancer
- had a relapse of cancer

- were being treated for cancer

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 2,5 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 2,5 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 2,5 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 2,5**

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 2,5:

- 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 prasugrel and ticagrelor (see section Warnings and Precautions))
- 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 2,5, if you take the following, because the effect of NEBIVOPEN 2,5 may be reduced:

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

### **NEBIVOPEN 2,5 with food and drink**

NEBIVOPEN 2,5 may be taken with or without food.

### **Pregnancy and breastfeeding**

Do not take NEBIVOPEN 2,5 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 2,5. If you become pregnant while you are taking NEBIVOPEN 2,5, 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 2,5.

### **Driving and using machines**

NEBIVOPEN 2,5 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 2,5**

NEBIVOPEN 2,5 contains lactose monohydrate. If you have been told by your doctor that you have intolerance to some sugars contact your doctor before taking NEBIVOPEN 2,5.

### **3. How to take NEBIVOPEN 2,5**

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

Always take NEBIVOPEN 2,5 exactly as your doctor has instructed you. Check with your doctor or pharmacist if you are unsure.

#### **How much to take**

The usual dose is one NEBIVOPEN 2,5 tablet (2,5 mg) twice a day.

Swallow the tablet preferably with water.

Try to take the tablet at the same time every day (one tablet in the morning and one in the evening).

NEBIVOPEN 2,5 may be taken with or without food.

Talk to your doctor about other ways to take NEBIVOPEN 2,5 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 2,5 tablet through a nose-stomach tube.

NEBIVOPEN 2,5 will not be given to you on its own.

Your doctor will also tell you to take aspirin. If you get NEBIVOPEN 2,5 after an acute coronary syndrome, your doctor may tell you to also take clopidogrel or ticlopidine.

Your doctor will tell you how much of these to take (usually between 75 to 100 mg aspirin daily or a daily dose of 75 to 100 mg aspirin plus a daily dose of either 75 mg clopidogrel or a standard daily dose of ticlopidine).

### **When to start NEBIVOPEN 2,5**

Treatment with NEBIVOPEN 2,5 after an acute coronary syndrome should be started as soon as possible after stabilisation of the acute coronary syndrome, at the earliest 24 hours after admission to hospital and at the time when parenteral (via injection) anticoagulation therapy would normally be stopped.

Your doctor will tell you when to start treatment with NEBIVOPEN 2,5 if you have been diagnosed with coronary artery disease or peripheral artery disease.

Your doctor will tell you how long your treatment with NEBIVOPEN 2,5 will last.

### **If you take more NEBIVOPEN 2,5 than you should**

Taking too much NEBIVOPEN 2,5 increases the risk of bleeding.

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

### **If you forget to take NEBIVOPEN 2,5**

Do not take a double dose to make up for a forgotten tablet.

If you have missed a dose, take the next tablet at the usual time.

#### **If you stop taking NEBIVOPEN 2,5**

Take NEBIVOPEN 2,5 regularly and for as long as your doctor prescribes it.

Do not stop taking NEBIVOPEN 2,5 without talking to your doctor first. Your risk of having another heart attack or stroke or dying from a disease related to your heart or your blood vessels may increase if you stop taking NEBIVOPEN 2,5.

#### **4. Possible side effects**

NEBIVOPEN 2,5 can have side effects.

Not all side effects reported for NEBIVOPEN 2,5 are included in this leaflet. Should your general health worsen while taking NEBIVOPEN 2,5, please consult your doctor, pharmacist or other health care provider for advice.

If any of the following happens, stop taking NEBIVOPEN 2,5 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 2,5. You may need urgent medical attention or hospitalisation.

Like other similar medicines (antithrombotic agents), NEBIVOPEN 2,5 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)
- a reaction that causes rash, fever, inflammation of internal organs, hematologic abnormalities and systemic illness (DRESS syndrome).
- 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 in the stomach or bowel, blood in the urine and heavy menstrual bleeding (urogenital bleeding), nose bleed, bleeding in the gum
- bleeding into the eye (including bleeding from the whites of the eyes)
- bleeding into tissue or a cavity of the body (haematoma, bruising)
- coughing up blood
- bleeding from the skin or under the skin
- bleeding following an operation

- oozing of blood or fluid from surgical wound
- pain in the limbs
- impaired function of the kidneys (may be seen in tests performed by your doctor)
- fever
- stomach ache, indigestion, nausea and vomiting (feeling sick or being sick), constipation, diarrhoea
- low blood pressure (symptoms may be feeling dizzy or fainting when standing up)
- decreased general strength and energy (weakness, tiredness), headache, dizziness
- rash, itchy skin
- blood test may show an increase in some liver enzymes.

***Less frequently occurring side effects:***

- bleeding into the brain or inside the skull
- bleeding into a joint causing pain and swelling
- thrombocytopenia (low number of platelets, which are cells that help blood to clot)
- allergic reactions, including allergic skin reactions
- 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
- fainting
- feeling unwell
- dry mouth
- hives
- bleeding into a muscle
- cholestasis (decreased bile flow), hepatitis incl. hepatocellular injury (inflamed liver incl. liver injury)

- yellowing of the skin and eye (jaundice)
- 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 2,5.

**5. How to store NEBIVOPEN 2,5**

Store all medicines out of reach of children.

Store at or below 30 °C, in the original package. Do not remove the blisters from the carton until required for use.

Do not store in a bathroom.

Do not use NEBIVOPEN 2,5 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 2,5 contains**

The active substance is rivaroxaban. Each film-coated tablet contains 2,5 mg rivaroxaban.

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

### **What NEBIVOPEN 2,5 looks like and contents of the pack**

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

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

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**Hotline:** 0800 122 912

**This leaflet was last revised in**

14 June 2022

**Registration number**

58/8.2/0622

**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](mailto:Medinfo@aspenpharma.com)

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