

**WARNING: (A) PREMATURE DISCONTINUATION OF MYOROXA INCREASES THE RISK OF THROMBOTIC EVENTS,
(B) SPINAL/EPIDURAL HAEMATOMA****A. Premature discontinuation of MYOROXA increase the risk of thrombotic events:**

Premature discontinuation of any oral anticoagulant, including MYOROXA, increases the risk of thrombotic events. If anticoagulation with MYOROXA 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 MYOROXA 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 spinal deformity or spinal surgery
- Optimal timing between the administration of MYOROXA 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**

MYOROXA 10 mg film-coated tablets
MYOROXA 15 mg film-coated tablets
MYOROXA 20 mg film-coated tablets

Rivaroxaban

Contains sugar (lactose monohydrate 28,09 mg in MYOROXIA 10, 28,068 mg in MYOROXIA 15, and 28,09 mg in MYOROXIA 20)

Read all of this leaflet carefully before you start taking MYOROXIA

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other healthcare provider.
- MYOROXIA 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 MYOROXIA is and what it is used for
2. What you need to know before you take MYOROXIA
3. How to take MYOROXIA
4. Possible side effects
5. How to store MYOROXIA
6. Contents of the pack and other information

1. What MYOROXIA is and what it is used for

MYOROXIA 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.

MYOROXIA contains the active substance rivaroxaban and is used in adults to:

- prevent blood clots in the veins after a hip or knee replacement operation.
- 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 MYOROXIA

Do not take MYOROXIA:

- if you are allergic to rivaroxaban or any of the other ingredients of MYOROXIA (listed in section 6)
- if you are bleeding excessively (e.g., brain or stomach bleeding)

- if you have a disease called triple positive antiphospholipid syndrome (a disorder in which the immune system mistakenly attacks normal proteins in the blood resulting in increased risk of blood clots)
- if you have a lesion or condition that increases the risk of serious bleeding (e.g., stomach ulcer, cancerous tumour at risk of bleeding, recent surgery of the brain or eyes); brain or spinal injury, enlarged veins in the tube running from the throat to the stomach, weak arteries that ruptures easily)
- Avoid using MYOROXA along with other blood-thinning medications like heparin, enoxaparin, dalteparin, fondaparinux, warfarin, dabigatran etexilate, apixaban, etc. There are some cases where switching between blood thinners might be necessary (see section 3), or if heparin needs to be used to keep a catheter open (see Other medicines and MYOROXA)
- if you have an inherited bleeding disorder
- if you have a liver disease with or without a bleeding disorder; or an increased risk of bleeding (cirrhotic patients with Child Pugh B and C)
- if you are pregnant or breastfeeding.

Warnings and precautions

Talk to your doctor or pharmacist before taking MYOROXA.

Take special care with MYOROXA:

- 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 MYOROXA 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 sections Do not take MYOROXA and Other medicines and MYOROXA)
 - bleeding disorders
 - very high blood pressure, not controlled by medical treatment
 - 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 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 MYOROXA. Your doctor will decide, if you should be treated with MYOROXA and if you should be kept under closer observation.

If you need to have an operation:

- It is very important to take MYOROXA 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 MYOROXA before and after the injection or removal of the catheter 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

MYOROXA 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 MYOROXA

Always tell your healthcare provider if you are taking any other medicine. (This includes all 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., ketoconazole, fluconazole, 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)
- anti-inflammatory and pain relieving medicines (e.g., naproxen or acetylsalicylic acid)
- some medicines to treat depression (selective serotonin reuptake inhibitors (SSRIs) or serotonin norepinephrine reuptake inhibitors (SNRIs)).
- a medicine to treat abnormal heartbeat (e.g., dronedarone).

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

Pregnancy and breastfeeding

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 MYOROXA.

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

Driving and using machines

It is not always possible to predict to what extent MYOROXA may interfere with your daily activities. MYOROXA may cause dizziness or fainting (see section 4, 'Possible side effects'). You should not drive or use machines if you are affected by these symptoms.

MYOROXA contains lactose

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking MYOROXA. MYOROXA contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially "sodium free".

3. How to take MYOROXA

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

Always take MYOROXA exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

The usual dose:

- **to prevent blood clots in the veins after a hip or knee replacement operation**, is one tablet MYOROXA 10 mg once a day. Take the first tablet 6 - 10 hours after your operation. 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.

- **to prevent blood clots in the brain (stroke) and other blood vessels in your body if you have non-valvular atrial fibrillation**, is one tablet MYOROXA 20 mg once a day. If you have kidney problems, the dose may be reduced to one tablet MYOROXA 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**, is one tablet MYOROXA 15 mg twice a day for the first 3 weeks, and then after 3 weeks the usual dose is one tablet MYOROXA 20 mg once a day.

MYOROXA 10 can be taken with or without food.

MYOROXA 15 and MYOROXA 20 must be taken with food.

Swallow the tablet preferably with water.

If you have difficulty swallowing the tablet whole, talk to your doctor about other ways to take MYOROXA 15 mg or 20 mg. 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 MYOROXA 15 mg or 20 mg tablet through a stomach tube.

Try to take the tablet at the same time every day to help you to remember it. Take the tablet every day until your doctor tells you to stop. Your doctor will decide how long you must continue treatment.

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

If you take more MYOROXA than you should

Taking too much MYOROXA increases your risk of bleeding.

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

If you forget to take MYOROXA

- **If you are taking one MYOROXA 10 mg, or MYOROXA 15 mg, or MYOROXA 20 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 MYOROXA 15 mg tablet twice a day** and have missed a dose, take it as soon as you remember. Do not take more than two MYOROXA 15 mg tablets in a single day. If you forget to take a dose you can take two MYOROXA 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 MYOROXA 15 mg tablet twice a day.

If you stop taking MYOROXA

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

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

4. Possible side effects

MYOROXA can have side effects.

Not all side effects reported for MYOROXA are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking MYOROXA, please consult your healthcare provider for advice.

MYOROXA may cause bleeding which may potentially be life threatening. Excessive bleeding may lead to a sudden drop in blood pressure (shock). In some cases, the bleeding may not be obvious.

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

- swelling of the face, lips, mouth, tongue, or throat; difficulty swallowing; hives and breathing difficulties; sudden drop in blood pressure.

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

Tell your doctor immediately if you experience any of the following side effects which may be a sign of bleeding:

- 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.

Tell your doctor immediately if you experience skin reactions such as:

- spreading intense skin rash, blisters, or mucosal lesions, e.g., in the mouth or eyes (Stevens-Johnson syndrome/Toxic Epidermal Necrolysis).
- a medicine reaction that causes rash, fever, inflammation of internal organs, hematologic abnormalities, and systemic illness (DRESS syndrome).
- yellowing of the skin and eye (jaundice).

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

The following side effects have been reported for MYOROXA:

Frequent side effects:

- reduction in red blood cells which can make the skin pale and cause weakness or breathlessness
- bleeding in the stomach or bowel, urogenital bleeding (including blood in the urine and heavy menstrual 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
- swelling in the limbs
- pain in the limbs
- impaired function of the kidneys (may be seen in tests performed by your doctor)
- fever
- stomach ache, indigestion, feeling 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 tests may show an increase in some liver enzymes

Less frequent side effects:

- bleeding into the brain or inside the skull
- bleeding into a joint causing pain and swelling
- bleeding into a muscle
- 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
- cholestasis (decreased bile flow), hepatitis incl. hepatocellular injury (inflamed liver incl. liver injury)
- fainting
- feeling unwell
- localised swelling
- faster heartbeat

- collection of blood (haematoma) in the groin as a complication of the cardiac procedure where a catheter is inserted in your leg artery (pseudoaneurysm)
- dry mouth
- hives

Frequency unknown

- kidney failure after a severe bleeding
- 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)

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 or pharmacist. 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 MYOROXA.

5. How to store MYOROXA

Store all medicines out of reach of children.

Store at or below 25 °C.

Keep in the original packaging until required for use.

Do not use after the expiry date stated on the label.

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 MYOROXA contains

The active substance is rivaroxaban. Each tablet contains 10 mg, 15 mg or 20 mg rivaroxaban respectively.

The *core tablet* of all the strengths contain: microcrystalline cellulose, lactose monohydrate, croscarmellose sodium, hypromellose, sodium lauryl sulfate, colloidal anhydrous silica, magnesium stearate

The film-coating of MYOROXA 10:

Opadry Pink (04F540031) consisting of: hypromellose (E464), iron oxide red (E172), titanium dioxide (E171), macrogol (E1521).

The film-coating of MYOROXA 15:

Opadry Brown (04F565029) consisting of: hypromellose (E464), iron oxide red (E172), titanium dioxide (E171), macrogol (E1521).

The film-coating of MYOROXA 20:

Opadry Brown (04F565025) consisting of: hypromellose (E464), iron oxide red (E172), titanium dioxide (E171), macrogol (E1521).

What MYOROXA looks like and contents of the pack

MYOROXA 10: Light-red, round shaped, biconvex, film-coated tablets, debossed with "CS" on one side and plain on other side.

Transparent Aluminium//PVC/PVDC foil blisters in cartons. MYOROXA 10 pack sizes: 5, 10, 30 or 100 film-coated tablets.

MYOROXA 15: Red, round shaped, biconvex, film-coated tablets, debossed with "C4" on one side and plain on other side.

Transparent Aluminium//PVC/PVDC foil blisters in cartons. MYOROXA 15 pack sizes: 10, 14, 28, 42, 98 or 100 film-coated tablets.

MYOROXA 20: Brown-red, round shaped, biconvex, film-coated tablets, debossed with "C3" on one side and plain on other side.

Transparent Aluminium//PVC/PVDC foil blisters in cartons. MYOROXA 20 pack sizes: 10, 14, 28, 98 or 100 film-coated tablets.

Not all pack sizes may be marketed.

Holder of Certificate of Registration:

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