PATIENT INFORMATION LEAFLET

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

A. Premature discontinuation of XARELTO increase the risk of thrombotic events:
Premature discontinuation of any oral anticoagulant, including XARELTO, increases the risk of thrombotic events. If anticoagulation with XARELTO 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 XARELTO 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 XARELTO 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**

XARELTO 2.5 mg film-coated tablets
Rivaroxaban
Contains sugar: 33.92 mg lactose (as monohydrate)

Read all of this leaflet carefully before you start XARELTO 2.5
- 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.
- XARELTO 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 XARELTO 2.5 is and what it is used for

You have been given XARELTO 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.
  XARELTO 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.
  XARELTO 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.
  XARELTO 2.5 reduces the risk in adults of getting blot clots (atherothrombotic events).
  XARELTO 2.5 will not be given to you on its own. Your doctor will also tell you to take aspirin.

XARELTO 2.5 contains the active substance rivaroxaban and belongs to a group of medicines called antithrombotic medicines. 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 take XARELTO 2.5

Do not take XARELTO 2.5

- 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 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 breast-feeding

Do not take XARELTO 2.5 and tell your doctor if any of these apply to you.

Warnings and precautions
Talk to your doctor or pharmacist before taking XARELTO 2.5.
XARELTO 2.5 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 XARELTO 2.5
- if you have an increased risk of bleeding, as could be the case in situations such as:
  - 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 XARELTO 2.5"**)**
  - 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
- 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.

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 XARELTO 2.5. 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 XARELTO 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 XARELTO 2.5 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
XARELTO 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 XARELTO 2.5
Always tell your health care provider:
If you are taking any other medicines. This includes complementary or traditional medicines.

- **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, 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 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 XARELTO 2.5, because the effect of XARELTO 2.5 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 used for tuberculosis.

  If any of the above apply to you, tell your doctor before taking XARELTO 2.5, because the effect of XARELTO 2.5 may be reduced. Your doctor will decide, if you should be treated with XARELTO 2.5 and if you should be kept under closer observation.

Pregnancy and breastfeeding
Do not take XARELTO 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 XARELTO 2.5. If you become pregnant while you are taking this medicine, tell your doctor immediately, who will decide how you should be treated.

Driving and using machines
XARELTO 2.5 may cause dizziness (frequent side effect) or fainting (less frequent side effect) (see section 4, "Possible side effects"). You should not drive or use machines if you are affected by these symptoms.

XARELTO 2.5 contains lactose and sodium
If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.
XARELTO 2.5 contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially "sodium-free".

3. How to take XARELTO 2.5

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

Always take XARELTO 2.5 exactly as your doctor/pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

How much to take

The recommended dose is one 2.5 mg tablet twice a day. Take XARELTO 2.5 around the same time every day (for example, one tablet in the morning and one in the evening). XARELTO 2.5 can be taken with or without food.

If you have difficulty swallowing the whole tablet, talk to your doctor/pharmacist about other ways to take XARELTO 2.5. The tablet may be crushed and mixed with water or apple puree immediately before you take it.
If necessary, your doctor may also give you the crushed XARELTO 2.5 tablet through a nose - stomach tube.

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

Treatment with XARELTO 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 XARELTO 2.5 if you have been diagnosed with coronary artery disease or peripheral artery disease.
Your doctor will decide how long you must continue treatment.

If you take more XARELTO 2.5 than you should
Taking too much XARELTO 2.5 increases the risk of bleeding.

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

If you forget to take XARELTO 2.5
Do not take a double dose to make up for a missed dose. If you miss a dose, take your next dose at the usual time.

If you stop taking XARELTO 2.5
Take XARELTO 2.5 on a regular basis and for as long as your doctor keeps prescribing it.

Do not stop taking XARELTO 2.5 without talking to your doctor first. If you stop taking XARELTO 2.5, it may increase your risk of having another heart attack or stroke or dying from a disease related to your heart or your blood vessels.

If you have any further questions on the use of XARELTO 2.5, ask your doctor or pharmacist.

4. Possible side effects

XARELTO 2.5 can have side effects.

Not all side effects reported for XARELTO 2.5 are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking XARELTO 2.5, please consult your health care provider for advice.

Like other similar medicines (antithrombotic agents), XARELTO 2.5 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.

Possible side effects which may be a sign of bleeding
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, 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 skin reaction
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). The frequency of this side effect is very rare (up to 1 in 10,000).
- a drug reaction that causes rash, fever, inflammation of internal organs, hematologic abnormalities and systemic illness (DRESS syndrome). The frequency of this side effect is very rare (up to 1 in 10,000).

Possible side effects which may be a sign of severe allergic reactions
Tell your doctor/pharmacist immediately if you experience any of the following side effects:
- swelling of the face, lips, mouth, tongue or throat; difficulty swallowing; hives and breathing difficulties; sudden drop in blood pressure. The frequencies of these side effects are less frequent (anaphylactic reactions, including anaphylactic shock; may affect up to 1 in 10,000 people and angioedema and allergic oedema; may affect up to 1 in 100 people).

Overall list of possible side effects

Frequent (may affect up to 1 in 10 people)
- 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 (may affect up to 1 in 100 people)
- 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
- faster heartbeat
- 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)

Not known (frequency cannot be estimated from the available data)
- 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 any 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 XARELTO 2.5.

5. How to store XARELTO 2.5

Store all medicines out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and on each blister or bottle after EXP. The expiry date refers to the last day of that month.

Store at or below 30 °C.
Protect for light and moisture.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What XARELTO 2.5 contains
- The active substance is rivaroxaban. Each tablet contains 2.5 mg of rivaroxaban.
- The other ingredients are:
  croscarmellose sodium, lactose monohydrate, hypromellose 2910, iron oxide yellow (E 172), macrogol 3350, magnesium stearate, microcrystalline cellulose, sodium laurilsulphate, titanium dioxide (E 171). See section 2 "XARELTO 2.5 contains lactose and sodium".

What XARELTO 2.5 looks like and contents of the pack

XARELTO 2.5 mg film-coated tablets are light yellow, round, biconvex and marked with the BAYER-cross on one side and "2.5" and a triangle on the other side.

They come
- in blisters in cartons of 14, 20, 28, 30, 56, 60, 98, 168 or 196 film-coated tablets or
- in unit dose blisters in cartons of 10 x 1 or 100 x 1 or
- in multipacks comprising 10 cartons, each containing 10 x 1 film-coated tablets

Not all pack sizes may be marketed.

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