1.3.2 Patient Information Leaflet

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS **S4**

EUROPAN 200 mg, 200 mg, Film-coated tablets

Pazopanib

Sugar-free

Read all of this leaflet carefully before you start taking EUROPAN 200 mg

- 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.
- EUROPAN 200 mg 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 IS EUROPAN 200 mg AND WHAT IT IS USED FOR

EUROPAN 200 mg is a type of medicine called a protein kinase inhibitor. It works by preventing the activity of proteins that are involved in the growth and spread of cancer cells. EUROPAN 200 mg is used in adults to treat kidney cancer that is advanced or has spread to other organs.

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE EUROPAN 200 mg

Do not take EUROPAN 200 mg:

- if you are hypersensitive (allergic) to pazopanib or any of the other ingredients of EUROPAN 200 mg (listed in section 6).

Warnings and precautions

Talk to your doctor or pharmacist before taking EUROPAN 200 mg.

Special care should be taken with EUROPAN 200 mg:

- if you have liver disease. Your dcotor will monitor your liver function closely (with blood tests).
- if you have high blood pressure. EUROPAN 200 mg can raise your blood pressure. Your blood pressure will be monitored before you take EUROPAN 200 mg and while you are taking it. If you have high blood pressure you will be treated with medicines to reduce it.
- if you experience a rapid onset of symptoms including headache, seizures, extreme tiredness and confusion, hypertension, and blindness. EUROPAN 200 mg can cause swelling of the brain. This condition is diagnosed by your doctor and is called posterior reversible encephalopathy syndrome (PRES)/ reversible posterior leukoencephalopathy syndrome (RPLS), which requires immediate medical attention.
- if you have trouble breathing, shortness of breath, cough, chest pain and unexplained weight loss. EUROPAN 200 mg can cause inflammation and scarring of the lungs. This condition is diagnosed by your doctor and is called interstitial lung disease (ILD)/ pneumonitis, which requires immediate medical attention.
- if you have had heart failure or a heart attack.
- if you have been diagnosed with changes in heart rhythm (QT prolongation). EUROPAN 200 mg can affect heart rhythm which in some people can develop into a potentially serious heart condition known as torsade de pointes. This can result in a very fast heartbeat causing a sudden loss of consciousness.
- if you have been diagnosed with heart disease or previous stroke.
- if you have had problems with bleeding, blood clots, narrowing of the arteries or weakening of arteries/ aneurysm.

- if you have had stomach or bowel problems such as perforation (hole) or fistula (abnormal passages forming between parts of the intestine).
- if you are going to have an operation. Your doctor will stop EUROPAN 200 mg at least 7 days before your operation as it may affect wound healing. Your treatment will be restarted when the wound has adequately healed.
- if you have thyroid problems.
- if you have kidney disease and excess protein in urine (after urine tests)
- if you have been diagnosed with rapid growing tumours, a high tumour burden (large sized tumour/s and/or large number of cancer cells), renal dysfunction, dehydration, high uric acid levels in blood (after blood tests), your doctor will monitor you for a condition called tumour lysis syndrome. This is when tumour cells release their contents into the bloodstream.
- if you diagnosed with serious infection/s.
- if you are pregnant, planning to get pregnant or fall pregnant during treatment with EUROPAN 200 mg.
- If you are taking any other medicines, especially those mentioned below in section "*Other medicines and EUROPAN 200 mg*". Your doctor will assess all your other concurrent medicines to lessen the risk of drug interactions.

Children

The safety and efficacy of EUROPAN 200 mg in children have not been established.

Other medicines and EUROPAN 200 mg

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

Some medicines may affect how EUROPAN 200 mg works or make it more likely that you will have side effects. EUROPAN 200 mg can also affect how some other medicines work. These include:

- ketoconazole, itraconazole, clarithromycin, telithromycin, voriconazole, rifampicin (used to treat infection).
- atazanavir, indinavir, nelfinavir, ritonavir, saquinavir (used to treat HIV).

- nefazodone (used to treat depression).
- lapatinib, paclitaxel, irinotecan, cetuximab (used to treat cancers)
- midazolam (used as a sedative)
- simvastatin and possible other statin (used to treat high cholesterol levels)
- dextromethorphan (included in certain cough mixtures or cold and flu medication)
- medicines that reduce stomach acid. e.g. proton pump inhibitor such as esomerprazole, H_2 antagonists or antacids

Tell your doctor or pharmacist if you take any of these.

EUROPAN 200 mg with food and drink

Don't take EUROPAN 200 mg with food, as it affects the way the medicine is absorbed. Take it at least two hours after a meal or one hour before a meal (see section 3). Do not drink grapefruit juice while you are being treated with EUROPAN 200 mg as this may increase the chance of side effects.

Pregnancy and breastfeeding

Pregnancy

EUROPAN 200 mg is not recommended if you are pregnant. The effect of EUROPAN 200 mg during pregnancy is not known. Use a reliable method of contraception while you are taking EUROPAN 200 mg. Tell your doctor if you are pregnant, planning to get pregnant or fall pregnant during treatment with EUROPAN 200 mg.

Breastfeeding

The effect of EUROPAN 200 mg during breastfeeding is not known. Do not breast feed while taking EUROPAN 200 mg. Talk to your doctor about this.

Fertility

Fertility may be affected by treatment with EUROPAN 200 mg. Talk to your doctor about this.

Driving and using machines

The effect of EUROPAN 200 mg when driving or using machines is not known. Avoid driving or using machines if you feel dizzy, tired or weak, or if your energy levels are low.

3. HOW TO TAKE EUROPAN 200 mg

Do not share medicines prescribed for you with any other person.
Always take EUROPAN 200 mg exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

The usual dose is EUROPAN 800 mg (4 tablets) taken once a day. This is the maximum dose per day. Your doctor may need to reduce your dose if you get side effects.

Do not take EUROPAN 200 mg with food. Take it at least two hours after a meal, or one hour before a meal. For example, you could take it two hours after breakfast or one hour before lunch. Take EUROPAN 200 mg at about the same time each day. Swallow the tablets whole with water, one after the other. Do not break or crush the tablets as this affects the way the medicine is absorbed and may increase the chance of side effects.

If you take more EUROPAN 200 mg than you should

If you take too many tablets, contact a doctor or pharmacist for advice. If possible show them the pack, or this leaflet.

If you forget to take EUROPAN 200 mg

Do not take a double dose to make up for a forgotten dose. Just take your next dose at the usual time.

If you stop taking EUROPAN 200 mg

Do not stop EUROPAN 200 mg without advice. Take EUROPAN 200 mg for as long as your doctor recommends. Do not stop unless your doctor advises you to.

4. POSSIBLE SIDE EFFECTS

EUROPAN 200 mg can have side effects. Not all side effects reported for EUROPAN 200 mg are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking EUROPAN 200 mg, please consult your health care provider for advice.

If any of the following happens, stop taking / using EUROPAN 200 mg and tell your doctor immediately or go to the casualty department at your nearest hospital:

- Swelling of the brain (reversible posterior leukoencephalopathy syndrome):
  EUROPAN 200 mg can, on rare occasions, cause swelling of the brain, which may be life threatening. Symptoms include loss of speech, change of vision, seizure (fits), confusion and high blood pressure. Stop taking EUROPAN 200 mg and seek medical help if you get any of these symptoms, or if you get headache accompanied with any of these symptoms.
- Hypertensive crisis (sudden and severe rise in blood pressure):
  EUROPAN 200 mg can, on occasion, cause a sudden and severe rise in blood pressure. This is known as a hypertensive crisis. Your doctor will monitor your blood pressure while you are taking EUROPAN 200 mg. Signs and symptoms of a hypertensive crisis may include severe chest pain, severe headache, blurred vision, confusion, nausea, vomiting, severe anxiety, shortness of breath, seizures (fits) and fainting. Stop taking EUROPAN 200 mg and seek medical help if you develop hypertensive crisis.

- Heart conditions, such as cardiac dysfunction/ heart failure, heart attack:
  The risks of these problems may be higher for people with an existing heart problem, or who are taking other medicines. You will be checked for any heart problems while you are taking EUROPAN 200 mg. EUROPAN 200 mg can affect how well your heart pumps or can increase the likelihood of having a heart attack. Signs and symptoms include irregular or fast heartbeat, rapid fluttering of your heart, fainting, chest pain or pressure, pain in your arms, back, neck or jaw, shortness of breath and leg swelling. Seek medical help if you get any of these symptoms.

- Changes in heart rhythm (QT prolongation):
  EUROPAN 200 mg can affect heart rhythm which in some people can develop into a potentially

serious heart condition known as torsade de pointes. This can result in a very fast heartbeat causing a sudden loss of consciousness. Tell your doctor if you notice any unusual changes in your heart beat, such as beating too fast or too slow.

- Stroke:

  EUROPAN 200 mg can increase your likelihood of having a stroke. Signs and symptoms of stroke may include numbness or weakness on one side of your body, difficulty talking, headache and dizziness. Seek medical help if you get any of these symptoms.

- Bleeding:

  EUROPAN 200 mg can cause severe bleeding in the digestive system (such as stomach, oesophagus, rectum or intestine), or the lungs, kidneys, mouth, vagina and brain, although this is uncommon. Symptoms include passing blood in the stools or passing black stools, passing blood in the urine, stomach pain and coughing or vomiting up blood. Seek medical help if you get any of these symptoms.

- Perforation and fistula:

  EUROPAN 200 mg can cause a tear (perforation) in your stomach or intestinal wall or the development of an abnormal connection between two parts of your digestive tract (a fistula). Signs and symptoms may include severe stomach pain, nausea and/or vomiting, fever and development of a hole (perforation) in the stomach, intestine or bowel from which bloody or foul smelling pus is released. Seek medical help if you get any of these symptoms.

- Liver problems:

  EUROPAN 200 mg can cause problems with your liver which may develop into serious conditions such as liver dysfunction and liver failure, which may be fatal. Your doctor will be checking your liver enzymes while you are taking EUROPAN 200 mg. Signs that your liver may not be working properly may include yellowing of your skin or the whites of your eyes (jaundice), dark urine, tiredness, nausea, vomiting, loss of appetite, pain on the right side of your stomach area (abdomen) and bruising easily. Seek medical help immediately if you get any of these symptoms.

- Blood clots (Deep vein thrombosis (DVT) and pulmonary embolism):

  EUROPAN 200 mg may cause blood clots in your veins, especially in your legs (deep vein thrombosis or DVT), which may also travel to your lungs (pulmonary embolism). Signs and symptoms may include sharp chest pain, shortness of breath, rapid breathing, leg pain and swelling of your arms and hands or legs and feet

- Thrombotic microangiopathy (TMA):

  EUROPAN 200 mg may cause blood clots in the small blood vessels in the kidneys and brain accompanied by a decrease in red blood cells and cells involved in clotting (thrombotic microangiopathy, TMA). Signs and symptoms may include bruising easily, high blood pressure, fever, confusion, drowsiness, seizures (fits) and decrease in urine output. Seek medical help if you get any of these symptoms.

- Tumour lysis syndrome

  EUROPAN 200 mg can cause a fast breakdown of cancer cells resulting in tumour lysis syndrome, which in some people may be fatal. Symptoms may include irregular heartbeat, seizures (fits), confusion, muscle cramps or spasms, or decrease in urine output. Seek medical help if you get any of these symptoms.

- Infections

  Infections occurring while you take EUROPAN 200 mg may possibly become serious. Symptoms of infections may include fever, flu-like symptoms such as cough, tiredness and body aches that do not go away, shortness of breath and/or wheezing, pain while urinating, cuts and scrapes or wounds that are red, warm, swollen or painful. Seek medical help if you get any of these symptoms.

- Lung inflammation

  EUROPAN 200 mg can, on rare occasions, cause lung inflammation (interstitial lung disease, pneumonitis), which in some people can be fatal. Symptoms include shortness of breath or cough

that will not go away. You will be checked for any lung problems while you are taking EUROPAN 200 mg. Seek medical help if you get any of these symptoms.

- Thyroid problems

  EUROPAN 200 mg can lower the amount of thyroid hormone produced in your body. This can result in weight increase and tiredness. You will be checked for thyroid hormone levels while you are taking EUROPAN 200 mg. Tell your doctor if you notice significant weight gain or tiredness.

- Blurry or impaired vision

  EUROPAN 200 mg can cause separation or tear of the lining of the back part of the eye (retinal detachment or tear). This can result in blurry or impaired vision. Tell your doctor if you notice any change in your vision.

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:

Frequent side effects:

- infections
- decrease in the number of blood platelets (seen in blood tests)
- decrease in the number of white blood cells (seen in blood tests)
- underactive thyroid gland (seen in blood tests)
- loss of appetite
- abnormally low body weight (anorexia)
- decrease in phosphate in the blood (seen in blood tests)
- changes in the levels of other different chemicals / enzymes in the blood. (seen in blood tests)
- dehydration
- difficulty sleeping
- taste disturbance or loss of taste
- headache

- dizziness
- lack of energy, feeling weak or tired
- tingling or prickling, “pins-and-needles” sensation often in the arms, hands, legs or feet
- numbness of hands or feet
- blurred vision
- high blood pressure
- hot flushes
- nose bleeds
- diarrhoea
- dry mouth or mouth ulcers
- increase in bilirubin (a substance produced by the liver) (seen in blood tests)
- changes in hair colour
- loss of skin pigment
- muscle, joint, tendon or chest pain, muscle spasms
- protein in the urine (seen in urine tests)
- feeling or being sick (nausea or vomiting)
- stomach pain
- weight loss
- sore mouth
- unusual hair loss or thinning
- skin rash, possibly involving peeling of the skin
- redness and swelling of the palms of the hands or soles of the feet
- increase in liver enzymes (seen in blood tests)
- decrease in albumin in the blood (seen in blood tests)
- indigestion, bloating, flatulence
- abnormal drowsiness
- chest pain, shortness of breath, leg pain, and swelling of the legs/feet. These could be signs of a blood clot in your body (thromboembolism). If the clot breaks off, it may travel to your lungs and this may be life threatening or even fatal.
- heart becomes less effective at pumping blood around the body (cardiac dysfunction)

- slow heartbeat
- high blood pressure
- hot flush / flushing of skin
- sudden shortness of breath, especially when accompanied with sharp pain in the chest and /or rapid breathing (pulmonary embolism)
- nose bleeds
- hoarseness
- shortness of breath
- cough
- coughing up blood
- diarrhoea
- nausea
- vomiting
- stomach pain
- sores in the mouth (stomatitis)
- heartburn (dyspepsia)
- gassiness
- bloating
- mouth ulcers
- dry mouth
- increase in bilirubin levels in the blood (see in blood tests)
- liver disease
- change in hair colour
- redness, swelling, pain, blisters on the palms of the hands and/or the soles of the feet (hand-foot symdrome)
- hair loss
- rash
- skin lightening
- skin dryness, redness or itchiness
- excessive sweating

- joint and muscle pain
- muscle twitch or spasm
- increase protein levels in urine (seen in urine tests)
- swelling caused by fluid of face, hands, ankles, feet or eyelids
- chest pain
- abnormal liver function (seen in blood tests)
- weight loss
- increase in creatinine (a substance produced in muscles) (seen in blood or urine tests)
- increase in lipase (an enzyme involved in digestion) (seen in blood tests)
- decrease in white blood cell count (seen in blood tests)
- increase in thyroid stimulating hormone (see in blood tests)
- increae in urea in the blood (see in blood tests)

Less frequent side effects:

- infection of the gums
- inflammation of the lining of the abdominal cavity (peritonitis)
- tumour pain
- increase in the number of red blood cells
- decrease in magnesium in the blood (seen in blood tests)
- tumour lysis syndrome resulting from a fast breakdown of cancer cells
- loss of sensation or feeling in one or more parts of your body (hypoaesthesia)
- temporary fall in blood supply to the brain (transient ischaemic attack)
- sleepiness
- stroke
- swelling of the brain (posterior reversible encephalopathy/ reversible posterior leukoencephalopathy syndrome)
- change in the colour of eyelashes
- retinal tear (detachments)
- decrease in heart rate
- interruption of blood supply to part of the heart or heart attack (myocardial infarction)

- heart failure
- partial interruption of blood supply to part of the heart (myocardial ischaemia)
- sudden sharp increase in blood pressure (hypertensive crisis)
- severe bleeding in the digestive system (such as stomach, oesophagus or intestine), or the kidneys, vagina and brain
- an enlargement and weakening of a blood vessel wall or a tear in a blood vessel wall (aneurysms and artery dissections)
- runny nose
- bleeding in the lung
- collapsed lung with air trapped in the space between the lung and chest, often causing shortness of breath (pneumothorax)
- inflammation of the lung (pneumonitis)
- inflammation of the pancreas (pancreatitis)
- bleeding from the rectum
- bloody stools
- bleeding in the stomach or bowels
- frequent bowel movements
- hole (perforation) in stomach or intestine
- bleeding from the mouth
- abnormal passages forming between parts of the intestine (fistula)
- vomiting blood
- yellowing of the skin or whites of the eyes (jaundice)
- liver failure/ damage
- change in nail colour
- peeling of skin
- increased sensitivity of the skin to sunlight
- rashes which may be itchy or inflamed (flat or raised spots or blisters)
- pain experienced in bones, muscles, ligaments, tendons, and nerves (musculoskeletal pain)
- bleeding in the bladder
- heavy or irregular menstrual periods

- sensation of coldness, with shivering
- increased in liver enzymes (seen in blood tests)
- decrease in blood sugar level (see in blood tests)
- heart rhythm disturbance (QT prolongation)
- abnormal thyroid function test (seen in blood tests)

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 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: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of EUROPAN 200 mg.

5. HOW TO STORE EUROPAN

Store at or below 25 °C.

Store all medicines out of reach of children.

Store in the original package / container.

Do not use this medicine after the expiry date which is stated on the packaging after "EXP". The expiry date refers to the last day of the month.

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 EUROPAN 200 mg contains:

The active substance is pazopanib (as hydrochloride).

The other ingredients are microcrystalline cellulose, povidone K-30, sodium starch glycolate, magnesium stearate, purified water, opadry YS-1-14762-A pink (titanium dioxide, hypromellose, macrogol, polysorbate 80, iron oxide red)

What EUROPAN 200 mg looks like and contents of the pack

EUROPAN 200 mg is a pink film-coated capsule-shaped tablets, debossed with "173" on one side and plain on the other side.

The 30 or 90 or 120 tablets are packed in HDPE containers with child-resistant PP caps (with liner), and a desiccant cylinder.

Holder of Certificate of Registration

Eurolab (Pty) Ltd

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Woodmead, 2144

This leaflet was last revised in

Registration Number

To be allocated