Applicant: Teva Pharmaceuticals (Pty) Ltd	**Product name:** PAZOTEV 200 & PAZOTEV 400 **Dosage form & strength:** Each film-coated tablet contains pazopanib hydrochloride equivalent to 400 mg pazopanib

APPROVED PATIENT INFORMATION LEAFLET:

SCHEDULING STATUS: S4

PAZOTEV 200 and 400, film-coated tablets

Pazopanib

Sugar free

Read all of this leaflet carefully before you take PAZOTEV:

- 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.
- PAZOTEV 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 PAZOTEV IS AND WHAT IT IS USED FOR

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE PAZOTEV

3. HOW TO TAKE PAZOTEV

4. POSSIBLE SIDE EFFECTS

5. HOW TO STORE PAZOTEV

6. CONTENTS OF THE PACK AND OTHER INFORMATION

1. WHAT PAZOTEV IS AND WHAT IT IS USED FOR:

PAZOTEV 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.

PAZOTEV 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 PAZOTEV:

Do not take PAZOTEV:

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

Warnings and precautions:

Take special care with PAZOTEV:

- if you have liver disease
- if you have had prior collapse of a lung
- if you have had heart failure or a heart attack
- if you have heart disease
- if you have had problems with bleeding, blood clots or narrowing of the arteries
- if you have or have had an aneurysm (enlargement and weakening of a blood vessel wall) or a tear in a blood vessel wall
- if you have had stomach or bowel problems such as perforation (hole) or fistula (abnormal passages forming between parts of the intestine)
- if you have thyroid problems
- if you have problems with your kidney function

High blood pressure and PAZOTEV:

PAZOTEV can raise your blood pressure. Your blood pressure will be checked before you take PAZOTEV and while you are taking it. If you have high blood pressure you will be treated with medicines to reduce it.

- Tell your doctor if you have high blood pressure.

If you are going to have an operation:

Your doctor will stop PAZOTEV at least 7 days before your operation as it may affect wound healing. Your treatment will be restarted when the wound has adequately healed.

Conditions you need to look out for:

PAZOTEV can make some conditions worse or cause serious side effects. You must look out for certain symptoms while you are taking PAZOTEV to reduce the risk of any problems. See **section 4**.

Children and adolescents:

PAZOTEV is not recommended for people aged under 18.

Other medicines and PAZOTEV:

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

Some medicines may affect how PAZOTEV works or make it more likely that you'll have side effects. PAZOTEV can also affect how some other medicines work. These include:

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

- simvastatin and possibly other statins (used to treat high cholesterol levels)
- medicines that reduce stomach acid. The type of medicine that you are taking to reduce your stomach acid (e.g., proton pump inhibitor, H_2 antagonists or antacids) may affect how PAZOTEV is taken. Please consult your doctor or nurse for advice.

PAZOTEV with food and drink:

Don't take PAZOTEV 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 PAZOTEV as this may increase the chance of side effects.

Pregnancy, breastfeeding and fertility:

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 PAZOTEV.

Use a reliable method of contraception while you're taking PAZOTEV, and at least for 2 weeks after, to prevent pregnancy.

If you do become pregnant during treatment with PAZOTEV, tell your doctor.

Male patients (including those who have had vasectomies) who have partners who are either pregnant or who could become pregnant (including those who use other methods of contraception) should use condoms during sexual intercourse while taking PAZOTEV and for at least 2 weeks after the last dose.

PAZOTEV is not recommended if you are pregnant. The effect of PAZOTEV during pregnancy is not known.

Don’t breastfeed while taking PAZOTEV. It is not known whether the ingredients in PAZOTEV pass into breast milk. Talk to your doctor about this.

Fertility may be affected by treatment with PAZOTEV. Talk to your doctor about this.

Driving and using machines:

PAZOTEV can have side effects that may affect your ability to drive or use machines.
Avoid driving or using machines if you feel dizzy, tired or weak, or if your energy levels are low.

It is not always possible to predict to what extent PAZOTEV may interfere with the daily activities of a patient. Patients should ensure that they do not engage in driving or use machines until they are aware of the measure to which PAZOTEV affects them.

PAZOTEV contains sodium:

This medicine contains less than 1 mmol sodium (23 mg) per film-coated tablet, that is to say essentially ‘sodium-free’.

3. HOW TO TAKE PAZOTEV:

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

The usual dose is two PAZOTEV 400 mg tablets (800 mg pazopanib) taken once a day. This is the maximum dose per day. Your doctor may need to reduce your dose if you get side effects.

Don’t take PAZOTEV with food. Take it at least two hours after a meal, or one hour before a meal (see **section 3**). For example, you could take it two hours after breakfast or one hour before lunch. Take PAZOTEV 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.

Your doctor will tell you how long your treatment with PAZOTEV will last. If you have the impression that the effect of PAZOTEV is too strong or too weak, tell your doctor or pharmacist.

If you take more PAZOTEV than you should:

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 PAZOTEV:

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

If you stop taking PAZOTEV:

Don’t stop unless your doctor advises you to.

4. POSSIBLE SIDE EFFECTS:

PAZOTEV can have side effects.

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

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

- swelling of the hands, feet, ankles, face, lips and mouth or throat, which may cause difficulty in swallowing or breathing,
- rash or itching,
- fainting.

These are all very serious side effects. If you have them, you may have had a serious reaction to PAZOTEV. 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:

- **Swelling of the brain:**

  which may be life threatening and symptoms include:

- loss of speech
- change of vision
- seizure (fits)
- confusion
- high blood pressure

- **Hypertensive crisis:**

  (sudden and severe rise in blood pressure), 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)
- fainting

- **Heart condition:**

  PAZOTEV 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
- leg swelling

- PAZOTEV 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 heartbeat, such as beating too fast or too slow.

- **Stroke:**

PAZOTEV 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
- dizziness

- **Bleeding:**

  PAZOTEV 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
- coughing or vomiting up blood

- **Perforation and fistula:**

  PAZOTEV 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
- development of a hole (perforation) in the stomach, intestine or bowel from which bloody or foul-smelling pus is released

- **Liver problems:**

  PAZOTEV 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 PAZOTEV. 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)
- bruising easily

- **Blood clots:**

  PAZOTEV 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
- swelling of your arms and hands or legs and feet

  PAZOTEV 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)
- decrease in urine output

- **Tumour lysis syndrome:**

  PAZOTEV 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 immediately if you get any of these symptoms.

- **Infections:**

  Infections occurring while you take PAZOTEV 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, scrapes or wounds that are red, warm, swollen or painful

- **Lung inflammation:**

  PAZOTEV 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 PAZOTEV.

- **Thyroid problems:**

  PAZOTEV 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 PAZOTEV.

- **Blurry or impaired vision:**

PAZOTEV 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 serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:

Frequent side effects:

- infections and an abnormally low count of a type of white blood cell (neutrophils)
- decrease in the number of blood platelets (cells that help blood to clot)
- decrease in disease-fighting cells
- underactive thyroid gland
- decreased appetite, dehydration, low levels of serum phosphate
- eating disorder (anorexia)
- difficulty sleeping
- taste disturbance or loss of taste, headache, dizziness, lack of energy, feeling weak or tired
- tingling, weakness or numbness of the hands, arms, legs or feet
- blurred vision
- blockage of blood flow to the heart muscle, heart rhythm disorder causing fast heartbeats
- high blood pressure, hot flushes, reddening of the face
- 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
- nose bleeding, hoarseness, shortness of breath, coughing up blood, chest pain
- diarrhoea

- feeling or being sick (nausea or vomiting)
- stomach pain, indigestion, bloating, flatulence, redness and inflammation of the oral mucosa (stomatitis)
- dry mouth or mouth ulcers, inflamed or sore mouth
- chemical-driven liver damage, abnormal liver function, increase in bilirubin (a substance produced by the liver)
- changes in hair colour, unusual hair loss or thinning, loss of skin pigment
- redness and swelling of the palms of the hands or soles of the feet
- burning, prickling, itching or tingling skin sensation, sensation of coldness, with shivering
- skin disorders, redness, itching, dry skin, excessive sweating
- muscle, joint, tendon or chest pain, muscle spasms
- protein in the urine
- abnormal heavy bleeding at menstruation and between periods, vaginal bleeding unrelated to menstruation
- tiredness, swelling caused by fluid of face, hands, ankles, feet or eyelids
- an inflammation of the mucosa with burning or tingling sensation
- decreased weight, decreased white blood cell count, increased blood pressure
- side effects that may show up in your blood or urine tests:

  underactive thyroid gland

  abnormal liver function

  increase in bilirubin (a substance produced by the liver)

  increase in lipase (an enzyme involved in digestion)

  increase in creatinine (a substance produced in muscles)

  increase in enzymes found in the liver and kidney

  increase in enzymes released when your liver or muscles are damaged

increase in the digestive enzyme (amylase)

increase in gamma-glutamyltransferase, an enzyme found throughout the body changes in the levels of other different chemicals/enzymes in the blood.

Your doctor will inform you of the results of the blood tests.

Less frequent side effects:

- inflammation of the lining of the abdominal cavity (peritonitis)
- inflammation of the gums
- tumour pain
- blood clots accompanied by a decrease in red blood cells and cells involved in clotting (thrombotic microangiopathy, TMA). These may harm organs such as the brain and kidneys
- increase in the number of red blood cells
- decrease in magnesium levels in your blood
- tumour lysis syndrome resulting from a fast breakdown of cancer cells
- stroke (cerebrovascular accident)
- hypoaesthesia (numbness), temporary fall in blood supply to the brain (transient ischaemic attack)
- abnormal drowsiness
- posterior reversible encephalopathy and leukoencephalopathy (swelling in the brain accompanied by headaches, vision problems and seizure)
- damage to the retina (tissue at the back of the eye)
- eyelash discolouration
- slow heartbeat
- interruption of blood supply to part of the heart or heart attack (myocardial infarction)

- fast heart rhythm (*Torsades de Pointes*)
- heart failure (cardiac dysfunction)
- sudden sharp increase in blood pressure (hypertensive crisis)
- runny nose
- collapsed lung with air trapped in the space between the lung and chest, often causing shortness of breath (pneumothorax)
- inflammation of the lung (pneumonitis), leaking of blood from blood vessels in the windpipe or airways into the main lung
- inflammation of the pancreas (pancreatitis)
- bleeding from the anus, usually with stools
- vomiting blood
- severe bleeding in the digestive system (such as mouth, stomach, oesophagus or intestine), or the kidneys, vagina, urinary tract and brain
- bleeding into the retroperitoneal space
- abnormal passages forming between parts of the intestine (fistula)
- hole (perforation) in stomach or intestine
- frequent bowel movements, black tarred stools, rectal bleeding
- yellowing of the skin or whites of the eyes (jaundice)
- liver inflamed, not working well or damaged
- nail disorders, rashes which may be itchy or inflamed (flat or raised spots or blisters)
- increased sensitivity of the skin to sunlight
- decreased feeling or sensitivity, especially in the skin
- pain in the muscles, bones, ligaments, tendons, and nerves
- chills, erosions, ulceration of the mucous membranes
- heart rhythm disturbance (QT prolongation)

- increased liver enzymes, decreased blood glucose
- blood pressure changes, abnormal thyroid test function.

Frequency unknown:

- an enlargement and weakening of a blood vessel wall or a tear in a blood vessel wall (aneurysms and artery dissections).

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 Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website. By reporting side effects, you can help provide more information on the safety of PAZOTEV.

5. HOW TO STORE PAZOTEV:

Store all medicines out of reach of children.

Store at or below 25 °C.

Store in a dry place and protect from light and moisture.

Do not take the tablets after the expiry date which is printed on the outside of the pack.

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 PAZOTEV contains:

The active substance is pazopanib.

The other ingredients are:

Tablet core: Cellulose, microcrystalline, magnesium stearate, povidone K-30, sodium starch glycolate.

Tablet coating: Hypromellose, iron oxide red (E172), macrogol 400, polysorbate 80, titanium dioxide (E171).

What PAZOTEV looks like and contents of the pack:

PAZOTEV 200: Capsule-shaped, pink, film-coated tablet with '200' debossed on one side, with dimensions 14,3 mm x 5,7 mm ± 5 %.

PAZOTEV 400: Capsule-shaped, white, film-coated tablet with '400' debossed on one side, with dimensions 18,0 mm x 7,1 mm ± 5 %.

PAZOTEV 200 and 400 film-coated tablets are packed in aluminium- PVC/PE/PVDC blisters or in white, plastic high-density polyethylene (HDPE) bottles with screwed mouth that are stoppered with a white, plastic (PP) child resistant cap.

Holder of Certificate of Registration:

Teva Pharmaceuticals (Pty) Ltd.

Maxwell Office Park

Magwa Crescent West

Waterfall City

Midrand

Gauteng

2090

South Africa

Tel: (011) 055 0200

Registration numbers:

PAZOTEV 200: 57/26/0150

PAZOTEV 400: 57/26/0151

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