PAZOTRI® (PAZOPANIB) F.C. TABLETS

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PAZOTRI® (PAZOPANIB) F.C. TABLETS FOR ORAL USE
Read this patient information carefully before you start taking Pazotri® because it answers some common questions about Pazotri®. This medication is prescribed for your current condition, therefore do not use it, in similar cases and do not recommend it to others.
To report SUSPECTED ADVERSE REACTIONS, contact Noavaran Daroui Kimia Co. at +982188012946 or send email to medical@kimia-pharma.co

Read this patient Information carefully before you start taking Pazotri® because it contains important information for you. This leaflet does not take the place of talking with your healthcare provider about your medical condition or treatment.

COMPOSITION

Each film coated tablet Pazotri® 200 mg contains: Pazopanib (as HCl) 200 mg.
Each film coated tablet Pazotri® 400 mg contains: Pazopanib (as HCl) 400 mg.

Mechanism of action

Pazotri® is a small-molecule tyrosine kinase inhibitor of growth factor receptors associated with angiogenesis and tumor cell proliferation.

Pharmacokinetic

Absorption

Pazotri® is absorbed orally with median time to achieve peak concentrations of 2 to 4 hours after a dose.

Distribution

Binding of Pazotri® to human plasma protein in vivo was greater than 99% with no concentration dependence over the range of 10 to 100 mcg/mL. In vitro studies suggest that Pazotri® is a substrate for P-gp and BCRP.

Metabolism

In vitro studies demonstrated that Pazotri® is metabolized by CYP3A4 with a minor contribution from CYP1A2 and CYP2C8.

Excretion

Pazotri® has a mean half-life of 31 hours after administration of the recommended dose of 800 mg. Elimination is primarily via feces with renal elimination accounting for < 4% of the administered dose.

INDICATION

Pazotri® is a kinase inhibitor indicated for the treatment of adults with:

- Advanced renal cell carcinoma.
- Advanced soft tissue sarcoma who have received prior chemotherapy.

The safety and effectiveness of Pazotri® in pediatrics patients have not been established.

Dosage and administration

- 800 mg orally once daily without food (at least 1 hour before or 2 hours after a meal).
- Baseline moderate hepatic impairment – 200 mg orally once daily. Not recommended in patients with severe hepatic impairment.

Severe and fatal hepatotoxicity has been observed in clinical trials. Monitor hepatic function and interrupt, reduce, or discontinue dosing as recommended.

Side effects / Adverse reactions

It should be noted that these side effects do not occur in all patient. **These are not all the possible side effects of Pazotri®. For more information, ask your healthcare provider or pharmacist.** Pazotri® May cause serious side effects including:

- **Irregular or fast heartbeat or fainting.**
- **Heart failure.** This is a condition where your heart does not pump as well as it should and may cause you to have shortness of breath.
- **Heart attack or stroke.** Heart attack and stroke can happen with Pazotri® and may cause death. Symptoms may include: chest pain or pressure, pain in your arms, back, neck or jaw, shortness of breath, numbness or weakness on one side of your body, trouble talking, headache, or dizziness.
- **Blood clots.** Blood clots may form in a vein, especially in your legs (deep vein thrombosis or DVT). Pieces of a blood clot may travel to your lungs (pulmonary embolism). This may be life-threatening and cause death. Symptoms may include: new chest pain, trouble breathing or shortness of breath that starts suddenly, leg pain, and swelling of the arms and hands, or legs and feet, a cool or pale arm or leg.
- **Thrombotic microangiopathy (TMA) including thrombotic thrombocytopenia purpura (TTP) and hemolytic uremic syndrome (HUS).** TMA is a condition involving blood clots that can happen while taking Pazotri®. TMA is accompanied by a decrease in red blood cells and cells that are involved in clotting. TMA may harm organs such as the brain and kidneys.
- **Bleeding problems.** These bleeding problems may be severe and cause death. Symptoms may include: unusual bleeding, bruising, or wounds that do not heal.
- **Tear in your stomach or intestinal wall (perforation) or an abnormal connection between two parts of your gastrointestinal tract (fistula).** Symptoms may include: pain, swelling in your stomach area, vomiting blood, and black sticky stools.
- **Lung problems.** Pazotri® may cause lung problems that may lead to death. Tell your healthcare provider right away if you get a cough that will not go away or shortness of breath.
- **Posterior Reversible Encephalopathy Syndrome (PRES).** PRES is a condition that can happen while taking Pazotri® that may cause death. Symptoms may include: headaches, seizures, lack of energy, confusion, high blood pressure, loss of speech, blindness or changes in vision, and problems thinking.
- **Arterial Thromboembolic Events.** Arterial thromboembolic events have been observed and can be fatal. Pazotri® has not been studied in patients who have had an arterial thromboembolic event within the previous 6 months. Permanently discontinue Pazotri® in case of an arterial thromboembolic event.
- **High blood pressure. High blood pressure can happen with Pazotri®, including a sudden and severe rise in blood pressure which may be life-threatening.** These blood pressure increases usually happen in the first several months of treatment. Your blood pressure should be well controlled before you start taking Pazotri®. Your healthcare provider should begin checking your blood pressure within 1 week of you starting Pazotri® and often during treatment to make sure that your blood pressure is well controlled. **Have someone call your healthcare provider or get medical help right away** for you, if you get symptoms of a severe increase in blood pressure, including: severe chest pain, severe headache, blurred vision, confusion, nausea and vomiting, severe anxiety, shortness of breath, seizures, or you pass out (become unconscious).
- **Thyroid problems.** Your healthcare provider should check you for this during treatment with Pazotri®.
- **Tumor Lysis Syndrome (TLS).** TLS is a condition that can happen during treatment with Pazotri® that may cause death. TLS is caused by a fast breakdown of cancer cells. Your healthcare provider may do a blood test to check you for TLS. Call your healthcare provider or get emergency medical help right away if you develop any of these symptoms during treatment with Pazotri®: irregular heartbeat, seizures, confusion, muscle cramps or spasms, or a decrease in urine output.
- **Protein in your urine.** Your healthcare provider will check you for this problem. If there is too much protein in your urine, your healthcare provider may tell you to stop taking Pazotri®.
- **Serious infections. Serious infections can happen with Pazotri® and can cause death.** Symptoms of an infection may include: fever, cold symptoms, such as runny nose or sore throat that do not go away, flu symptoms, such as cough, tiredness, and body aches, pain when urinating, cuts, scrapes or wounds that are red, warm, swollen or painful.
- **Collapsed lung (pneumothorax).** A collapsed lung can happen with Pazotri®. Air may get trapped in the space between your lung and chest wall. This may cause you to have shortness of breath.
- **Risk of impaired wound healing.** Withhold Pazotri® for at least 1 week prior to elective surgery. Do not administer for at least 2 weeks following major surgery and until adequate wound healing. The safety of resumption of Pazotri® after resolution of wound healing complications has not been established.
- Depigmentation of the hair or skin may occur during treatment with Pazotri®.

The most common side effects

The most common side effects in people who take Pazotri® include:
• Diarrhea • Change in hair color • Nausea or vomiting • Loss of appetite

Other common side effects in people with advanced soft tissue sarcoma who take Pazotri® include:
• Decreased weight • feeling tired • Tumor pain • Muscle or bone pain • Stomach pain
• Headache • Taste changes • Trouble breathing • Change in skin color

Call your doctor for medical advice about side effect:
Pazotri® can cause serious liver problems including death. Your healthcare provider will do blood tests to check your liver before start and while you take Pazotri®. Tell your healthcare provider right away if you get any of these signs of liver problems during treatment with Pazotri®:
• yellowing of your skin or the whites of your eyes (jaundice) •dark urine • loss of appetite • pain on the right side of your stomach area (abdomen) • Tiredness • bruise easily •nausea or vomiting

Drug interaction

Tell your healthcare provider if you:

- take medicines that can affect how your liver enzymes work such as:
  - certain antibiotics (used to treat infections)
  - certain medicines used to treat depression
  - certain medicines used to treat HIV-1
  - medicines used to treat irregular heart beats
- take a medicine that contains simvastatin to treat high cholesterol levels
- take medicines that reduce stomach acid (e.g., esomeprazole)
- drink grapefruit juice. Do not eat grapefruit or drink grapefruit juice during treatment with Pazotri®. Grapefruit products may increase the amount of Pazotri® in your body.

Tell your healthcare provider about all the medicines you take including prescription and over-the-counter medicines, vitamins, and herbal supplements. Pazotri® may affect the way other medicines work and other medicines may affect how Pazotri® works.

Warnings

Before you take Pazotri®, tell your healthcare provider if you:

- Have heart problems or an irregular heartbeat including QT prolongation.
- Have or had liver problems. You may need a lower dose of Pazotri®, or your healthcare provider may prescribe a different medicine to treat your advanced renal cell cancer or advanced soft tissue sarcoma.
- Have high blood pressure.
- Have a history of a stroke.
- Have headaches, seizures, or vision problems.
- Have coughed up blood in the last 6 months.
- Had bleeding of your stomach or intestines in the last 6 months.
- Have a history of a tear (perforation) in your stomach or intestine, or an abnormal connection between two parts of your gastrointestinal tract (fistula).
- Have had blood clots in a vein or in the lung.
- Have thyroid problems.
- Had recent surgery or are going to have surgery.
- Have problems with your kidney function.
- Have any other medical conditions.
- Are pregnant or plan to become pregnant.
- Are breastfeeding or plan to breastfeed.

Contraindication

Pazotri® is not recommended in patients with:

- Severe hepatic impairment.
- Patients who have a history of hemoptysis, cerebral, or clinically significant gastrointestinal hemorrhage in the past 6 months and should not be used in those patients.

Use with caution in patients:

- Patients at risk for gastrointestinal perforation or fistula
- Patients at risk for arterial thrombotic events
- Hypertension

Missed dose

If you miss a dose of Pazotri® take it as soon as you remember. Do not take it if it is close (within 12 hours) to your next dose. Just take the next dose at your regular time. Do not take more than 1 dose of Pazotri® at a time.

OVERDOSE

Treatment of overdose with Pazotri® should consist of general supportive measures. There is no specific antidote for over dosage of Pazotri®.

Pregnancy and lactation

You should not become pregnant while you are taking Pazotri®. You should use effective birth control during treatment with Pazotri® and for at least 2 weeks after your final dose of Pazotri®. Males (including one who has had a vasectomy) with a sexual partner who is pregnant, or who could become pregnant (including those who use other forms of birth control) should use condoms during treatment with Pazotri® and for at least 2 weeks after the last dose of Pazotri®. It is not known if Pazotri® passes into your breast milk. Do not breastfeed during treatment with Pazotri® and for 2 weeks after the final dose.

Patient information

- Take Pazotri® exactly as your healthcare provider tells you. Your healthcare provider will tell you how much Pazotri® to take.
- Do not crush Pazotri® tablets.
- Take Pazotri® on an empty stomach, at least 1 hour before or 2 hours after food.
- Do not eat grapefruit or drink grapefruit juice during treatment with Pazotri®. Grapefruit products may increase the amount of Pazotri® in your body.
- Your healthcare provider will test your urine, blood, and heart before you start and while you take Pazotri®.

Storage

- Store Pazotri® tablets below 30°C.
- Keep Pazotri® in the original container with the lid tightly closed.
- Keep out of the reach of children.
- Keep away from light and moisture.
- Use appropriate precautions for handling and disposal of cytotoxic drugs.

Packaging

Bottle of 30 F.C. Tablets

References

www.accessdata.fda.gov/drugsatfda_docs/label/2020/022465s028lbl.pdf

Manufactured By
Noavaran Daroui Kimia Co. Tehran, Iran.
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