Zotrix (Pazopanib Hydrochloride INN) Innerleaf design

Color: Pantone 185 C & Metallic Coated 8483 C

L - 300 mm X W - 195 mm

Zotrix™
Pazopanib Hydrochloride INN

Jenphar
Bangladesh

جـنـفـار
بنغلاديش

Composition:

Zotrix 200 Tablet: Each film coated tablet contains Pazopanib Hydrochloride INN equivalent to Pazopanib 200 mg.

Zotrix 400 Tablet: Each film coated tablet contains Pazopanib Hydrochloride INN equivalent to Pazopanib 400 mg.

Clinical Pharmacology:

Pazopanib is a multi-tyrosine kinase inhibitor of vascular endothelial growth factor receptor (VEGFR-1, VEGFR-2, VEGFR-3), platelet-derived growth factor receptor (PDGFR-α and -β), fibroblast growth factor receptor (FGFR-1 and-3), cytokine receptor (Kit), interleukin-2 receptor inducible T-cell kinase (Itk), leukocyte-specific protein tyrosine kinase (Lck), and transmembrane glycoprotein receptor tyrosine kinase (c-Fms).

Indication:

Pazopanib tablet is indicated for the treatment of patients with-
1. advanced renal cell carcinoma (RCC) and
2. advanced soft tissue sarcoma (STS) who have received prior chemotherapy.

Dose & Administration:

Recommended Dosing: 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.

Contra-indication: None.

Warning and precaution:

- Increases in serum transaminase levels and bilirubin were observed. Severe and fatal hepatotoxicity has occurred. Measure liver chemistries before the initiation of treatment and regularly during treatment.
- Prolonged QT intervals and torsades de pointes have been observed. Use with caution in patients at higher risk of developing QT interval prolongation. Monitoring electrocardiograms and electrolytes should be considered.
- Cardiac dysfunction such as congestive heart failure and decreased left ventricular ejection fraction (LVEF) has occurred. Monitor blood pressure and manage hypertension promptly. Baseline and periodic evaluation of LVEF is recommended in patients at risk of cardiac dysfunction.
- Fatal hemorrhagic events have been reported. Pazopanib has not been studied in 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.
- Arterial thromboembolic events have been observed and can be fatal. Use with caution in patients who are at increased risk for these events.
- Venous thromboembolic events (VTE) have been observed, including fatal pulmonary emboli (PE). Monitor for signs and symptoms of VTE and PE.
- Thrombotic microangiopathy (TMA), including thrombotic thrombocytopenic purpura (TTP) and hemolytic uremic syndrome (HUS) has been observed. Permanently discontinue Pazopanib if TMA occurs.
- Gastrointestinal perforation or fistula has occurred. Fatal perforation events have occurred. Use with caution in patients at risk for gastrointestinal perforation or fistula.
- Reversible Posterior Leukoencephalopathy Syndrome (RPLS) has been observed and can be fatal. Permanently discontinue Pazopanib in patients developing RPLS.
- Hypertension including hypertensive crisis has been observed. Blood pressure should be well controlled prior to initiating Pazopanib. Monitor blood pressure within one week after starting Pazopanib and frequently thereafter.
- Interruption of therapy with Pazopanib is recommended in patients undergoing surgical procedures.
- Hypothyroidism may occur. Monitoring of thyroid function tests is recommended.
- Proteinuria: Monitor urine protein. Interrupt treatment for 24-hour urine protein ≥3 grams and discontinue for repeat episodes despite dose reductions.
- Infection: Serious infections (with or without neutropenia), some with fatal outcome, have been reported. Monitor for signs and symptoms and treat active infection promptly. Interrupt or discontinue Pazopanib.
- Animal studies have demonstrated Pazopanib can severely affect organ growth and maturation during early post-natal development. The safety and effectiveness in pediatric patients have not been established.
- Pazopanib can cause fetal harm when administered to a pregnant woman. Women of childbearing potential should be advised of the potential hazard to the fetus and to avoid becoming pregnant while taking Pazopanib.

Side Effects:

The most common adverse reactions in patients with advanced renal cell carcinoma (≥20%) are diarrhea, hypertension, hair color changes (depigmentation), nausea, anorexia, and vomiting. The most common adverse reactions in patients with advanced soft tissue sarcoma (≥20%) are fatigue, diarrhea, nausea, decreased weight, hypertension, decreased appetite, hair color changes, vomiting, tumor pain, dysgeusia, headache, musculoskeletal pain, myalgia, gastrointestinal pain, and dyspnea.

Drug Interaction:

- *CYP3 A4 Inhibitors:* Avoid use of strong CYP3A4 inhibitors. If co-administration is warranted, reduce the dose of Pazopanib to 400 mg.
- *CYP3A4 Inducers:* Consider an alternate concomitant medication with no or minimal enzyme induction potential or avoid Pazopanib.
- *CYP Substrates:* Concomitant use of Pazopanib with agents with narrow therapeutic windows that are metabolized by CYP3A4, CYP2D6 or CYP2C8 is not recommended.
- Concomitant use of Pazopanib and simvastatin increases the risk of ALT elevations and should be undertaken with caution and close monitoring.
- *Drugs that raise Gastric pH:* Avoid concomitant use of Pazopanib with drugs that raise gastric pH. Consider short-acting antacids in place of proton pump inhibitors (PPIs) and H2 receptor antagonists. Separate antacid and Pazopanib dosing by several hours.

Use In Specific Populations:

Pregnancy Category D. Pazopanib can cause fetal harm when administered to a pregnant woman. There are no adequate and well-controlled studies of Pazopanib in pregnant women.

It is not known whether Pazopanib is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from Pazopanib, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use: The safety and effectiveness of Pazopanib in pediatric patients have not been established.

Geriatric Use: No overall differences in safety or effectiveness of Pazopanib were observed between these patients and younger patients

Hepatic Impairment: An analysis of data from a pharmacokinetic study of Pazopanib in patients with varying degrees of hepatic dysfunction suggested that no dose adjustment is required in patients with mild hepatic impairment.

Renal Impairment: Renal impairment is not expected to influence Pazopanib exposure, and dose adjustment is not necessary.

Overdose:

Treatment of overdose with Pazopanib should consist of general supportive measures. There is no specific antidote for overdosage of Pazopanib.

Storage:

Store in a cool and dry place below 30° C, protect from light. Keep out of the reach of children.

Packing:

Zotrix 200 mg Tablet: Each box contains 28 tablets and one packet silica gel in a sealed HDPE container.

Zotrix 400 mg Tablet: Each box contains 14 tablets and one packet silica gel in a sealed HDPE container.

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Manufactured by:
Jenphar Bangladesh Ltd.
Sreepur, Gazipur, Bangladesh.