Pazorest

Pazopanib Hydrochloride INN

Everest

COMPOSITION

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

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), lymphocyte-specific protein tyrosine kinase (Lck), and transmembrane glycoprotein receptor tyrosine kinase (cFms).

INDICATIONS AND USAGE

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

- advanced renal cell carcinoma (RCC)
- advanced soft tissue sarcoma (STS) who have received prior chemotherapy

Limitations of Use: The efficacy of Pazopanib for the treatment of patients with adipocytic STS or gastrointestinal stromal tumors has not been demonstrated.

DOSAGE AND ADMINISTRATION

Recommended dose: The recommended dosage is 800 mg orally once daily without food (at least 1 hour before or 2 hours after a meal) until disease progression or unacceptable toxicity.

Swallow tablets whole. Do not crush tablets due to the potential for increased rate of absorption, which may affect systemic exposure.

If a dose is missed, it should not be taken if it is < 12 hours until the next dose.

Dosage Modifications for Adverse Reactions

Recommended Dose Reductions of Pazopanib for Adverse Reactions

Dose reduction	For RCC	For STS
First	400 mg orally once daily	600 mg orally once daily
Second	200 mg orally once daily	400 mg orally once daily

Permanently discontinue Pazopanib in patients unable to tolerate the second dose reduction.

CONTRAINDICATIONS

None.

WARNINGS AND PRECAUTIONS

Hepatic Toxicity

Liver should be monitored regularly during treatment.

QT Prolongation and Torsades de Pointes

Patients who are at significant risk of developing QTc prolongation should be monitored and taking taking antiarrhythmics or other medications that may prolong QT interval.

Cardiac Dysfunction

Blood pressure and clinical signs or symptoms of congestive heart failure should be monitored and managed as appropriate.

Hemorrhagic Events

Pazopanib should be withheld and resumed at reduced dose or should be permanently discontinued based on severity of hemorrhagic events.

Arterial Thromboembolic Events

Pazopanib should be discontinued permanently in case of an arterial thromboembolic event.

Venous Thromboembolic Events

Pazopanib should be withheld and then resumed at same dose or should be permanently discontinued based on severity of Venous Thromboembolic Events.

Thrombotic Microangiopathy (TMA)

Signs and symptoms of Thrombotic Microangiopathy should be monitored and should be discontinued permanently in patients developing TMA.

Interstitial Lung Disease/Pneumonitis

Patients with pulmonary symptoms indicative of ILD/ pneumonitis should be monitored. Pazopanib should be permanently discontinued in patients who develop ILD or pneumonitis.

Posterior Reversible Encephalopathy Syndrome

Pazopanib should be permanently discontinued in patients who develop Posterior Reversible Encephalopathy Syndrome (PRES).

Hypertension

Blood pressure should be monitored as clinically indicated and should be initiated and adjusted with antihypertensive therapy as appropriate.

Risk of Impaired Wound Healing

Pazopanib should not be administered for at least 2 weeks following major surgery and until adequate wound healing.

Proteinuria

Baseline and periodic urinalysis should be perfomed during treatment with follow up measurement of 24-hour urine protein as clinically indicated.

SIDE EFFECTS

The most common adverse reactions reported are diarrhea, hypertension, hair color changes (depigmentation), nausea, anorexia, vomiting, fatigue, decreased weight, decreased appetite, tumor pain, musculoskeletal pain, headache, dysgeusia, dyspnea, and skin hypopigmentation.

DRUG INTERACTIONS

Effect of Other Drugs on Pazopanib

Strong CYP3A4 Inhibitors

Coadministration of Pazopanib with strong CYP3A4 inhibitors should be avoided or dose should be reduced as it increases pazopanib concentrations.

Strong CYP3A4 Inducers

Coadministration of Pazopanib with strong CYP3A4 inducers should be avoided or discontinued as it may decrease plasma Pazopanib concentrations.

Transporters

Coadministration of strong inhibitors of P-gp or BCRP should be avoided as it may increase Pazopanib concentrations.

Effects of Pazopanib on Other Drugs

CYP Substrates

The concomitant use of Pazopanib with agents with narrow therapeutic windows that are metabolized by CYP3A4, CYP2D6, or CYP2C8 is not recommended as it may result in inhibition of the metabolism of these products and create the potential for serious adverse reactions.

Concomitant Use With Simvastatin

Concomitant use of Pazopanib with simvastatin increases the incidence of ALT elevations and thus Pazopanib should be withheld and then resumed at reduced dose, or be permanently discontinued based on severity of hepatotoxicity.

Concomitant Use With Gastric Acid-Reducing Agents

Concomitant use of Pazopanib with esomeprazole, a PPI should be avoided as it decreases the exposure of Pazopanib.

Drugs That Prolong the QT Interval

Coadministration of Pazopanib should be avoided with drugs known to prolong the QT/QTc interval since it is associated with QTc interval prolongation.

USE IN SPECIFIC POPULATIONS

Pregnancy

Based on animal reproduction studies and its mechanism of action, Pazopanib can cause fetal harm when administered to a pregnant woman. There is no available data on Pazopanib use in pregnant women. Pregnant women should be informed about potential risk of using Pazopanib to fetus.

Lactation

There is no data on the presence of Pazopanib or its metabolites in either human milk or its effects on the breastfed infant or on milk production. Because of the potential for serious adverse reactions in breastfed infants, advise women not to breastfeed during treatment with Pazopanib and for 2 weeks after the final dose.

Females and Males of Reproductive Potential

Pazopanib can cause fetal harm when administered to a pregnant woman.

Pregnancy Testing

Verify pregnancy status of females of reproductive potential prior to starting treatment with Pazopanib.

Contraception

Females

Advise females of reproductive potential to use effective contraception during treatment with Pazopanib and for at least 2 weeks after the last dose.

Males

Advise males (including those who have had vasectomies) with female partners of reproductive potential to use condoms during treatment with Pazopanib and for at least 2 weeks after the last dose.

Infertility

Based on findings from animal studies, Pazopanib may impair fertility in females and males of reproductive potential while receiving treatment.

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 patients aged ≥ 65 years and younger patients.

Renal Impairment

No dose adjustment is recommended for patients with renal impairment.

Hepatic Impaired

No dose adjustment is required in patients with mild to moderate or severe hepatic impairment.

PHARMACEUTICAL INFORMATION

Storage Condition

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

HOW SUPPLIED

PAZOREST tablet: Each HDPE container contains 60 film coated tablets, each of which contains Pazopanib 200 mg.

Manufactured by
Everest Pharmaceuticals Ltd.
BSCIC I/A, Kanchpur, Narayanganj, Bangladesh
www.everestpharmabd.com

1901000200