Reganex

Regorafenib INN

Jenphar Bangladesh | جنفار بنغلاديش

Composition:
Reganex 40 Tablet: Each film coated tablet contains Regorafenib Monohydrate INN equivalent to Regorafenib 40 mg.

Pharmacology:
Regorafenib is a multikinase inhibitor; it targets kinases involved with tumor angiogenesis, oncogenesis, and maintenance of the tumor microenvironment which results in inhibition of tumor growth. Specifically, it inhibits VEGF receptors 1-3, KIT, PDGFR-alpha, PDGFR-beta, RET, FGFR1 and 2, TIE2, DDR2, TrkA, Eph2A, RAF-1. BRAF, $BRAF^{V600E}$, SAPK2, PTK5, and Abl.

Indications:
- Metastatic colorectal cancer (CRC) who have been previously treated with fluoropyrimidine, oxaliplatin and irinotecan-based chemotherapy, an anti-VEGF therapy, and, if RAS wild-type, an anti-EGFR therapy.
- Locally advanced, unresectable or metastatic gastrointestinal stromal tumor (GIST) who have been previously treated with imatinib mesylate and sunitinib malate.
- Hepatocellular carcinoma (HCC) who have been previously treated with sorafenib.

Dosage and Administration:
Recommended Dose: 160 mg orally, once daily for the first 21 days of each 28-day cycle. Continue treatmet until disease progression or unacceptable toxicity.

Contraindications:
None.

Warning and precaution:
Hepatotoxicity: Monitor liver function tests. Withhold and then reduce or discontinue Regorafenib based on severity and duration.

Infections: Withhold Regorafenib in patients with worsening or severe infections.

Hemorrhage: Permanently discontinue Regorafenib for severe or life-threatening hemorrhage.

Gastrointestinal perforation or fistula: Discontinue Regorafenib.

Dermatologic toxicity: Withhold and then reduce or discontinue Regorafenib depending on severity and persistence of dermatologic toxicity.

Hypertension: Temporarily or permanently withhold Regorafenib for severe or uncontrolled hypertension.

Cardiac ischemia and infarction: Withhold Regorafenib for new or acute cardiac ischemia/infarction and resume only after resolution of acute ischemic events.

Reversible posterior leukoencephalopathy syndrome (RPLS): Discontinue Regorafenib.

Side Effect:
Common side effects may include: Infection, Anaemia, Thrombocytopenia & Leukopenia, Hypothyroidism, Hypokalemia, Hypophosphatemia, Hypocalcaemia, Hyponatremia, Hypomagnesaemia, Hyperuricemia, Dehydration, Headache, Tremor, Haemorrhage, Hypertension, Dysphonia, Diarrhoea, Stomatitis, Vomiting, Nausea, Taste disorders, Dry mouth, GERD, Gastroenteritis, Hyperbilirubinemia, Increase in transaminases, Hand-foot skin reaction, Rash, Alopecia, Dry skin, Exfoliative rash, Muscle spasm, Proteinuria, Asthenia/fatigue, Pain, Fever, Mucosal inflammation, Weight loss, Increase in amylase & lipase, Abnormal International normalized ratio.

Rare side effects may include: Keratoacanthoma/Squamous cell carcinoma of the skin, Hypersensitivity reaction, Posterior reversible encephalopathy syndrome (PRES), Myocardial infarction & ischaemia, Hypertensive crisis, Gastrointestinal perforation, Gastrointestinal fistula, Pancreatitis, Severe liver injury, Nail disorder , Erythema multiforme, Stevens-Johnson syndrome, Toxic epidermal necrolysis.

Use in Specific Populations:
Pregnancy: May cause fetal harm.

Lactation: There are no data on the presence of Regorafenib or its metabolites in human milk, the effects of Regorafenib on the breastfed infant, or on milk production.

Pediatric Use: The safety and efficacy of Regorafenib in pediatric patients less than 18 years of age have not been established.

Geriatric Use: No overall differences in safety and efficacy relative to younger adults, but grade 3 or 4 hypertension occurred more frequently in geriatric patients.

Hepatic Impairment: No dose adjustment is recommended in patients with mild or moderate hepatic impairment. Closely monitor patients with hepatic impairment for adverse reactions. Regorafenib is not recommended for use in patients with severe hepatic impairment.

Renal Impairment: No dose adjustment is recommended for patients with renal impairment. The pharmacokinetics of Regorafenib have not been studied in patients who are on dialysis and there is no recommended dose for this patient population.

Drug Interaction:
Medicine:
Effect of Regorafenib on Cytochrome P450 Substrates: In vitro studies suggested that Regorafenib is an inhibitor of CYP2C8, CYP2C9, CYP2B6, CYP3A4 and CYP2C19. In vitro studies suggested that Regorafenib is not an inducer of CYP1A2, CYP2B6, CYP2C19, and CYP3A4 enzyme activity.

Effect of CYP3A4 Strong Inducers on Regorafenib: The mean AUC of Regorafenib decreased by 50%.

Effect of CYP3A4 Strong Inhibitors on Regorafenib: The mean AUC of Regorafenib increased by 33%.

Effect of Neomycin on Regorafenib: No clinically meaningful effect on the mean AUC of Regorafenib was observed. The effects of other antibiotics on the exposure of Regorafenib and its active metabolites have not been studied.

Effect of Regorafenib on BCRP Substrates: Administration of Regorafenib prior to administration of a single dose of Rosuvastatin, a BCRP substrate, resulted in a 3.8-fold increase in mean exposure (AUC) of Rosuvastatin and a 4.6-fold increase in Cmax

Food: Depending on the amount of fat, food may help the absorption of Regorafenib.

Overdose:
There is no specific antidote for overdose with Regorafenib. In the event of an overdose, monitor the patient for adverse reactions and provide appropriate supportive care.

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

Packaging:
Reganex 40 mg Tablet: Each box contains 12 film coated tablets and one packet silica gel in a sealed HDPE container.

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