Regotab™

Regorafenib Monohydrate INN Film Coated Tablet

DESCRIPTION

Regotab™ is a preparation of Regorafenib Monohydrate. Regorafenib is a small molecule inhibitor of multiple membrane-bound and intracellular kinases involved in normal cellular functions and in pathologic processes such as oncogenesis, tumor angiogenesis, and maintenance of the tumor microenvironment. In *in vitro* biochemical or cellular assays, Regorafenib or its major human active metabolites M-2 and M-5 inhibited the activity of RET, VEGFR1, VEGFR2, VEGFR3, KIT, PDGFR-alpha, PDGFR-beta, FGFR1, FGFR2, TIE2, DDR2, Trk2A, Eph2A, RAF-1, BRAF, $BRAF^{V600E}$, SAPK2, PTK5, and Abl at concentrations of Regorafenib that have been achieved clinically. In *in vivo* models, Regorafenib demonstrated anti-angiogenic activity in a rat tumor model, and inhibition of tumor growth as well as anti-metastatic activity in several mouse xenograft models including some for human colorectal carcinoma.

INDICATIONS

Metastatic colorectal cancer (CRC) who have been previously treated with fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, an anti-VEGF therapy, and, if KRAS wild type, an anti-EGFR therapy.

DOSAGE AND ADMINISTRATION

Recommended Dose: 160 mg orally, once daily for the first 21 days of each 28-day cycle. Take Regorafenib with food (a low-fat breakfast).

CONTRAINDICATIONS

None

SIDE EFFECTS

- Asthenia/fatigue
- Decreased appetite and food intake
- Hand-foot skin reaction (HFSR) [palmar-plantar erythrodysesthesia (PPE)] diarrhea, mucositis, weight loss
- Infection
- Hypertension
- Dysphonia

PRECAUTION AND WARNING

- Hemorrhage: Permanently discontinue Regorafenib for severe or life-threatening hemorrhage.
- Dermatological toxicity: Interrupt and then reduce or discontinue Regorafenib depending on severity and persistence of dermatologic toxicity.
- Hypertension: Temporarily or permanently discontinue 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 in patients who developed RPLS.
- Gastrointestinal perforation or fistula: Discontinue Regorafenib in patients who develop gastrointestinal perforation or fistula.
- Wound healing complications: Stop Regorafenib before surgery. Discontinue in patients with wound dehiscence.

DRUG INTERACTIONS

- Strong CYP3A4 inducers: Avoid strong CYP3A4 inducers. (e.g. Rifampicin, Phenytoin, Carbamazepine, Phenobarbital)
- Strong CYP3A4 inhibitors: Avoid strong CYP3A4 inhibitors. (e.g. Clarithromycin, St. John's Wort)

USE IN PREGNANCY AND LACTATION

Pregnancy Category D. Based on its mechanism of action, Regorafenib can cause fetal harm when administered to a pregnant woman. There are no adequate and well-controlled studies with Regorafenib in pregnant women. Regorafenib was embryolethal and teratogenic in rats and rabbits at exposures lower than human exposures at the recommended dose, with increased incidences of cardiovascular, genitourinary, and skeletal malformations. If this drug is used during pregnancy or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to a fetus.

It is unknown whether Regorafenib or its metabolites are excreted in human milk. In rats, Regorafenib and its metabolites are excreted in milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from Regorafenib, a decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

PHARMACEUTICAL PRECAUTION

Do not store above 25 °C temperature. Keep away from light and wet place. Keep out of reach of children.

PACKAGING

Regotab™ Tablet: Box containing 4 strips of 7 tablets each. Each tablet contains Regorafenib Monohydrate INN equivalent to Regorafenib 40 mg.

SK+F ONCOLOGY
Manufactured by
ESKAYEF PHARMACEUTICALS LIMITED
RUPGANJ, NARAYANGANJ, BANGLADESH
TM TRADEMARK
R/PM1559 V01