Resinib (Sunitinib) Innerleaf design

Pantone Metallic Coated 8483 C & Pantone 185 C

W - 190 mm X L - 300 mm

Resinib™

Sunitinib

Jenphar Bangladesh | جنفار بنغلاديش

Composition:
Resinib 12.5 Capsule: Each capsule contains Sunitinib Malate INN equivalent to Sunitinib 12.5 mg.
Resinib 25 Capsule: Each capsule contains Sunitinib Malate INN equivalent to Sunitinib 25 mg.
Resinib 37.5 Capsule: Each capsule contains Sunitinib Malate INN equivalent to Sunitinib 37.5 mg.
Resinib 50 Capsule: Each capsule contains Sunitinib Malate INN equivalent to Sunitinib 50 mg.

Pharmacology:
Sunitinib is a small molecule that inhibits multiple receptor tyrosine kinases (RTKs), some of which are implicated in tumor growth, pathologic angiogenesis, and metastatic progression of cancer. Sunitinib was evaluated for its inhibitory activity against a variety of kinases (>80 kinases) and was identified as an inhibitor of platelet-derived growth factor receptors (PDGFRα and PDGFRβ), vascular endothelial growth factor receptors (VEGFR1, VEGFR2 and VEGFR3), stem cell factor receptor (KIT), Fms-like tyrosine kinase-3 (FLT3), colony stimulating factor receptor Type 1 (CSF-1R), and the glial cell-line derived neurotrophic factor receptor (RET). Sunitinib inhibition of the activity of these RTKs has been demonstrated in biochemical and cellular assays, and inhibition of function has been demonstrated in cell proliferation assays. The primary metabolite exhibits similar potency compared to sunitinib in biochemical and cellular assays. Sunitinib inhibited the phosphorylation of multiple RTKs (PDGFRβ, VEGFR2, KIT) in tumor xenografts expressing RTK targets *in-vivo* and demonstrated inhibition of tumor growth or tumor regression and/or inhibited metastases in some experimental models of cancer. Sunitinib demonstrated the ability to inhibit growth of tumor cells expressing dysregulated target RTKs (PDGFR, RET, or KIT) *in-vitro* and to inhibit PDGFRβ- and VEGFR2-dependent tumor angiogenesis *in-vivo*.

Indication:
Gastrointestinal Stromal Tumor (GIST): Resinib is indicated for the treatment of gastrointestinal stromal tumor after disease progression on or intolerance to imatinib mesylate.
Advanced Renal Cell Carcinoma (RCC): Resinib is indicated for the treatment of advanced renal cell carcinoma.
Advanced Pancreatic Neuroendocrine Tumors (pNET): Resinib is indicated for the treatment of progressive, well-differentiated pancreatic neuroendocrine tumors in patients with unresectable locally advanced or metastatic disease.

Dose & administration:
Recommended Dose for GIST and RCC: The recommended dose of Resinib for gastrointestinal stromal tumor (GIST) and advanced renal cell carcinoma (RCC) is one 50 mg oral dose taken once daily, on a schedule of 4 weeks on treatment followed by 2 weeks off (Schedule 4/2). Resinib may be taken with or without food.
Recommended Dose for pNET: The recommended dose of Resinib for pancreatic neuroendocrine tumors (pNET) is 37.5 mg taken orally once daily continuously without a scheduled off-treatment period. Resinib may be taken with or without food.
Dose Modification:
Dose interruption and/or dose modification in 12.5 mg increments or decrements is recommended based on individual safety and tolerability. The maximum dose administered in the Phase 3 pNET study was 50 mg daily.
Strong CYP3A4 inhibitors such as ketoconazole may increase Resinib plasma concentrations. A dose reduction for Resinib to a minimum of 37.5 mg (GIST and RCC) or 25 mg (pNET) daily should be considered if Resinib must be co-administered with a strong CYP3A4 inhibitor.
CYP3A4 inducers such as rifampin may decrease Resinib plasma concentrations. A dose increase for Resinib to a maximum of 87.5 mg (GIST and RCC) or 62.5 mg (pNET) daily should be considered if Resinib must be co-administered with a CYP3A4 inducer. If dose is increased, the patient should be monitored carefully for toxicity.

Route of administration: Oral

Contra-indication:
None.

Warning and precaution:
1. Hepatotoxicity, including liver failure, has been observed. Monitor liver function tests before initiation of treatment, during each cycle of treatment, and as clinically indicated. Resinib should be interrupted for Grade 3 or 4 drug-related hepatic adverse events and discontinued if there is no resolution. Do not restart Resinib if patients subsequently experience severe changes in liver function tests or have other signs and symptoms of liver failure.
2. Women of childbearing potential should be advised of the potential hazard to the fetus and to avoid becoming pregnant.
3. Cardiac toxicity including left ventricular ejection fraction declines to below the lower limit of normal and cardiac failure including death have occurred. Monitor patients for signs and symptoms of congestive heart failure.
4. Prolonged QT intervals and Torsade de Pointes have been observed. Use with caution in patients at higher risk for developing QT interval prolongation. When using Resinib, monitoring with on-treatment electrocardiograms and electrolytes should be considered.
5. Hypertension may occur. Monitor blood pressure and treat as needed.
6. Hemorrhagic events including tumor-related hemorrhage have occurred. Perform serial complete blood counts and physical examinations.
7. Thyroid dysfunction may occur. Patients with signs and/or symptoms suggestive of hypothyroidism or hyperthyroidism should have laboratory monitoring of thyroid function performed and be treated as per standard medical practice.
8. Adrenal hemorrhage was observed in animal studies. Monitor adrenal function in case of stress such as surgery, trauma or severe infection.

Adverse effects:
The most common adverse reactions (≥20%) are fatigue, asthenia, fever, diarrhea, nausea, mucositis/stomatitis, vomiting, dyspepsia, abdominal pain, constipation, hypertension, peripheral edema, rash, hand-foot syndrome, skin discoloration, dry skin, hair color changes, altered taste, headache, back pain, arthralgia, extremity pain, cough, dyspnea, anorexia, and bleeding.

Special population:

Use in pregnancy & lactation:
Pregnancy: Pregnancy Category D. Resinib can cause fetal harm when administered to a pregnant woman.
Nursing Mothers: Resinib excreted in human milk and because of the potential for serious adverse reactions in nursing infants from Resinib, 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 efficacy of Resinib in pediatric patients have not been established.

Geriatric Use: No overall differences in safety or effectiveness were observed between younger and older patients.

Hepatic Impairment: No dose adjustment to the starting dose is required when administering Resinib to patients with Child-Pugh Class A or B hepatic impairment.

Renal Impairment: No adjustment to the starting dose is required when administering Resinib to patients with mild, moderate, and severe renal impairment. Subsequent dose modifications should be based on safety and tolerability.

Drug interaction:
CYP3A4 Inhibitors: Strong CYP3A4 inhibitors such as ketoconazole may increase Resinib plasma concentrations. Selection of an alternate concomitant medication with no or minimal enzyme inhibition potential is recommended. Concurrent administration of Resinib with the strong CYP3A4 inhibitor, ketoconazole, resulted in 49% and 51% increases in the combined (sunitinib + primary active metabolite) Cmax and AUCo-∞ values, respectively, after a single dose of Resinib in healthy volunteers. Co-administration of Resinib with strong inhibitors of the CYP3A4 family (e.g., ketoconazole, itraconazole, clarithromycin, atazanavir, indinavir, nefazodone, nelfinavir, ritonavir, saquinavir, telithromycin, voriconazole) may increase Resinib concentrations. Grapefruit may also increase plasma concentrations of Resinib. A dose reduction for Resinib should be considered when it must be co-administered with strong CYP3A4 inhibitors.

CYP3A4 Inducers: CYP3A4 inducers such as rifampin may decrease Resinib plasma concentrations. Selection of an alternate concomitant medication with no or minimal enzyme induction potential is recommended. Concurrent administration of Resinib with the strong CYP3A4 inducer, rifampin, resulted in a 23% and 46% reduction in the combined (sunitinib + primary active metabolite) Cmax and AUCo-∞ values, respectively, after a single dose of Resinib in healthy volunteers. Co-administration of Resinib with inducers of the CYP3A4 family (e.g., dexamethasone, phenytoin, carbamazepine, rifampin, rifabutin, rifapentin, phenobarbital) may decrease Resinib concentrations. A dose increase for Resinib should be considered when it must be co-administered with CYP3A4 inducers.

Overdose:
Treatment of overdose with Resinib should consist of general supportive measures. There is no specific antidote for over dosage with Resinib. If indicated, elimination of unabsorbed drug should be achieved by emesis or gastric lavage. A few cases of accidental overdose have been reported; these cases were associated with adverse reactions consistent with the known safety profile of Resinib, or without adverse reactions.

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

Packing:
Resinib 12.5 Capsule: Each box contains 14 capsules and one packet silica gel in a sealed HDPE container.
Resinib 25 Capsule: Each box contains 14 capsules and one packet silica gel in a sealed HDPE container.
Resinib 37.5 Capsule: Each box contains 14 capsules and one packet silica gel in a sealed HDPE container.
Resinib 50 Capsule: Each box contains 14 capsules and one packet silica gel in a sealed HDPE container.

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

12001864 Ver.:01