Ibrunib (Ibrutinib INN) Innerleaf

Pantone Metallic Coated 8483 c W - 193 mm X H - 303 mm

Ibrunib™
Ibrutinib

Jenphar Bangladesh | جـنـفـار بنغلاديش

Composition:
Ibrunib 140 Capsule: Each capsule contains Ibrutinib INN 140 mg.

Clinical Pharmacology:
Ibrutinib is a small-molecule inhibitor of BTK. Ibrutinib forms a covalent bond with a cysteine residue in the BTK active site, leading to inhibition of BTK enzymatic activity. BTK is a signaling molecule of the B-cell antigen receptor (BCR) and cytokine receptor pathways. BTK's role in signaling through the B-cell surface receptors results in activation of pathways necessary for B-cell trafficking, chemotaxis, and adhesion. Nonclinical studies show that ibrutinib inhibits malignant B-cell proliferation and survival in vivo as well as cell migration and substrate adhesion in vitro.

Indications:
Mantle Cell Lymphoma:
Ibrutinib is indicated for the treatment of patients with Mantle Cell Lymphoma (MCL) who have received at least one prior therapy.
Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma:
Ibrutinib is indicated for the treatment of patients with chronic lymphocytic leukemia.
Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma with 17p deletion Ibrutinib is indicated for the treatment of patients with chronic lymphocytic leukemia.
Waldenstrom Macroglobulinemia (WM):
Ibrutinib is indicated for the treatment of patients with Waldenstrom Macroglobulinemia (WM).
Marginal Zone Lymphoma:
Ibrutinib is indicated for the treatment of patients with marginal zone lymphoma (MZL) who require systemic therapy and have received at least one prior anti-CD 20-based therapy.

Dosage and Administrationt:
Dosing Guidelines:
Administer Ibrutinib orally once daily at approximately the same time each day. Swallow the capsules whole with water. Do not open, break, or chew the capsules.

Dosage:
Mantle Cell Lymphoma and Marginal Zone Lymphoma:
The recommended dose of Ibrutinib for MCL and MZL is 560 mg (four 140 mg capsules) orally once daily until disease progression or unacceptable toxicity.
Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma and Waldenstrom Macroglobulinemia (WM):
The recommended dose of Ibrutinib for CLL/SLL and WM is 420 mg (three 140 mg capsules) orally once daily until disease progression or unacceptable toxicity.
The recommended dose of Ibrutinib for CLL/SLL when used in combination with bendamustine and rituximab (administered every 28 days for up to 6 cycles) is 420 mg (three 140 mg capsules) orally once daily until disease progression or unacceptable toxicity.
Dose Modifications for Adverse Reactions
Interrupt Ibrutinib therapy for any Grade 3 or greater non-hematological toxicities, Grade 3 or greater neutropenia with infection or fever, or Grade 4 hematological toxicities. Once the symptoms of the toxicity have resolved to Grade 1 or baseline (recovery), Ibrutinib therapy may be reinitiated at the starting dose. If the toxicity reoccurs, reduce dose by one capsule (140 mg per day). A second reduction of dose by 140 mg may be considered as needed. If these toxicities persist or recur following two dose reductions, discontinue Ibrutinib.

Toxicity Occurrence	MCL and MZL Dose Modification After Recovery Starting Dose=560mg	CLL/SLL and WM Dose Modification After Recovery Starting Dose=420mg
First	Restart at 560 mg daily	Restart at 420 mg daily
Second	Restart at 420 mg daily	Restart at 280 mg daily
Third	Restart at 280 mg daily	Restart at 140 mg daily
Fourth	Discontinue Ibrutinib	Discontinue Ibrutinib

Dose Modifications for Use with CYP3A Inhibitors:
Avoid co-administration with strong or moderate CYP3A inhibitors and consider alternative agents with less CYP3A inhibition. Concomitant use of strong CYP3A inhibitors which would be taken chronically (e.g., ritonavir, indinavir, nelfinavir, saquinavir, boceprevir, telaprevir, nefazodone) is not recommended. For short-term use (treatment for 7 days or less) of strong CYP3A inhibitors (e.g., antifungals and antibiotics) consider interrupting Ibrutinib therapy until the CYP3A inhibitor is no longer needed. Reduce Ibrutinib dose to 140 mg if a moderate CYP3A inhibitor must be used (e.g., fluconazole, darunavir, erythromycin, diltiazem, atazanavir, aprepitant, amprenavir, fosamprenavir, crizotinib, imatinib, verapamil, and ciprofloxacin). Patients taking concomitant strong or moderate CYP3A inhibitors should be monitored more closely for signs of Ibrutinib toxicity.
Dose Modifications for Use in Hepatic Impairment:
For patients with mild liver impairment (Child-Pugh class A), the recommended dose is 140 mg daily (one capsule). Avoid the use of Ibrutinib in patients with moderate or severe hepatic impairment (Child-Pugh classes B and C).
Missed Dose:
If a dose of Ibrutinib is not taken at the scheduled time, it can be taken as soon as possible on the same day with are turn to the normal schedule the following day. Extra capsules of Ibrutinib should not be taken to make up for the missed dose.

Contraindications:
Hypersensitivity to the active substance or to any of the excipients.

Warning and precaution:
- Hemorrhage: Monitor for bleeding.
- Infections: Monitor patients for fever and infections and evaluate promptly.
- Cytopenias: Check complete blood counts monthly.
- Atrial Fibrillation: Monitor patients for atrial fibrillation.
- Second Primary Malignancies: Other malignancies have occurred in patients, including skin cancers, and other carcinomas.
- Tumor Lysis Syndrome (TLS): Monitor patients at risk for TLS (e.g. high tumor burden).
- Embryo-Fetal Toxicity: Can cause fetal harm. Advise women of the potential risk to a fetus and to avoid pregnancy while taking the drug.

Adverse Effect:
Hemorrhage, Infections, Cytopenias, Atrial Fibrillation, Hypertension, Second Primary Malignancies and Tumor Lysis Syndrome.
Additional Important Adverse Reactions: Diarrhea, Visual Disturbance.

Use In Specific Populations:
Pregnancy
Pregnancy catagory D. Ibrutinib can cause fetal harm based on findings from animal studies.
Lactation
There is no information regarding the presence of Ibrutinib or its metabolites in human milk, the effects on the breast fed infant, or the effects on milk production.
Pediatric Use
The safety and effectiveness of Ibrutinib in pediatric patients has not been established.
Geriatric Use
No overall differences in effectiveness were observed between younger and older patients. Anemia (all grades) and Grade 3 or higher pneumonia occurred more frequently among older patients treated with Ibrutinib.
Hepatic Impairment
Ibrutinib is metabolized in the liver. In a hepatic impairment study, data showed an increase in Ibrutinib exposure. The safety of Ibrutinib has not been evaluated in cancer patients with mild to severe hepatic impairment by Child-Pugh criteria. Monitor patients for signs of Ibrutinib toxicity and follow dose modification guidance as needed. It is not recommended to administer Ibrutinib to patients with moderate or severe hepatic impairment.

Drug Interaction:
CYP3A Inhibitors:
Ibrutinib is primarily metabolized by cytochrome P450 enzyme 3A (CYP3A). Avoid concomitant administration of Ibrutinib with strong or moderate inhibitors of CYP3A. Patients taking concomitant strong or moderate CYP3A4 inhibitors should be monitored more closely for signs of Ibrutinib toxicity. Avoid grape fruit and Seville oranges during Ibrutinib treatment, as these contain moderate inhibitors of CYP3A.
CYP3A Inducers:
Administration of Ibrutinib with rifampin, astrong CYP3A inducer, decreased Ibrutinib Cmax and AUC. Avoid concomitant use of strong CYP3A inducers (e.g., carbamazepine, rifampin, phenytoin, and St. John'sWort). Consider alternative agents with less CYP3A induction.

Over Dose:
There is no specific experience in the management of Ibrutinib over dose in patients. Closely monitor patients who ingest more than the recommended dosage and provide appropriate supportive treatment.

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

Packaging:
Ibrunib 140 Capsule: Each box contains 60 capsules and one packet silica gel in a sealed HDPE container.

12001850 Ver.: 01

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