Dasatin (Dasatinib) Innerleaf

Pantone Metallic Coated 8483 C W - 190 mm X L - 300 mm

Dasatin™
Dasatinib

Jenphar Bangladesh | جنفار بنغلاديش

Composition:
Dasatin 20 mg Tablet: Each film coated tablet contains Dasatinib Monohydrate INN equivalent to Dasatinib 20 mg.
Dasatin 100 mg Tablet: Each film coated tablet contains Dasatinib Monohydrate INN equivalent to Dasatinib 100 mg.

Pharmacology:
Dasatinib, at nanomolar concentrations, inhibits the following kinases: BCR-ABL, SRC family (SRC, LCK, YES, FYN), c-KIT, EPHA2, and PDGFRβ. Based on modeling studies, Dasatinib is predicted to bind to multiple conformations of the ABL kinase. *In vitro*, Dasatinib was active in leukemic cell lines representing variants of imatinib mesylate sensitive and resistant disease. Dasatinib inhibited the growth of chronic myeloid leukemia (CML) and acute lymphoblastic leukemia (ALL) cell lines overexpressing BCR-ABL. Under the conditions of the assays, Dasatinib was able to overcome Imatinib resistance resulting from BCR-ABL kinase domain mutations, activation of alternate signaling pathways involving the SRC family kinases (LYN, HCK) and multi-drug resistance gene overexpression.

Indications:
Dasatin is indicated for the treatment of adults with
- Newly diagnosed Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) in chronic phase.
- Chronic, accelerated, or myeloid or lymphoid blast phase Ph+ CML with resistance or intolerance to prior therapy including Imatinib.
- Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL) with resistance or intolerance to prior therapy.

Dasatinib is indicated for the treatment of pediatric patients 1 year of age and older with
- Ph+ CML in chronic phase.
- Newly diagnosed Ph+ ALL in combination with chemotherapy.

Dose & administration:
Adult dose:
The recommended starting dose of Dasatinib for chronic phase CML is 100 mg administered orally once daily. The recommended starting dose of Dasatinib for accelerated phase CML, myeloid or lymphoid blast phase CML, or Ph+ ALL is 140 mg administered orally once daily. Tablets should not be crushed or cut; they should be swallowed whole. Dasatinib can be taken with or without a meal, either in the morning or in the evening. In clinical studies, treatment with Dasatinib was continued until disease progression or until no longer tolerated by the patient. The effect of stopping treatment after the achievement of a complete cytogenetic response (CCyR) has not been investigated.
Pediatric dose:
The recommended starting dose for pediatrics is based on body weight as shown in Table 1. The recommended dose should be administered orally once daily with or without food. Recalculate the dose every 3 months based on changes in body weight, or more often if necessary.

Table 1. Dasatinib for Pediatric Patients[a]

Body Weight (kg)[b]	Daily Dose (mg)
10 to less than 20	40 mg
20 to less than 30	60 mg
30 to less than 45	70 mg
At least 45	100 mg

a. For pediatric patients with Ph+ ALL, begin Dasatinib therapy on or before day 15 of induction chemotherapy, when diagnosis is confirmed and continue for 2 years
b. Tablet dosing is not recommended for patients weighing less than 10 kg.

Dose Modification:
Concomitant Strong CYP3A4 inducers: The use of concomitant strong CYP3A4 inducers may decrease Dasatinib plasma concentrations and should be avoided (eg, dexamethasone, phenytoin, carbamazepine, rifampin, rifabutin, phenobarbital). St. John's Wort may decrease Dasatinib plasma concentrations unpredictably and should be avoided. If patients must be coadministered a strong CYP3A4 inducer, based on pharmacokinetic studies, a Dasatinib dose increase should be considered. If the dose of Dasatinib is increased, the patient should be monitored carefully for toxicity. Concomitant Strong CYP3A4 inhibitors: CYP3A4 inhibitors (eg, ketoconazole, itraconazole, clarithromycin, atazanavir, indinavir, nefazodone, nelfinavir, ritonavir, saquinavir, telithromycin, and voriconazole) may increase Dasatinib plasma concentrations. Grapefruit juice may also increase plasma concentrations of Dasatinib and should be avoided.

Contra-indication:
None.

Warning and precaution:
1. Myelosuppression: Severe thrombocytopenia, neutropenia, and anemia may occur and require dose interruption or reduction. Monitor complete blood counts regularly.
2. Bleeding Related Events (mostly associated with severe thrombocytopenia): CNS and gastrointestinal hemorrhages, including fatalities, have occurred. Severe hemorrhage may require treatment interruptions and transfusions. Use Dasatinib with caution in patients requiring medications that inhibit platelet function or anticoagulants.
3. Fluid Retention: Dasatinib is associated with fluid retention, sometimes severe, including ascites, edema, and pleural and pericardial effusions. Manage with appropriate supportive care measures.
4. QT Prolongation: Use Dasatinib with caution in patients who have or may develop prolongation of the QT interval.
5. Congestive Heart Failure, Left Ventricular Dysfunction and Myocardial Infarction: Monitor patients for signs or symptoms consistent with cardiac dysfunction and treat appropriately.
6. Fetal harm may occur when administered to a pregnant woman. Women should be advised of the potential hazard to the fetus and to avoid becoming pregnant.

Side Effect:
Most common adverse reactions (≥10%) in patients included myelosuppression, fluid retention events, diarrhea, headache, skin rash, hemorrhage, dyspnea, fatigue, nausea, and musculoskeletal pain.

Special populations:
Pregnancy: Pregnancy category D. Based on limited human data, Dasatinib can cause fetal harm when administered to a pregnant woman.
Lactation: No data are available regarding the presence of Dasatinib in human milk, the effects of the drug on the breastfed child, or the effects of the drug on milk production.
Pediatric Use: The safety profile of Dasatinib in pediatric subjects was comparable to that reported in studies in adult subjects with chronic phase CML. Monitor bone growth and development in pediatric patients.
Geriatric Use: No differences in confirmed Complete Cytogenetic Response (cCCyR) and MMR were observed between older and younger patients.
Hepatic Impairment: No dose adjustment is necessary in patient with hepatic impairment. Caution is recommended when administering Dasatinib to patients with hepatic impairment.
Renal Impairment: There are currently no clinical studies with Dasatinib in patients with impaired renal function. Less than 4% of Dasatinib and its metabolites are excreted via the kidney.

Drug interaction:
Strong CYP3A4 Inhibitors: The coadministration with strong CYP3A inhibitors may increase Dasatinib concentrations. Increased Dasatinib concentrations may increase the risk of toxicity. Avoid concomitant use of strong CYP3A4 inhibitors. If concomitant administration of a strong CYP3A4 inhibitor cannot be avoided, consider a Dasatinib dose reduction.
Strong CYP3A4 Inducers: The coadministration of Dasatinib with strong CYP3A inducers may decrease Dasatinib concentrations. Decreased Dasatinib concentrations may reduce efficacy. Consider alternative drugs with less enzyme induction potential. If concomitant administration of a strong CYP3A4 inducer cannot be avoided, consider a Dasatinib dose increase.
Gastric Acid Reducing Agents: The coadministration of Dasatinib with a gastric acid reducing agent may decrease the concentrations of Dasatinib. Decreased Dasatinib concentrations may reduce efficacy. Do not administer H2 antagonists or proton pump inhibitors with Dasatinib. Consider the use of antacids in place of H2 antagonists or proton pump inhibitors. Administer the antacid at least 2 hours prior to or 2 hours after the dose of Dasatinib. Avoid simultaneous administration of Dasatinib with antacids.

Overdose:
Experience with overdose of Dasatinib in clinical studies is limited to isolated cases. The highest overdosage of 280 mg per day for 1 week was reported in two patients and both developed severe myelosuppression and bleeding. Since Dasatinib is associated with severe myelosuppression, monitor patients who ingest more than the recommended dosage closely for myelosuppression and give appropriate supportive treatment.

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

Packing:
Dasatin 20 mg Tablet: Each box contains 30 film coated tablets and one packet silica gel in a sealed HDPE container.
Dasatin 100 mg Tablet: Each box contains 30 film coated tablets and one packet silica gel in a sealed HDPE container.

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

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