HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use IMATINIB MESYLATE TABLETS safely and effectively. See full prescribing information for IMATINIB MESYLATE TABLETS.

IMATINIB MESYLATE tablets, for oral use
Initial U.S. Approval: 2001

---------- RECENT MAJOR CHANGES ----------

Warnings and Precautions (5) 1/2015

---------- INDICATIONS AND USAGE ----------

Imatinib mesylate is a kinase inhibitor indicated for the treatment of:

- Newly diagnosed adult and pediatric patients with Philadelphia chromosome positive chronic myeloid leukemia (Ph+ CML) in chronic phase (1.1)
- Patients with Philadelphia chromosome positive chronic myeloid leukemia (Ph+ CML) in blast crisis (BC), accelerated phase (AP), or in chronic phase (CP) after failure of interferon-alpha therapy (1.2)
- Adult patients with relapsed or refractory Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL) (1.3)
- Adult patients with myelodysplastic/myeloproliferative diseases (MDS/MPD) associated with PDGFR (platelet-derived growth factor receptor) gene re-arrangements (1.5)
- Adult patients with aggressive systemic mastocytosis (ASM) without the D816V c-Kit mutation or with c-Kit mutational status unknown (1.6)
- Adult patients with hypereosinophilic syndrome (HES) and/or chronic eosinophilic leukemia (CEL) who have the FIP1L1-PDGFRα fusion kinase (mutational analysis or FISH demonstration of CHIC2 allele deletion) and for patients with HES and/or CEL who are FIP1L1-PDGFRα fusion kinase negative or unknown (1.7)
- Adult patients with unresectable, recurrent and/or metastatic dermatofibrosarcoma protuberans (DFSP) (1.8)

---------- DOSAGE AND ADMINISTRATION ----------

- Adults with Ph+ CML CP (2.1): 400 mg/day
- Adults with Ph+ CML AP or BC (2.1): 600 mg/day
- Pediatrics with Ph+ CML CP (2.2): 340 mg/m^2/day
- Adults with Ph+ ALL (2.3): 600 mg/day
- Adults with MDS/MPD (2.5): 400 mg/day
- Adults with ASM (2.6): 100 mg/day or 400 mg/day
- Adults with HES/CEL (2.7): 100 mg/day or 400 mg/day
- Adults with DFSP (2.8): 800 mg/day
- Patients with mild to moderate hepatic impairment (2.11): 400 mg/day
- Patients with severe hepatic impairment (2.11): 300 mg/day

All doses of imatinib mesylate tablets should be taken with a meal and a large glass of water. Doses of 400 mg or 600 mg should be administered once-daily, whereas a dose of 800 mg should be administered as 400 mg twice a day. Imatinib mesylate tablets can be dissolved in water or apple juice for patients having difficulty swallowing. Daily dosing of 800 mg and above should be accomplished using the 400 mg tablet to reduce exposure to iron.

---------- DOSAGE FORMS AND STRENGTHS ----------

Tablets (scored): 100 mg and 400 mg (3)

---------- CONTRAINDICATIONS ----------

None (4)

---------- WARNINGS AND PRECAUTIONS ----------

- Edema and severe fluid retention have occurred. Weigh patients regularly and manage unexpected rapid weight gain by drug interruption and diuretics (5.1, 6.1, 6.9)
- Cytopenias, particularly anemia, neutropenia, and thrombocytopenia, have occurred. Manage with dose reduction or dose interruption and in rare cases discontinuation of treatment. Perform complete blood counts weekly for the first month, biweekly for the second month, and periodically thereafter (5.2)
- Severe congestive heart failure and left ventricular dysfunction have been reported, particularly in patients with comorbidities and risk factors. Patients with cardiac disease or risk factors for cardiac failure should be monitored and treated (5.3)
- Severe hepatotoxicity including fatalities may occur. Assess liver function before initiation of treatment and monthly thereafter or as clinically indicated. Monitor liver function when combined with chemotherapy known to be associated with liver dysfunction (5.4)
- Grade 3/4 hemorrhage has been reported in clinical studies in patients with newly diagnosed CML (5.5)
- Gastrointestinal perforations, some fatal, have been reported (5.6)
- Cardiogenic shock/left ventricular dysfunction has been associated with the initiation of imatinib mesylate in patients with conditions associated with high eosinophil levels (e.g., HES, MDS/MPD and ASM) (5.7)
- Bullous dermatologic reactions (e.g., erythema multiforme and Stevens- Johnson syndrome) have been reported with the use of imatinib mesylate (5.8)
- Hypothyroidism has been reported in thyroidectomy patients undergoing levothyroxine replacement. Closely monitor TSH levels in such patients (5.9)
- Fetal harm can occur when administered to a pregnant woman. Women should be apprised of the potential harm to the fetus (5.10, 8.1)
- Growth retardation occurring in children and pre-adolescents receiving imatinib mesylate has been reported. Close monitoring of growth in children under imatinib mesylate treatment is recommended (5.11, 6.11)
- Tumor lysis syndrome. Close monitoring is recommended (5.12)
- Reports of motor vehicle accidents have been received in patients receiving imatinib mesylate. Caution patients about driving a car or operating machinery (5.13)

---------- ADVERSE REACTIONS ----------

The most frequently reported adverse reactions (≥30%) were edema, nausea, vomiting, muscle cramps, musculoskeletal pain, diarrhea, rash, fatigue and abdominal pain (6.1, 6.9)

To report SUSPECTED ADVERSE REACTIONS, contact Sun Pharmaceutical Industries, Inc. at 1-800-818-4555 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

---------- DRUG INTERACTIONS ----------

- CYP3A4 inducers may decrease imatinib mesylate C_{max} and AUC (2.11, 7.1)
- CYP3A4 inhibitors may increase imatinib mesylate C_{max} and AUC (7.2)
- Imatinib mesylate is an inhibitor of CYP3A4 and CYP2D6 which may increase the C_{max} and AUC of other drugs (7.3, 7.4)
- Patients who require anticoagulation should receive low-molecular weight or standard heparin and not warfarin (7.3)

---------- USE IN SPECIFIC POPULATIONS ----------

- There is no experience in children less than 1 year of age (8.4)
- Pregnancy: Sexually active female patients should use highly effective contraception during treatment (5.10)

See 17 for PATIENT COUNSELING INFORMATION

Revised: 11/2015