Imaceva™

Imatinib

COMPOSITION

Imaceva™ 100: Each film coated tablet contains Imatinib Mesylate BP equivalent to 100 mg of Imatinib free base.

Imaceva™ 400: Each film coated tablet contains Imatinib Mesylate BP equivalent to 400 mg of Imatinib free base.

PHARMACOLOGY

Imatinib mesylate is a protein-tyrosine kinase inhibitor that inhibits the BCR-ABL tyrosine kinase; the constitutive abnormal tyrosine kinase created by the Philadelphia chromosome abnormality in CML. Imatinib inhibits proliferation and induces apoptosis in BCR-ABL positive cell lines as well as fresh leukemic cells from Philadelphia chromosome-positive chronic myeloid leukemia. Imatinib inhibits colony formation in assays using ex vivo peripheral blood and bone marrow samples from CML patients.

INDICATION

Imatinib is indicated for the treatment of:

• Newly diagnosed adult and pediatric patients with Philadelphia chromosome positive chronic myeloid leukemia (Ph+CML) in chronic phase. 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.

• Adult patients with relapsed or refractory Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ALL). Pediatric patients with newly diagnosed Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ALL) in combination with chemotherapy.

• Adult patients with myelodysplastic/myeloproliferative diseases (MDS/MPD) associated with PDGFR (platelet-derived growth factor receptor) gene re-arrangements as determined with an FDA-approved test.

• Adult patients with aggressive systemic mastocytosis (ASM) without the D816V c-Kit mutation as determined with an FDA-approved test or with c-Kit mutational status unknown.

• 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.

• Adult patients with unresectable, recurrent and/or metastatic dermatofibrosarcoma protuberans (DFSP).

• Patients with Kit (CD117) positive unresectable and/or metastatic malignant gastrointestinal stromal tumors (GIST).

• Adjuvant treatment of adult patients following resection of Kit (CD117) positive GIST.

DOSAGE AND ADMINISTRATION

The recommended dose for Imatinib are: • Adults with Ph+CML CP: 400 mg/day; • Adults with Ph+CML AP or BC: 600 mg/day; • Pediatrics with Ph+CML CP: 340 mg/m2/day; • Adults with Ph+ALL: 600 mg/day; • Pediatrics with Ph+ALL: 340 mg/m2/day; •Adults with MDS/MPD: 400 mg/day; • Adults with ASM: 100 mg/day or 400 mg/day; • Adults with HES/CEL: 100 mg/day or 400 mg/day; • Adults with DFSP: 800 mg/day; • Adults with metastatic and/or unresectable GIST: 400 mg/day; • Adjuvant treatment of adults with GIST: 400 mg/day; • Patients with mild to moderate hepatic impairment: 400 mg/day; • Patients with severe hepatic impairment: 300 mg/day.

SIDE EFFECTS

The most frequently reported adverse reactions (greater than or equal to 30%) were edema, nausea, vomiting, muscle cramps, musculoskeletal pain, diarrhea, rash, fatigue and abdominal pain.

WARNINGS AND PRECAUTIONS

- Edema and severe fluid retention have occurred. Weigh patients regularly and manage unexpected rapid weight gain by drug interruption and diuretics.
- Cytopenias, particularly anemia, neutropenia, and thrombocytopenia, have occurred. Manage with dose reduction, dose interruption, or discontinuation of treatment. Perform complete blood counts weekly for the first month, biweekly for the second month, and periodically thereafter.
- Severe congestive heart failure and left ventricular dysfunction have been reported, particularly in patients with comorbidities and risk factors. Monitor and treat patients with cardiac disease or risk factors for cardiac failure.
- 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.
- Renal toxicity. A decline in renal function may occur in patients receiving Imatinib. Evaluate the renal function at baseline and during therapy, with attention to risk factors for renal dysfunction.

CONTRAINDICATION

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

USE IN PREGNANCY AND LACTATION

Imatinib can cause fetal harm when administered to a pregnant woman based on human and animal data. Imatinib and its active metabolite are excreted into human milk. Because of the potential for serious adverse reactions in breastfed infants from Imatinib, advise a lactating woman not to breastfeed during treatment and for 1 month after the last dose.

USE IN SPECIAL POPULATION

Pediatric Use: The safety and effectiveness of Imatinib have been demonstrated in pediatric patients with newly diagnosed Ph+chronic phase CML and Ph+ALL. There are no data in children under 1 year of age.

Geriatric Use: The efficacy of Imatinib was similar in older and younger patients.

Hepatic Impairment: Mild and moderate hepatic impairment do not influence exposure to Imatinib impairment. Reduce the dose by 25% for patients with severe hepatic impairment.

Renal Impairment: Dose reductions are necessary for patients with moderate and severe renal impairment.

OVERDOSE

In the event of overdose the patient should be observed and be given appropriate symptomatic treatment.

DRUG-DRUG INTERACTION

CYP3A4 inducers may decrease Imatinib Cmax and area under the curve (AUC). CYP3A4 inhibitors may increase Imatinib Cmax and AUC. Imatinib is an inhibitor of CYP3A4 and CYP2D6 which may increase the Cmax and AUC of other drugs. Patients who require anticoagulation should receive low-molecular-weight or standard heparin and not warfarin.

STORAGE

Keep away from light & moisture, store in cool & dry place. Store below 30°C. Keep out of the reach of the childrens.

HOW SUPPLIED

Imaceva™ 100: Each box contains 3 blister of 10 tablets.

Imaceva™ 400: Each box contains 3 blister of 10 tablets.

Manufactured by

SQUARE PHARMACEUTICALS LTD. BANGLADESH