**Indications**

- Newly diagnosed Philadelphia positive (Ph+) chronic myeloid leukemia (CML). CML is blast crisis, accelerated phase, or in chronic phase after failure of interferon-alpha treatment.
- A new treatment following failure of either (BCR-ABL) positive patients with Ph+ CML after failure of bone marrow transplantation or remission induction with interferon alpha.
- Ablation of palpable or refractory post-acute lymphoblastic leukemia (ALL) (in combination with chemotherapy).
- Metastatic gastrointestinal stromal tumor (GIST) (KIT (CD117) positive).
- Unresectable, recurrent, or metastatic gastrointestinal stromal tumor (GIST). Adjuvant treatment following resection of Kit (CD117) positive.
- Hypereosinophilic syndrome and/or associated with platelet-derived growth factor receptor (PDGFR) gene rearrangement.
- Angioectatic dermatofibrosarcoma protuberans (DFSP).
- Newly diagnosed Ph+ ALL (in combination with chemotherapy).

**Pharmacokinetics**

- Mostly metabolized by the CYP3A4 enzyme system to N-desmethyl imatinib, which is as active as imatinib. Excreted mostly in excreted unchanged in urine.
- 5% excreted unchanged in urine.
- Mostly metabolized by the CYP3A4 enzyme system.

**Action**

Inhibits kinases which may be produced by malignant cell lines.

**Contraindications/Precautions**

- Pregnancy Category D
- Use cautiously in: Hepatic impairment (dose should be decreased).
- Hypersensitivity; Potentially fatal for fetal harm; Lactation: Potential for fecal protein in breast milk; breastfeeding should be avoided.

**Adverse Reactions/Side Effects**

- **Gastrointestinal:** nausea, vomiting, diarrhea.
- **Hemat:** neutropenia, anemia, petechiae.
- **Hepatic:** transaminases increased.
- **Cardiovascular:** edema, hypokalemia, pericardial infusion, anasarca, superficial edema and fluid retention.
- **Cutaneous:** rash, pruritus, skin changes.
- **General:** malaise, weakness.
- **Hypersensitivity:** rash, fever.
- **Metabolic:** hypothyroidism.

**Drug Interactions**

- **Drug-Dose:** blood levels and effects may be increased.
- **Drug-Food:** grapefruit juice.

**Half-life:** imatinib — 18 hr; 3-desmethyl imatinib — 40 hr.

**TIME-ACTION PROFILE (blood levels of imatinib)**

- **ROUTE**
  - **ONSET**
  - **PEAK**
  - **DURATION**
- **PO** unknown
- **2–4 hr**
- **24 hr**

**Contraindications/Precautions**

- Contraindicated in: Hypersensitivity; Pregnancy Category D; Lactation: Potential for breast milk; breastfeeding should be avoided.

**Adverse Reactions/Side Effects**

- **Gastrointestinal:** nausea, vomiting, diarrhea.
- **Hemat:** neutropenia, anemia, petechiae.
- **Hepatic:** transaminases increased.
- **General:** malaise, weakness.
- **Hypersensitivity:** rash, fever.
- **Metabolic:** hypothyroidism.

**Drug Interactions**

- **Drug-Dose:** blood levels and effects may be increased.
- **Drug-Food:** grapefruit juice.
Route/Dosage

Chronic Myeloid Leukemia
PO (Adults): Chronic phase—400 mg once daily, may be 7 to 600 mg once daily; accelerated phase or blast crisis—600 mg once daily, may be 7 to 800 mg/day given as 400 mg more daily based on response and circumstances.

PO (Children): Newly diagnosed Ph+ CML—340 mg/m2/day (not to exceed 600 mg); CML recurrent after failure of bone marrow transplant or resistance to interferon alpha—260 mg/m2/day.

Gastrointestinal Stromal Tumors
PO (Adults): Metastatic or unresectable—400 mg/day; may be up to 400 mg twice daily if well tolerated and response insufficient; Adjuvant treatment after resection—400 mg/day.

Ph+ Acute Lymphoblastic Leukemia
PO (Adults): 600 mg/day.
PO (Children): 340 mg/m2/day (not to exceed 600 mg).

Myelodysplastic/Myloliproliferative Diseases
PO (Adults): 400 mg/day.

Aggressive Systemic Mastocytosis
PO (Adults): 400 mg/day. For patients with eosinophilia—100 mg/day; q to 400 mg/day if well tolerated and response insufficient.

Hypereosinophilic Syndrome and/or Chronic Eosinophilic Leukemia
PO (Adults): 400 mg/day. For patients with FIP1L1–PDGFRa fusion kinase—100 mg/day; increase to 400 mg/day if well tolerated and response insufficient.

Dermatofibrosarcoma Proscarba
PO (Adults): 800 mg/day.

Hepatic Impairment
PO (Adults): p dose by 25% in severe hepatic impairment.

Renal Impairment
PO (Adults): CC 40–50 mL/min—Do not exceed dose of 600 mg/day; CC 20–39 mL/min—initial dose by 50%; as tolerated.

NURSING IMPLICATIONS

Assessment
- Monitor for fluid retention. Weigh regularly, and assess for signs of peripheral edema, pericardial effusion, pulmonary edema, ascites (dyspnea, peripheral edema, swelling in face and ankles, weight gain). Evaluate unexpected weight gain. Fluid retention is usually dose related, more common in accelerated phase or blast crisis, and in more common in the elderly. Treatment usually involves diuretics, supportive therapy, and interruption of imatinib.
- Monitor growth rate in children and adolescents; may cause decrease in growth.
- Monitor vital signs; may cause fever.
- Monitor for tumor lysis syndrome (malignant disease progression, high WBC counts, hyperuricemia, hypercalcemia, hyperphosphatemia, hypocalcemia, and/or electrolyte disturbances). Prevent by maintain adequate hydration and correcting any acidosis prior to starting imatinib.
- Lab Test Considerations: Monitor liver function before and monthly during treatment or when clinically indicated. May cause transaminases and bilirubin which usually lasts 1 week and may require dose reduction or interruption. If bilirubin is ≥3 times the upper limit of normal or transaminases are ≥5 times the upper limit of normal, withhold dose until bilirubin levels return to ≤1.5 times the upper limit of normal and transaminase levels to ≤2.5 times the upper limit of normal. Treatment may then be continued at reduced levels (patients on 400 mg/day should receive 300 mg/day and patients receiving 600 mg/day should receive 400 mg/day).
- Monitor CBC weekly for the first month, biweekly for the second month, and periodically during therapy. May cause neutropenia and thrombocytopenia, usually lasting 2–3 weeks or 3–4 weeks, respectively, and anemia. Usually requires dose reduction, but may require discontinuation (see Implementation).
- Patients receiving chronic phase, myelodysplastic/myeloproliferative disease, aggressive systemic mastocytosis, and hypereosinophilic syndrome and/or chronic eosinophilic leukemia treatment who develop an ANC ≤1.0 x 109/L and/or platelets ≤50 x 109/L should stop imatinib until ANC ≥1.5 x 109/L and platelets ≥75 x 109/L. Then resume imatinib treatment at 400 mg or 600 mg/day.
- Patients receiving accelerated phase and blast crisis treatment or Ph+ acute lymphoblastic leukemia who develop an ANC < 0.5 x 109/L and/or platelets < 10 x 109/L should stop imatinib until ANC ≥1.5 x 109/L and platelets ≥75 x 109/L.
CONTINUED

**imatinib**

- 10% should determine if cytopenia is related to leukemia via marrow aspirate or biopsy. If cytopenia is unrelated to leukemia, reduce dose to 400 mg/day. If cytopenia persists for 2 wk, reduce dose to 300 mg/day. If cytopenia persists for 4 wk and is still unrelated to leukemia, stop imatinib until ANC ≥ 10,000/mm³ and platelets ≥ 100,000/mm³. Reduce treatment at 300 mg/day.

- Patients receiving aggressive systemic mastocytosis with eosinophilia or hypereosinophilic syndrome and/or chronic eosinophilic leukemia with 

- FIP1L1 – PDGFRa fusion kinase— who develop ANC ≤ 0.5 × 10⁹/L and platelets ≤ 50 × 10⁹/L should stop imatinib until ANC > 1.5 × 10⁹/L and platelets > 75 × 10⁹/L. Resume treatment at previous dose.

- Monitor for hypokalemia.

**Potential Nursing Diagnoses**

- High alert: fatalities have occurred with incorrect administration of chemotherapeutic agents. Before administering, clarify all ambiguous orders; double check single, daily, and course-of-therapy dose limits; have second practitioner independently double check original orders and dose calculations. Therapy should be initiated by physician experienced in the treatment of patients with chronic myeloid leukemia.

- Patients requiring anticoagulation should receive low-molecular-weight or standard heparin, not warfarin.

- Treatment should be continued as long as patient continues to benefit.

- PO: Administer with food and a full glass of water to minimize GI irritation.

- Tablets may be dispersed in water or apple juice (50 mL for the 100 mg and 100 mL for the 400 mg tablets) and stirred with a spoon for patients unable to swallow pills. Administer immediately after suspension.

- Doses for children may be given once daily or divided into two doses, one in morning and one in evening.

- Administer doses > 800 mg/day as 400 mg twice daily to decrease exposure to iron.

**Implantation**

- Regular drug name.
- Genetic Implication.
- CONTINUED

---

**Patient/Family Teaching**

- Explain purpose of imatinib to patient.

- Advise patient to avoid grapefruit and grapefruit juice during therapy.

- Advise patients to avoid driving or other activities requiring alertness and concentration on medications known.

- Advise female patients to notify health care professional if pregnancy is planned or suspected; avoid breastfeeding.

**Evaluation/Desired Outcomes**

- Decrease in production of leukemic cells in patients with CML, M1, and ALL.

- Malignant cells in GIST, MDS, MF, AML, and DFSP.

- Why was this drug prescribed for your patient?