Dasatinib (das-uh-tin-ib)

**Special**

**Pharmacologic: enzyme inhibitors**

**Pregnancy Category D**

**Indications**

Chronic, accelerated, or myeloid or lymphoid blast phase Philadelphia chromosome positive (Ph+)- Chronic myeloid leukemia (CML) chronic phase resistant/intolerant to prior therapy (including imatinib). Newly diagnosed chronic phase Ph+ - CML. Ph+ acute lymphoblastic leukemia (Ph+ ALL) resistant/intolerant to prior therapy.

**Action**

Inhibits tyrosine kinases resulting in inhibition of leukemic cell lines, including those resistant to imatinib.

**Therapeutic Effects: Decreased progression of leukemias.

**Pharmacokinetics**

**Absorption:** Well absorbed following oral administration. Absorption is pH dependent.

**Distribution:** Extensively distributed into extravascular space.

**Protein Binding:** 96%.

**Metabolism and Excretion:** Mostly as metabolites.

**Half-life:** 3–5 hr.

**Time/ACTION PROFILE**

**ROUTE**

**ONSET**

**PEAK**

**DURATION**

**PO**

P.O.

2–5 hr.

12 hr.

**Interactions**

**Drug-Drug:** The following drugs may ↓ dasatinib levels and risk of toxicity by inhibiting CYP3A4 (e.g., clarithromycin, dexamethasone, diltiazem, ergot alkaloids, ritonavir, telithromycin) should be administered with caution because of their narrow therapeutic indices and the unpredictability of enzyme inhibition.

**Drug-Food:** Grapefruit juice may ↑ levels and risk of toxicity.

**Drug-Natural Products:** St. John's wort may ↑ levels and effectiveness; avoid concurrent use.

**Drug-Lifestyle:** Smoking, alcohol, obesity, exercise, stress may affect therapeutic indices and the unpredictability of enzyme inhibition.

**Contraindications/Precautions**

Contraindicated in: OB, Lactation: Pregnancy or lactation. CML.

**Warnings/Precautions:** Use Cautiously in: OB, Lactation: Decreased levels and risk of toxicity by inducing CYP3A4.

**Adverse Reactions/Side Effects**

**CNS:** seizures, confusion, depression, dizziness, headache, insomnia, malaise, syncope, vertigo.

**CV:** edema, hypertension, hypotension, MI, PRLL, QT interval prolongation.

**EENT:** conjunctivitis, dry eye, sinusitis.

**EENT:** photosensitivity, pigment disorder, sweating, urticaria.

**GI:** anorexia, constipation, diarrhea, flatulence, nausea, vomiting.

**GU:** renal failure, urinary tract infection.

**Hemat:** bleeding, fever.

**MS:** gynecomastia.

**Musculoskeletal:** myalgia, myositis.

**Respiratory:** bronchospasm, dyspnea, hypoxia, PLE.

**Skin:** alopecia, rash, urticaria.

**Surgical:** increased risk of bleeding.

**Other:** photosensitivity, pigmentation, sweating, urticaria.

**Other:** headache, hypocalcemia.

**Other:** rare: agranulocytosis, fever, sepsis, thrombocytopenia, toxic epidermal necrolysis, neutropenia, thrombocytopenia, systemic inflammatory response syndrome, tumor lysis syndrome.

**Other:** life-threatening: bleeding events, anemia, hemorrhage, tenosynovitis.

**Other:** death.

**Other:** discontinued.

**Dosage**

**PO**

Adults: 100 mg q.d.; or 70 mg q.d. in those unable to tolerate 100 mg q.d. The dose of dasatinib may be required. If concurrent use is required, ↓ dose of dasatinib may be required. The following drugs may ↓ dasatinib levels and risk of toxicity by inhibiting CYP3A4 (e.g., clarithromycin, dexamethasone, diltiazem, ergot alkaloids, ritonavir, telithromycin) should be administered with caution because of their narrow therapeutic indices and the unpredictability of enzyme inhibition.

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**Warnings/Precautions:** Use Cautiously in: OB, Lactation: Decreased levels and risk of toxicity by inducing CYP3A4.
Route/Dosage
Accelerated, or myeloid or lymphoid blast phase CML, or Ph + ALL
PO (Adults): 140 mg once daily; may increase to 180 mg once daily (hematologic or cytogenetic response is not achieved). Concurrent strong CYP3A4 inhibitor—initiate at 140 mg once daily.

Chronic phase CML
PO (Adults): 80 mg once daily; may increase to 140 mg once daily for hematologic or cytogenetic response is not achieved. Concurrent strong CYP3A4 inhibitor—initiate at 20 mg once daily.

NURSING IMPLICATIONS
Assessment
● Monitor for fluid retention. Weight regularly, and assess for signs of peripheral edema, pulmonary edema, ascites (pitting), pericardial effusion, pleural effusion, pulmonary edema, ascites (dyspnea, periorbital edema, swelling in feet and ankles, weight gain). Evaluate unexpected weight gain.
● Monitor CBC weekly for the first 2 mo, then monthly during therapy or when clinically indicated. May cause Grade 3 or 4 thrombocytopenia requiring platelet transfusions and/or platelets stopping and resuming therapy and with each Rx refill in case of changes.

Potential Nursing Diagnoses
Hypokalemia or hypomagnesemia should be corrected before administration. May cause dizziness. Caution patients to avoid driving or other activities requiring alertness.

Implementation
High Alert: Adverse effects have occurred with incorrect administration of chemotherapy agents. Before administering, clarify all ambiguous orders. Double check single, daily, and course-of-therapy dose limits; have second practitioner independently double check original order and dose calculations. Therapy should be initiated by physicians experienced in the treatment of patients with chronic myeloid leukemia.

PO: Administer without regard to meals. Swallow tablets whole; do not crush, break or chew.

● Patients receiving chronic phase treatment who develop an ANC < 0.5 x 10^9/L and/or platelets < 50 x 10^9/L should stop dasatinib until ANC > 0.5 x 10^9/L and/or platelets > 50 x 10^9/L. Then resume dasatinib treatment at original dose if recovery occurs 7 days. If recovery does not occur within 21 days, stop dasatinib and resume at 80 mg once daily for 2nd episode or 50 mg once daily for 3rd episode for newly diagnosed patients or discontinuation of patient is required or intolerant to prior therapy including imatinib.

● Patients receiving accelerated phase and blast crisis treatment who develop an ANC < 0.5 x 10^9/L and/or platelets < 50 x 10^9/L. Then resume dasatinib treatment at original dose if recovery occurs. If cytopenia is related to leukemia, consider dose escalation to 180 mg once daily.

● Advise patient to notify health care professional immediately if fever, bleeding, or easy bruising, swelling, weight gain, or increasing shortness of breath or signs and symptoms of pulmonary arterial hypertension (shortness of breath, fatigue, and swelling ankles and legs) occur.

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- Instruct patient to notify health care professional of all Rx or OTC medications, vitamins, or herbal products being taken or if lactose intolerant and consult health care professional before taking any new medications. Advise patient to avoid taking medicines that reduce stomach acid to improve absorption. Medicines that neutralize stomach acid, such as antacids, may be used up to 2 hrs before or 2 hrs after dasatinib dose.

- Inform patient that headache and musculoskeletal pain may occur, notify health care professional if severe.

- May have intragraft effects. Advise patient to use effective contraception and to notify health care professional if pregnancy is planned or suspected, or if breastfeeding. Women who are pregnant or may become pregnant should avoid handling crushed or broken tablets. Men receiving dasatinib should be advised to use a condom to avoid pregnancy in their partner.

Evaluation/Desired Outcomes

- Decreased progression of leukemia. Most cytogenic responses occurred after 12 wks of therapy. Treatment should be continued as long as patient continues to benefit or until therapy is no longer tolerated by patient.

Why was this drug prescribed for your patient?