Dasatinib

Class:
_Antineoplastic agent, Tyrosine Kinase Inhibitor.

Indications:
_Chronic myelogenous leukemia (CML), Philadelphia chromosome-positive (Ph+), newly diagnosed in chronic phase.
_ CML, Ph+, resistant or intolerant.
_ Acute lymphoblastic leukemia (ALL), Ph+

Available dosage form in the hospital:
70 mg, tablet.
50 mg, tablet.
20 mg, tablet

Trade Names:
Sprycel

Doses: Note: The effect of discontinuation after complete cytogenetic remission is achieved has not been studied.

-Chronic myelogenous leukemia (CML), Philadelphia chromosome-positive (Ph+), newly diagnosed in chronic phase:
Oral: 100 mg once daily until disease progression or unacceptable toxicity. In clinical studies, a dose escalation to 140 mg once daily was allowed in patients not achieving hematologic or cytogenetic response at recommended initial dosage.

-CML, Ph+, resistant or intolerant:
-Oral: Chronic phase: 100 mg once daily until disease progression or unacceptable toxicity. In clinical studies, a dose escalation to 140 mg once daily was allowed in patients not achieving hematologic or cytogenetic response at recommended initial dosage.
-Accelerated or blast phase: 140 mg once daily until disease progression or unacceptable toxicity. In clinical studies, a dose escalation to 180 mg once daily was allowed in patients not achieving hematologic or cytogenetic response at recommended initial dosage.

-Acute lymphoblastic leukemia (ALL), Ph+:
Oral: 140 mg once daily until disease progression or unacceptable toxicity. In clinical studies, a dose escalation to 180 mg once daily was allowed in patients not achieving hematologic or cytogenetic response at recommended initial dosage.

-Dosage adjustment for concomitant CYP3A4 inhibitors:
Avoid concomitant administration with strong CYP3A4 inhibitors (eg, clarithromycin, itraconazole, ketoconazole, nefazodone, protease inhibitors, telithromycin, voriconazole, grapefruit juice); if concomitant administration with a strong CYP3A4 inhibitor cannot be avoided, consider reducing dasatinib from 100 mg once daily to 20 mg once daily **or** from 140 mg once daily to 40 mg once daily, with careful monitoring. If reduced dose is not tolerated, the strong CYP3A4 inhibitor must be discontinued or dasatinib therapy temporarily held until concomitant inhibitor use has ceased. When a strong CYP3A4 inhibitor is discontinued, allow a washout period (~1 week) prior to adjusting dasatinib dose upward.

-Dosage adjustment for concomitant CYP3A4 inducers:
Avoid concomitant administration with strong CYP3A4 inducers (eg, carbamazepine, dexamethasone, phenobarbital, phenytoin, rifampin, St John's wort); if concomitant administration with a strong CYP3A4 inducer cannot be avoided, consider increasing the dasatinib dose with careful monitoring.

Geriatric
Refer to adult dosing.

Renal Impairment:

No dosage adjustment provided in the manufacturer's labeling. However, <4% of dasatinib and metabolites are renally excreted.

Hepatic Impairment:

No dosage adjustment necessary; use with caution.

Dosing: Adjustment for Toxicity

-Hematologic toxicity:

-*Chronic phase CML* (100 mg daily starting dose): For ANC <500/mm^3 or platelets <50,000/mm^3, withhold treatment until ANC ≥1000/mm^3 and platelets ≥50,000/mm^3; then resume treatment at the original starting dose if recovery occurs in ≤7 days. If platelets <25,000/mm^3 or recurrence of ANC <500/mm^3 for >7 days, withhold treatment until ANC ≥1000/mm^3 and platelets ≥50,000/mm^3; then resume treatment at 80 mg once daily (second episode). For third episode, further reduce dose to 50 mg once daily (for newly-diagnosed patients) or discontinue (for patients resistant or intolerant to prior therapy)

-*Accelerated or blast phase CML and Ph+ ALL* (140 mg once daily starting dose): For ANC <500/mm^3 or platelets <10,000/mm^3, if cytopenia unrelated to leukemia, withhold treatment until ANC ≥1000/mm^3 and platelets ≥20,000/mm^3; then resume treatment at the original starting dose. If cytopenia recurs, withhold treatment until ANC ≥1000/$mm^3$and platelets ≥20,000/mm^3; then resume treatment at 100 mg once daily (second episode) or 80 mg once daily (third episode). For cytopenias related to leukemia (confirm with marrow aspirate or biopsy), consider dose escalation to 180 mg once daily.

-Nonhematologic toxicity: Withhold treatment until toxicity improvement or resolution; if appropriate, resume treatment at a reduced dose based on the event severity. Fluid retention is managed with diuretics and supportive care. Effusions may require diuretics and/or dose interruption. Corticosteroids (eg, prednisone 20 mg/day for 3 days) may be considered for pleural or pericardial effusion with significant symptoms (hold dasatinib and reinitiate at a decreased dose when effusion resolves). Rash may be managed with steroids (topical or systemic), treatment interruption, dose reduction, or discontinuation (NCCN CML guidelines v.2.2013). Discontinue with confirmed pulmonary arterial hypertension.

Common side effects:

Cardiovascular: Fluid retention, superficial edema, Generalized edema , pericardial effusion , CHF/cardiac dysfunction ; includes cardiac failure, cardiomyopathy, diastolic dysfunction, ejection fraction decreased, left ventricular dysfunction, ventricular failure); arrhythmia, chest pain, flushing, hypertension, palpitation **Central nervous system**: Headache, fatigue, fever , CNS bleeding (≤3%; grades 3/4: ≤3%), chills, depression, dizziness, insomnia, pain, somnolence

Dermatologic: Rash ; includes drug eruption, erythema, erythema multiforme, erythematous rash, erythrosis, exfoliative rash, follicular rash, heat rash, macular rash, maculopapular rash, milia, papular rash, pruritic rash, pustular rash, skin exfoliation, skin irritation, urticaria vesiculosa, vesicular rash)

Endocrine & metabolic: Hypophosphatemia (grades 3/4), hypokalemia (grades 3/4), hypocalcemia (grades 3/4) **Gastrointestinal**: Diarrhea, nausea, vomiting , abdominal pain

Hematologic: Thrombocytopenia , neutropenia , anemia , hemorrhage, neutropenic fever

Neuromuscular & skeletal: Musculoskeletal pain, myalgia , arthralgia

Respiratory: Pleural effusion , dyspnea

Miscellaneous: Infection (9% to 12%, includes bacterial, fungal, viral)

Pregnancy Risk Factor: D