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bortezomib (bor-tez-o-mib)

Velcade

Classification
Therapeutic: antineoplastics
Pharmacologic: proteasome inhibitors

Pregnancy Category D

Indications
Multiple myeloma (as initial therapy or after progression); with melphalan and prednisone. Mantle cell lymphoma after at least one other therapy.

Action
Inhibits proteasome, a regulator of intracellular protein catabolism, resulting in disruption of various intracellular processes. Cytotoxic to a variety of cancerous cells.

Therapeutic Effects: Death of rapidly replicating cells, particularly malignant ones.

Pharmacokinetics
Absorption: IV administration results in complete bioavailability.
Distribution: Unknown.
Metabolism and Excretion: Mostly metabolized by the liver (P450 enzymes); excretion is unknown.
Half-life: 9–15 hr.

TIME/ACTION PROFILE
ROUTE ONSET PEAK DURATION
IV unknown 38 days* unknown
*Median time to response based on clinical parameters

Contraindications/Precautions
Contraindicated in: Hypersensitivity to bortezomib, boron, or mannitol; Intra-thecal administration (may cause death); OB: Potential fetal harm; Lactation: Potentially serious drug reaction in nursing infants. Use Cautiously in: OB: Women with childbearing potential; Moderate to severe hepatic impairment (may q levels, risk of toxicity); History of or risk factors for HF; Pedi: Safety not established.

Adverse Reactions/Side Effects
CNS: PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY, REVERSIBLE POSTERIOR LEUKOENCEPHALOPATHY SYNDROME (RPLS), fatigue, malaise, weakness, diarrhea, syncope.
CV: hypotension, HF.
EENT: blurred vision, diplopia.
GI: LIVER FAILURE, anorexia, constipation, diarrhea, nausea, vomiting.
Hemat: BLEEDING, anemia, neutropenia, thrombocytopenia.
Neuro: peripheral neuropathy.
Misc: fever, tumor lysis syndrome.

Interactions
Drug-Drug: Concurrent neurotoxic medications including amiodarone, some antivirals, nitrofurantoin, isoniazid, or HMG-CoA reductase inhibitors may ↑ risk of peripheral neuropathy.

Route/Dosage
Previously Untreated Multiple Myeloma
IV, Subcut (Adults): 1.3 mg/m2 twice weekly for Cycles 1–4 (days 1, 4, 8, 11, 22, 25, 29 and 32; no treatment during cycle 3), then once weekly for Cycles 5–9 (days 1, 8, 22, and 29; no treatment during Cycle 7); further cycles/doses depend on response and toxicity.
Relapsed Multiple Myeloma and Mantle Cell Lymphoma
IV, Subcut (Adults): 1.3 mg/m2 twice weekly for 2 wk (days 1, 4, 8, and 11), followed by a 10–day rest; further cycles/doses depend on response and toxicity.
Hepatic Impairment
IV (Adults): Moderate or severe hepatic impairment—0.7 mg/m2 per injection for the first cycle, then 1 to 1.5 mg/m2 per injection or ↓ further to 0.5 mg/m2 per injection, based on tolerability.

NURSING IMPLICATIONS
Assessment
• Monitor visual signs frequently during therapy. May cause severe and irreversible hypopigmentation requiring adjustment of antihypertensives, hydration, or administration of amphotericin B.
• Monitor for GI adverse effects. May require antimotility, antidiarrheals, and fluid and electrolyte replacement to prevent dehydration. Weigh weekly, modify diet as tolerated.

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Monitor for signs and symptoms of tumor lysis syndrome (tachypnea, tachycardia, hypotension, pulmonary edema). Patients with high tumor burden prior to treatment are at increased risk.

Monitor for signs of RPLS (headache, seizure, lethargy, confusion, blindness). Hypertension may or may not be present. May occur within 16 hr to 1 yr of initiation of therapy. Treat hypertension if present and discontinue bortezomib therapy. Symptoms usually resolve within days.

Assess for any new signs or symptoms that may be suggestive of PML, an opportunistic infection of the brain caused by the JC virus, that leads to death or severe disability; withhold dose and notify health care professional promptly. Bortezomib exposure may begin gradually but usually worsen rapidly. Symptoms vary depending on which part of brain is infected. Mental function declines rapidly and progressively, causing dementia; speaking becomes increasingly difficult; partial blindness; difficulty walking; headache; seizures may occur. Diagnosis is usually made via gadolinium-enhanced MRI and CSF analysis. Risk of PML increases with the number of infusions. Withhold bortezomib at first sign of PML.

Lab Test Considerations:
Monitor CBC and platelet count frequently during therapy. The nadir of thrombocytopenia is day 11 and recovery is usually by next cycle. Occurs more commonly in cycles 1 and 2, but may occur throughout therapy. May require discontinuation of therapy.

Monitor blood glucose levels closely in patients taking oral hypoglycemic agents; may require adjustment of antidiabetic agent dose.

Potential Nursing Diagnoses
Risk for injury (Adverse Reactions)

Implementation

Should be administered under the supervision of a physician experienced in the use of antineoplastic therapy.

Prepare solution in a biologic cabinet. Wear gloves, gown, and mask, while handling medication. Discard equipment in specially designated containers.

IV Administration

pH: 2.0–6.5.

Subcut: Reconstitute each vial with 1.4 mL of 0.9% NaCl. Concentration: 2.5 mg/mL. Solution should be clear and colorless; do not administer solutions that are discolored or contain particulate matter. May inject into thigh or abdomen; rotate injection sites. Inject into sites at least 1 inch from other sites and avoid tender, bruised, erythematous, or indurated sites. If local injection site reactions occur, may inject a less concentrated (1 mg/mL) solution.

Direct IV: Reconstitute each vial with 3.5 mL of 0.9% NaCl. Concentration: 1 mg/mL. Administer reconstituted solution within 8 hr at room temperature; 3 of the 8 hr may be stored in a syringe. Rate: Administer as a 3–5 second bolus injection twice weekly for 2 wk followed by a 10 day rest period. At least 72 hr should elapse between consecutive doses.

If peripheral neuropathy is Grade 1 (paresthesia or loss of reflexes without pain or loss of function) continue prescribed dose. If peripheral neuropathy is Grade 2 with pain or Grade 3 (interfering with activities of daily living) withhold dose until toxicity resolves, then re-initiate with a reduced dose of 0.7 mg/m² and decrease frequency to once/wk.

Patient/Family Teaching

Inform patient that dehydration may occur with vomiting or diarrhea. Advise patient to maintain fluid intake and to notify health care professional of diarrhea or vomiting.

Inform patient to contact health care professional if they experience new or worsening signs of peripheral neuropathy (tingling, numbness, pain, weakness, loss of sensation in the feet or hands). PML (progressive weakness on one side of the body or clumsiness of limbs; disturbance of vision; changes in thinking, memory, and orientation leading to confusion and personality changes; or signs of deterioration (dizziness, fainting) due to vomiting or diarrhea, rash, shortness of breath, cough, swelling of feet, ankles, or legs, confusion, persistent headache, reduced reflexes, increase in BP or blurred vision) occur.

May cause dizziness and blurred vision. Caution patient to avoid driving or other activities requiring alertness until response to medication is known.

Inform patient to notify health care professional of all Rx or OTC medications, vitamins, or herbal products being taken and consult health care professional before taking Rx, OTC, or herbal products.
Continued

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Advise diabetic patients taking oral hypoglycemic agents to monitor blood glucose frequently and notify health care professional of changes in blood sugar.

Advise patient of the need for contraception and to avoid breast feeding during therapy. Patient should notify health care professional immediately if pregnancy is suspected.

Evaluation/Desired Outcomes

Decrease in serum and urine myeloma protein.

Decrease in size and spread of malignancy.

Why was this drug prescribed for your patient?