

You Are Invited



Treatment of Multiple Myeloma – Where is it Going?

Presented by

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6:00 PM**

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Program Background*

This educational offering from Millennium Pharmaceuticals, Inc., has been developed in collaboration with preeminent thought leaders, and is designed to address the contemporary challenges of medical oncologists, pharmacists, oncology nurses, and other health care providers who care for patients with hematologic malignancies. Each program will discuss the comprehensive clinical evidence of VELCADE® (bortezomib) for Injection in MM or MCL, including a review of VELCADE pharmacology, efficacy, safety, dosing, and administration.

* Please note that this is not a CME-accredited program.

VELCADE® (bortezomib) for Injection is indicated for the treatment of patients with multiple myeloma. VELCADE® (bortezomib) for Injection is indicated for the treatment of patients with mantle cell lymphoma who have received at least 1 prior therapy.

Please see Important Safety Information for VELCADE on the back.



Indications and Important Safety Information for VELCADE® (bortezomib)

INDICATIONS:

- VELCADE is indicated for the treatment of patients with multiple myeloma. VELCADE is indicated for the treatment of patients with mantle cell lymphoma who have received at least 1 prior therapy.

CONTRAINDICATIONS:

- VELCADE is contraindicated in patients with hypersensitivity to bortezomib, boron, or mannitol.

WARNINGS AND PRECAUTIONS:

- VELCADE should be administered under the supervision of a physician experienced in the use of antineoplastic therapy. Complete blood counts (CBC) should be monitored frequently during treatment with VELCADE.

Pregnancy Category D:

- Women of childbearing potential should avoid becoming pregnant while being treated with VELCADE.

Peripheral Neuropathy:

- VELCADE treatment causes a peripheral neuropathy that is predominantly sensory. However, cases of severe sensory and motor peripheral neuropathy have been reported. Patients with pre-existing symptoms (numbness, pain or a burning feeling in the feet or hands) and/or signs of peripheral neuropathy may experience worsening peripheral neuropathy (including \geq Grade 3) during treatment with VELCADE. Patients should be monitored for symptoms of neuropathy, such as a burning sensation, hyperesthesia, hypoesthesia, paresthesia, discomfort, neuropathic pain or weakness. Patients experiencing new or worsening peripheral neuropathy may require change in the dose and schedule of VELCADE. The long-term outcome of peripheral neuropathy has not been studied in mantle cell lymphoma.

Hypotension:

- Hypotension (postural, orthostatic, and hypotension NOS) has been observed throughout therapy. Caution should be used when treating patients with a history of syncope, patients receiving medications known to be associated with hypotension, and patients who are dehydrated.

Cardiac Disorders:

- Acute development or exacerbation of congestive heart failure and new onset of decreased left ventricular ejection fraction have been reported, including reports in patients with no risk factors for decreased left ventricular ejection fraction. Patients with risk factors for, or who have existing heart disease should be closely monitored. There have been isolated cases of QT-interval prolongation in clinical studies; causality has not been established.

Pulmonary Disorders:

- There have been reports of acute diffuse infiltrative pulmonary disease of unknown etiology such as pneumonitis, interstitial pneumonia, lung infiltration and Acute Respiratory Distress Syndrome (ARDS) in patients receiving VELCADE. Some of these events have been fatal.
- There have been reports of pulmonary hypertension associated with VELCADE administration in the absence of left heart failure or significant pulmonary disease.

Reversible Posterior Leukoencephalopathy Syndrome (RPLS):

- There have been reports of RPLS in patients receiving VELCADE. RPLS is a rare, reversible, neurological disorder which can present with seizure, hypertension, headache, lethargy, confusion, blindness, and other visual and neurological disturbances.

Gastrointestinal Adverse Events:

- VELCADE treatment can cause nausea, diarrhea, constipation, and vomiting sometimes requiring use of antiemetic and antidiarrheal medications. Ileus can occur. Fluid and electrolyte replacement should be administered to prevent dehydration.

Thrombocytopenia/Neutropenia:

- VELCADE is associated with thrombocytopenia and neutropenia.
- Platelet counts should be monitored prior to each dose of VELCADE. Patients experiencing thrombocytopenia may require change in the dose and schedule of VELCADE. There have been reports of gastrointestinal and intracerebral hemorrhage in association with VELCADE. Transfusions may be considered.

Tumor Lysis Syndrome:

- Because VELCADE is a cytotoxic agent and can rapidly kill malignant cells, the complications of tumor lysis syndrome may occur.

Hepatic Events:

- Cases of acute liver failure have been reported in patients receiving multiple concomitant medications and with serious underlying medical conditions.

Patients with Hepatic Impairment:

- VELCADE exposure is increased in patients with moderate or severe hepatic impairment. These patients should be treated with VELCADE at reduced starting doses and closely monitored for toxicities.

ADVERSE EVENT DATA:

- **Previously Untreated MM:** In the phase 3 VELCADE with melphalan and prednisone study, the most commonly reported adverse events were thrombocytopenia (52% vs 47%), neutropenia (49% vs 46%), nausea (48% vs 28%), peripheral neuropathy (47% vs 5%), diarrhea (46% vs 17%), anemia (43% vs 55%), constipation (37% vs 16%), neuralgia (36% vs 1%), leukopenia (33% vs 30%), vomiting (33% vs 16%), pyrexia (29% vs 19%), fatigue (29% vs 26%), lymphopenia (24% vs 17%), anorexia (23% vs 10%), asthenia (21% vs 18%), cough (21% vs 13%), insomnia (20% vs 13%), and edema peripheral (20% vs 10%).
- **Relapsed MM and MCL:** In the integrated analysis of 1163 patients in phase 2 and 3 studies, the most commonly reported adverse events were asthenic conditions (including fatigue, malaise, and weakness) (64%), nausea (55%), diarrhea (52%), constipation (41%), peripheral neuropathy NEC (including peripheral sensory neuropathy and peripheral neuropathy aggravated) (39%), thrombocytopenia and appetite decreased (including anorexia) (each 36%), pyrexia (34%), vomiting (33%), anemia (29%), edema (23%), headache, paresthesia and dysesthesia (each 22%), dyspnea (21%), and cough and insomnia (each 20%). Twenty percent (20%) of patients experienced at least 1 episode of \geq Grade 4 toxicity, most commonly thrombocytopenia (5%) and neutropenia (3%).

In the integrated analysis, a total of 50% of patients experienced serious adverse events (SAEs). The most commonly reported SAEs included pneumonia (7%), pyrexia (6%), diarrhea (5%), vomiting (4%), and nausea, dehydration, dyspnea and thrombocytopenia (each 3%).

DRUG INTERACTIONS:

- Patients who are concomitantly receiving VELCADE and drugs that are inhibitors or inducers of cytochrome P450 3A4 should be closely monitored for either toxicities or reduced efficacy.

USE IN SPECIFIC POPULATIONS:

Nursing Mothers:

- It is not known whether bortezomib is excreted in human milk. Because of the potential for serious adverse reactions in nursing infants from VELCADE, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use:

- The safety and effectiveness of VELCADE in children has not been established.

Patients with Renal Impairment:


- Dosing adjustments of VELCADE are not necessary for patients with renal insufficiency. In patients undergoing dialysis, VELCADE should be administered after the dialysis procedure.

Patients with Diabetes:

- During clinical trials, hypoglycemia and hyperglycemia were reported in diabetic patients receiving oral hypoglycemics. Patients on oral antidiabetic agents receiving VELCADE treatment may require close monitoring of their blood glucose levels and adjustment of the dose of their antidiabetic medication.

Please see accompanying full Prescribing Information.



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