

DRUG INFO

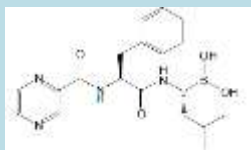


UNIT FARMASI
HOSPITAL KOTA MARUDU

ISSUE:02/21

Introduction

VELCADE® for Injection contains **bortezomib** which is an **antineoplastic agent**. **Bortezomib** is a modified dipeptidyl boronic acid. The chemical name for bortezomib, the monomeric boronic acid, is [(1R)-3-methyl-1-[[[(2S)-1-oxo-3-phenyl-2-[(pyrazinylcarbonyl)amino]propyl]amino]butyl]boro nic acid.



Indication

Treatment of adult patients with

1. Multiple Myeloma (MM)
2. Mantle Cell Lymphoma

Mechanism of Action

Bortezomib is a reversible inhibitor of the chymotrypsin-like activity of the 26S proteasome in mammalian cells.

The 26S proteasome is a large protein complex that degrades ubiquitinated proteins. The ubiquitin-proteasome pathway plays an essential role in regulating the intracellular concentration of specific proteins, thereby maintaining homeostasis within cells.

Inhibition of the 26S proteasome prevents this targeted proteolysis, which can affect multiple signaling cascades within the cell. This disruption of normal homeostatic mechanisms can lead to cell death.

Dosage and Administration

- For **subcutaneous or intravenous use only**. Each route of administration has a **different reconstituted concentration**
- The recommended starting dose of VELCADE is **1.3 mg/m²** administered either as a 3 to 5 second bolus intravenous injection or subcutaneous injection.
- Retreatment for multiple myeloma: May retreat starting at the last tolerated dose.
- Hepatic Impairment: Use a lower starting dose for patients with moderate or severe hepatic impairment.
- Dose must be **individualized** to prevent overdose.

REFERENCES:

Field-Smith, A., Morgan, G., & Davies, F. (2006). Bortezomib (Velcade?) in the treatment of multiple myeloma. *Therapeutics And Clinical Risk Management*, 2(3), 271-279. doi: 10.2147/tcrm.2006.2.3.271

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Painuly, U., & Kumar, S. (2013). Efficacy of Bortezomib as First-Line Treatment for Patients with Multiple Myeloma. *Clinical Medicine Insights: Oncology*, 7, CMO.S7764. doi: 10.4137/cmo.s7764

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Warning and Precautions

- **Peripheral Neuropathy:** Manage with dose modification or discontinuation.
- **Hypotension:** Use caution when treating patients taking antihypertensives, with a history of syncope, or with dehydration.
- **Cardiac Toxicity:** Worsening of and development of cardiac failure has occurred. Closely monitor patients with existing heart disease or risk factors for heart disease.
- **Pulmonary Toxicity:** Acute respiratory syndromes have occurred. Monitor closely for new or worsening symptoms and consider interrupting VELCADE therapy.
- **Posterior Reversible Encephalopathy Syndrome:** Consider MRI imaging for onset of visual or neurological symptoms; discontinue VELCADE if suspected.
- **Gastrointestinal Toxicity:** Nausea, diarrhea, constipation, and vomiting may require use of antiemetic and antidiarrheal medications or fluid replacement.
- **Thrombocytopenia and Neutropenia:** Monitor complete blood counts regularly throughout treatment.
- **Tumor Lysis Syndrome:** Closely monitor patients with high tumor burden.
- **Hepatic Toxicity:** Monitor hepatic enzymes during treatment. Interrupt VELCADE therapy to assess reversibility.
- **Thrombotic Microangiopathy:** Monitor for signs and symptoms. Discontinue VELCADE if suspected.
- **Embryo-fetal Toxicity:** VELCADE can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and to avoid pregnancy.

Adverse Effect

Most commonly reported adverse reactions (incidence $\geq 20\%$) in clinical studies include nausea, diarrhea, thrombocytopenia, neutropenia, peripheral neuropathy, fatigue, neuralgia, anemia, leukopenia, constipation, vomiting, lymphopenia, rash, pyrexia, and anorexia.

REFERENCES:

Raaben, M., Grinwis, G., Rottier, P., & de Haan, C. (2010). The Proteasome Inhibitor Velcade Enhances rather than Reduces Disease in Mouse Hepatitis Coronavirus-Infected Mice. *Journal Of Virology*, 84(15), 7880-7885. doi: 10.1128/jvi.00486-10

Zhang, S., Kulkarni, A., Xu, B., Chu, H., Kourelis, T., & Go, R. et al. (2020). Bortezomib-based consolidation or maintenance therapy for multiple myeloma: a meta-analysis. *Blood Cancer Journal*, 10(3). doi: 10.1038/s41408-020-0298-1

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