



Submitted by:  
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**NCCN Guidelines Panel: Multiple Myeloma**

On behalf of Millennium: The Takeda Oncology Company, I respectfully request the NCCN Multiple Myeloma Guidelines Panel to review the enclosed data on the use of VELCADE® (bortezomib) as salvage therapy in patients with multiple myeloma.

**Specific Changes:**

- Inclusion of a footnote to bortezomib and bortezomib/dexamethasone as a salvage therapy in the Myeloma Therapy section (MYEL-D, 2 of 2) of the NCCN Clinical Practice Guidelines (NCCN Guidelines™) in Multiple Myeloma (version V2.2013), indicating that bortezomib±dexamethasone retreatment might be considered for use in patients who have relapsed ≥6 months after prior bortezomib treatment
- Inclusion of new data from a recently published prospective study employing bortezomib±dexamethasone retreatment as a salvage therapy within the narrative section of the Guidelines, specifically on page MS-24 of version V2.2013, where the current data on bortezomib±dexamethasone as salvage therapy are included
- Inclusion of the associated reference for the recently published data.

**FDA Clearance:** The FDA has approved VELCADE for the treatment of multiple myeloma, including in the relapsed setting. The recommended dose of VELCADE is 1.3 mg/m<sup>2</sup> on days 1, 4, 8, and 11 of 21-day cycles, administered either as a 3- to 5-second bolus intravenous injection or subcutaneous injection. Data from the study referenced below are not included in the US Prescribing Information for VELCADE.

**Rationale:** A prospective, international phase 2 study of bortezomib±dexamethasone retreatment in 130 patients with relapsed multiple myeloma (median 2 prior lines of therapy) who had relapsed ≥6 months after achieving a partial response or better (≥PR) with prior bortezomib-based therapy was fully published in March 2013 in the *British Journal of Haematology*. The main findings were:

- Retreatment with bortezomib±dexamethasone resulted in an overall response rate of 40%
- In patients who achieved a best confirmed response of ≥PR with retreatment, the median duration of response and time to progression were 6.5 and 8.4 months, respectively
- During bortezomib±dexamethasone retreatment, grade ≥3 adverse events (AEs) occurred in 60% of patients, the most common being thrombocytopenia (35%), diarrhea, neutropenia (each 7%), pneumonia (6%), and anemia (5%)
- Serious AEs, discontinuations due to AEs, and deaths due to AEs occurred in 32%, 21%, and 6% of patients, respectively
- Forty percent of patients experienced neuropathy events, including 9% grade 3 (no grade 4) neuropathy. The median time to improvement or resolution of neuropathy events was 1.5 and 8.9 months, respectively.

The following enclosures are submitted in support of the above proposed changes:

- Petrucci MT et al. A prospective, international phase 2 study of bortezomib retreatment in patients with relapsed multiple myeloma. *Br J Haematol* 2013;160(5):649–59
- VELCADE (bortezomib) for Injection. United States prescribing information, Rev 15, issued October 2012.

Yours sincerely

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