On behalf of Millennium Pharmaceuticals, Inc., I respectfully request the NCCN Multiple Myeloma Guidelines Panel to review the enclosed data on the use of VELCADE® (bortezomib) as induction therapy prior to stem cell transplantation (SCT), and as maintenance therapy, in patients with multiple myeloma (MM).

**Specific Changes:** Consider updating the NCCN guidelines with recently published and presented data from Phase 3 and Phase 2 studies of VELCADE-based induction regimens. Consider the inclusion of VELCADE as a Category 2A recommended treatment option for maintenance therapy, based upon recently published and presented data from Phase 3 studies.

**FDA Clearance:** The FDA has approved VELCADE for the treatment of multiple myeloma. Please refer to the enclosed prescribing information for the full FDA-approved indications and safety information.

**Rationale:** Final or updated results from five Phase 3 and two Phase 2 studies of VELCADE-based induction regimens in transplant-eligible patients have recently been published or presented, warranting updates to the NCCN guidelines and providing further support for the existing treatment recommendations:

- Final data from the IFM 2005-01 Phase 3 study demonstrating the superiority of VELCADE-dexamethasone versus VAD as induction have been published,¹ supporting the Category 1 recommendation for this regimen
- Final data from the GIMEMA MMY-3006 Phase 3 study demonstrating the superiority of VELCADE-thalidomide-dexamethasone versus thalidomide-dexamethasone as induction and consolidation have been published,² supporting the Category 1 recommendation for this regimen
  - In addition, updated data from the GEM05MENOS65³ and IFM 2007-02⁴ Phase 3 studies incorporating bortezomib-thalidomide-dexamethasone were presented at the 52⁰ Annual Meeting of the American Society of Hematology (ASH) in Orlando, Florida, in December 2010, and the 2010 Annual Meeting of the American Society of Clinical Oncology (ASCO) in Chicago, Illinois, in June 2010, respectively, providing further support for the Category 1 recommendation for this regimen as induction therapy
- Updated data from the HOVON-65/GMMG-HD4 Phase 3 trial demonstrating the superiority of VELCADE-doxorubicin-dexamethasone versus VAD as induction were presented at the ASH 2010 meeting,⁵ supporting the Category 1 recommendation for this regimen
- Updated data from the EVOLUTION Phase 2 study incorporating VELCADE-cyclophosphamide-dexamethasone induction,⁶ and new data from the IFM 2008 Phase 2 study of VELCADE-lenalidomide-dexamethasone as induction and consolidation,⁷ were also presented at the ASH 2010 meeting, supporting the Category 2A and 2B recommendations for these regimens, respectively
Regarding the use of VELCADE as maintenance therapy, final or updated results from four Phase 3(b) studies have recently been published or presented, supporting the inclusion of VELCADE as a Category 2A recommended treatment option for maintenance therapy:

- Updated data from the HOVON-65/GMMG-HD4 Phase 3 study incorporating VELCADE versus thalidomide as maintenance therapy following SCT were presented at the ASH 2010 meeting, demonstrating the good tolerability of VELCADE maintenance and the induction of additional responses.

- Updated data from the UPFFRONT Phase 3b study incorporating VELCADE maintenance following VELCADE-based induction were presented at the ASH 2010 meeting, demonstrating some increases in response rates without substantial increases in toxicity compared with induction therapy.

- Final data from the GEM05>65 and GIMEMA MM-03-05 Phase 3 studies incorporating VELCADE-thalidomide/prednisone as maintenance therapy following VELCADE-based induction therapy have been published, demonstrating increases in response rates during maintenance therapy and notable long-term outcomes.

These findings are supported by data from two Phase 2 studies of VELCADE as maintenance post-SCT or as post-induction maintenance in patients with high-risk disease.

The following enclosures (cited references) are included for your review (copyright-paid where applicable):


- VELCADE prescribing information.

Yours sincerely

Deya Corzo, MD
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