JANSSEN-ORTHO

NOTICE TO HOSPITALS
Important Safety Information on VELCADE*
(bortezomib mannitol boronic ester) for Injection

June 17th, 2005

To: Hospital Chief of Medical Staff

Please distribute to the relevant Departments of Oncology, Hematology, Cancer Wards, Oncology Clinics, Oncology Pharmacy and Nursing, and other involved professional staff and **post this NOTICE** as appropriate in your institution.

Subject: Rare reports of acute liver failure and other hepatic events, and reports of decreased left ventricular ejection fraction in patients treated with VELCADE

VELCADE (bortezomib mannitol boronic ester) is an antineoplastic agent indicated for the treatment of multiple myeloma patients who have relapsed following front-line therapy and are refractory to their most recent therapy. VELCADE has been issued marketing authorization with conditions, pending the results of studies to verify its clinical benefits. Over 24,000 patients have been treated with VELCADE worldwide.

Janssen-Ortho would like to inform you of important safety information pertaining to reports of decreased left ventricular ejection fraction, and rare reports of acute liver failure and other hepatic events in patients treated with VELCADE.

Cardiac Disorders

Acute development or exacerbation of congestive heart failure, and/or new onset of decreased left ventricular ejection fraction has been reported. Patients with risk factors for, or existing heart disease should be closely monitored.

Hepatic Events

Rare cases of acute liver failure have been reported in patients receiving multiple concomitant medications and with serious underlying medical conditions. Other reported hepatic events include asymptomatic increases in liver enzymes, hyperbilirubinemia, and hepatitis. Such changes may be reversible upon discontinuation of VELCADE. There is limited rechallenge information in these patients.

Janssen-Ortho Inc. will be working with Health Canada to update the Canadian labelling to include the information contained in this letter.

The current Prescribing Information is available on the Janssen-Ortho Inc. website at www.janssen-ortho.com. Updates to the Prescribing Information will be posted on this web site once available and will be provided for the next edition of the Compendium of Pharmaceuticals and Specialties.

Any suspected adverse events in patients receiving VELCADE should be reported to Janssen-Ortho Inc. or the Marketed Health Products Directorate at the following addresses:

Janssen-Ortho Inc.
19 Green Belt Drive
Toronto, Ontario
M3C 1L9
Or call toll free at 1-800-567-3331
Or email to dsscan@joica.jnj.com
Or fax to 416-449-2658

Canadian Adverse Drug Reaction Monitoring Program (CADRMP)
Marketed Health Products Directorate
HEALTH CANADA
Address Locator: 0701C
OTTAWA, Ontario, K1A 0K9
Local Tel: (613) 957-0337 or Local Fax: (613) 957-0335
Toll Free Tel: (866) 234-2345 or Toll Free Fax: (866) 678-6789
cadrmp@hc-sc.gc.ca

The ADR Reporting Form can be found in *The Compendium of Pharmaceuticals and Specialties*, or on the TPD web site, along with the ADR Guidelines at:
www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/adverse_e.pdf,
www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/adr_guideline_e.pdf

Your professional commitment in this regard has an important role in protecting the well-being of your patients by contributing to early signal detection and informed drug use.

These recommendations should be shared with your staff as appropriate to encourage their implementation in the interest of patient safety.

Should you have any questions or require additional information, please contact Janssen-Ortho Inc. Medical Information Department at 1-800-567-3331 from 9:00 am to 5:00 pm Monday to Friday Eastern Standard Time (EST) or by facsimile at 416-449-2658.

Sincerely,

Wendy Arnott, Pharm.D.
Vice President
Regulatory, Safety and Quality