PUBLIC COMMUNICATION
Health Canada Endorsed Important Safety Information on XGEVA® (denosumab)

31 May 2012

Subject: XGEVA® (denosumab) – Risk of decrease in blood calcium level with severe symptoms, including death

Amgen Canada Inc., in consultation with Health Canada, would like to inform you of new important safety information related to hypocalcemia (low calcium levels in the blood) associated with the use of XGEVA.

XGEVA is used for reducing the risk of developing cancer-related complications like broken bones and/or bone pain that need surgery or radiation. XGEVA is not used for reducing the risk of developing cancer-related complications in patients with multiple myeloma. XGEVA is administered as a single 120 mg injection under the skin given once every 4 weeks.

- Treatment with XGEVA can cause the lowering of calcium levels in the blood. Cases of low blood calcium with severe symptoms, including death, have been reported.
  - Signs and symptoms of low blood calcium may include confusion, muscle spasms, twitches, or cramps, seizures and irregularity of the heart rhythm. Contact your doctor if you develop any of these symptoms.
- This risk can be reduced by regular blood tests to check the calcium level before and during treatment with XGEVA and correcting calcium and vitamin D levels when necessary.

Amgen Canada is working with Health Canada to update the safety information for XGEVA and has sent a letter to health care professionals to inform them of this new important safety information. A copy of that letter is available on the Health Canada website (www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/index-eng.php). This information is also available at www.amgen.ca. Amgen Canada will continue to review new safety data for XGEVA, including post-marketing adverse event reports.

Managing marketed health product-related adverse reactions depends on health care professionals and consumers reporting them. Reporting rates determined on the basis of spontaneously reported post-marketing adverse reactions are generally presumed to underestimate the risks associated with health product treatments. Any case of severe symptomatic hypocalcemia or other serious or unexpected adverse reactions in patients receiving XGEVA (denosumab) should be reported to Amgen Canada Inc. or Health Canada at the following addresses:

Amgen Canada Inc.
6775 Financial Drive, Suite 100
Mississauga, Ontario L5N 0A4
Safety Tel: 1-866-512-6436 or Fax: 1-888-264-3655
Safety e-mail: safetycanada@amgen.com

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at www.healthcanada.gc.ca/medeffect
- Call toll-free at 1-866-234-2345
- Complete a Reporting Form and:
  - Fax toll-free to 1-866-678-6789, or
  - Mail to: Canada Vigilance Program
    Health Canada
    Postal Locator 0701E
    Ottawa, Ontario K1A 0K9

The Reporting Forms, postage paid labels, and Guidelines can be found on the MedEffect™ Canada Web site in the Adverse Reaction Reporting section.

http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php

For other health product inquiries related to this communication, please contact Health Canada at:
Marketed Health Products Directorate (MHPD)
E-mail: MHPD_DPSC@hc-sc.gc.ca
Telephone: 613-954-6522
Fax: 613-952-7738

Sincerely,

Clive Ward-Able, MD
Executive Medical Director
AMGEN Canada Inc.