Health Canada Endorsed Important Safety Information on Prolia®

AMGEN

11/16/2012 v1.0

Dear Healthcare Professional:

Subject: Association of Prolia® (denosumab) with Risk of Atypical Femoral Fracture

AMGEN Canada Inc., in consultation with Health Canada, would like to inform healthcare providers of new important safety information regarding the risk of atypical femoral fractures associated with PROLIA treatment.

PROLIA (denosumab) is indicated for the treatment of postmenopausal women with osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapy.

Atypical femoral fractures are subtrochanteric or proximal diaphyseal fractures that may occur with little or no trauma and which may be bilateral. Radiographic findings include simple transverse or oblique fracture with "beaking" of the cortex with diffuse cortical thickening of the proximal femoral shaft.[1] There have been no confirmed Canadian cases of atypical femoral fractures associated with PROLIA to date. Amgen has proactively evaluated the potential for atypical femoral fractures in patients treated with PROLIA in clinical trials and the postmarketing setting.

- Cases of atypical femoral fracture have been confirmed in patients receiving PROLIA participating in the ongoing open label extension study of the pivotal phase 3 fracture trial in postmenopausal osteoporosis (FREEDOM).
- Events of atypical femoral fracture have occurred very rarely (<1/10,000) based on 31,266 subject years of exposure to PROLIA in bone loss studies.
- During PROLIA treatment, healthcare professionals should advise the patients to report new or unusual thigh, hip, or groin pain. Patients presenting with such symptoms should be evaluated for an incomplete femoral fracture, and the contralateral femur should also be examined.

The Warnings and Precautions section of the PROLIA Product monograph have been updated to reflect this new information on atypical femoral fractures.

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 serious atypical femoral fracture or other serious or unexpected adverse reactions in patients receiving PROLIA should be reported to Amgen Canada Inc. or Health Canada.

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

To correct your mailing address or fax number, contact Amgen Canada Inc.

You can report any suspected adverse reactions associated with the use of health products to Health Canada by:

- Calling toll-free at 1-866-234-2345; or
- Visiting MedEffect Canada's Web page on Adverse Reaction Reporting (http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php) for information on how to report online, by mail or by fax

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

A copy of this 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.

Sincerely,

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

References:

1. Shane E, Burr D, Ebeling PR, et al. Atypical subtrochanteric and diaphyseal femoral fractures: report of a task force of the American Society of Bone and Mineral Research. *J Bone Miner Res*. 2010;25:2267-2294.