



Health Santé  
Canada Canada

Health Products and Food Branch  
Direction générale des produits de santé et des aliments

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This is duplicated text of a letter from **Novartis Pharmaceuticals Canada Inc.**  
Contact the company for a copy of any references, attachments or enclosures.

**Health Canada Endorsed Important Safety Information on  
Aredia\* (pamidronate disodium) and/or Zometa\* (zoledronic acid)**



November 5, 2004

**Subject: UPDATED SAFETY: POSSIBLE RELATIONSHIP OF AREDIA\*  
(PAMIDRONATE DISODIUM) AND/OR ZOMETA\* (ZOLEDRONIC ACID)  
WITH OSTEONECROSIS OF THE JAW**

Dear Health Care Professional:

Novartis would like to inform you of important new safety information related to spontaneous adverse drug reaction reports of osteonecrosis of the jaw (ONJ) in cancer patients who have received Aredia\* (pamidronate disodium) and/or Zometa\* (zoledronic acid) as a component of their therapy. A small number of cases of ONJ in non-cancer patients who have received other bisphosphonates, have also been reported in the literature. Aredia\* and Zometa\* are on the Canadian market for the treatment of the following conditions: Aredia\*: a) tumor-induced hypercalcemia; b) symptomatic Paget's disease of bone; and c) conditions associated with increased osteoclast activity: predominantly lytic bone metastases and multiple myeloma; Zometa\*: a) tumor-induced hypercalcemia; and b) bone metastases of solid tumors and osteolytic lesions of multiple myeloma. While causality between bisphosphonates and ONJ has not been established, recommendations for updating the current Prescribing Information/Product Monographs for Aredia\* and Zometa\* have been initiated. Up to May 14, 2004, a worldwide total of 217 cases of ONJ in cancer patients treated with either Aredia\* or Zometa\* have been reported to Novartis. Based on this number and an estimated 2.5 million patients treated worldwide with Aredia\* and/or Zometa\*, the estimated incidence of ONJ is approximately 1 per 10,000 treated persons. This letter outlines changes made to the "Precautions" and "Post Marketing Experience" sections of the Aredia\* (pamidronate disodium) Injection and Zometa\* (zoledronic acid) Injection Product Monographs.

- In the Product Monographs for both Aredia\* and Zometa\* the following information on osteonecrosis has been added under the **Precautions Section**.
- Osteonecrosis of the jaw (ONJ) has been reported in patients with cancer receiving treatment regimens including bisphosphonates. Many of these patients were also receiving chemotherapy and corticosteroids. The majority of reported cases have been associated with dental procedures such as tooth extraction. Many had signs of local infection including osteomyelitis.
- A dental examination with appropriate preventive dentistry should be considered prior to treatment with bisphosphonates in patients with concomitant risk factors (e.g. cancer, chemotherapy, radiotherapy, corticosteroids, poor oral hygiene).
- While on treatment, these patients should avoid invasive dental procedures if possible. For patients who develop ONJ while on bisphosphonate therapy, dental surgery may exacerbate the condition. For patients requiring dental procedures, there are no data available to suggest whether discontinuation of bisphosphonate treatment reduces the risk of ONJ. Clinical judgment of the treating physician should guide the management plan of each patient based on individual benefit/risk assessment.
- In the Product Monographs for both Aredia\* and Zometa\*, information on osteonecrosis has previously been added to the **Adverse Reactions** section under **Post-Marketing Experience**. This section, as well as the **Information For the Consumer** section, is being updated reflecting the most recent data.

Reporting rates determined on the basis of spontaneously reported post-marketing adverse events are generally presumed to underestimate the risks associated with drug treatments.

The identification, characterization, and management of marketed health product-related adverse events are dependent on the active participation of health care professionals in adverse drug reaction reporting programmes. Any occurrences of Osteonecrosis of the jaw (ONJ) observed and/or unexpected adverse events in patients receiving Aredia\* or Zometa\* should be reported to Novartis or Health Canada at the following addresses:

Novartis Pharmaceuticals Canada Inc.  
385 Bouchard Blvd.  
Dorval, (QC) H9S 1A9  
Phone:1-800-363-8883 (Medical Information)

**Any suspected adverse reaction can also be reported to:**

Canadian Adverse Drug Reaction Monitoring Program (CADRMP)  
Marketed Health Products Directorate  
HEALTH CANADA

Address Locator: 0701C

OTTAWA, Ontario, K1A 0K9

Tel: (613) 957-0337 or Fax: (613) 957-0335

To report an Adverse Reaction, consumers and health professionals may call toll free:

Tel: 866 234-2345

Fax: 866 678-6789

[cadmp@hc-sc.gc.ca](mailto:cadmp@hc-sc.gc.ca)

For other inquiries: please refer to contact information.

The [AR Reporting Form](#) and the [AR Guidelines](#) can be found on the Health Canada web site or in *The Canadian Compendium of Pharmaceuticals and Specialties*.

[http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/adverse\\_e.html](http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/adverse_e.html)

[http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/adr\\_guideline\\_e.html](http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/adr_guideline_e.html)

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.

Should you have any questions or require additional information regarding the use of Aredia\* (pamidronate disodium) and Zometa\* (zoledronic acid) please contact Novartis Pharmaceuticals Canada Inc., Medical Information at 1-800-363-8883 from 8:30 AM to 4:30 PM Monday to Friday Eastern Standard Time.

Sincerely,

***original signed by***

Pier-Giorgio Fontana, PHD  
Vice-President, Drug Regulatory Affairs

***original signed by***

Jean-Marie Leclerc, M.D., F.R.C.P. (c)  
Vice-President, Medical Affairs

<sup>Pr</sup>Aredia\* and <sup>Pr</sup>Zometa\* are registered trademarks.