The Health Products and Food Branch (HPFB) posts on the Health Canada website safety alerts, public health advisories, press releases and other notices as a service to health professionals, consumers, and other interested parties. These advisories may be prepared with Directorates in the HPFB which includes pre-market and post-market areas as well as market authorization holders and other stakeholders. Although the HPFB grants market authorizations or licenses for therapeutic products, we do not endorse either the product or the company. Any questions regarding product information should be discussed with your health professional.

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:
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

Aredia* and Zometa* are registered trademarks.