

ANEXOS

ANEXO 1

IMPORTANT DRUG PRECAUTION FOR DENTAL HEALTH PROFESSIONALS WITH PATIENTS BEING TREATED FOR CANCER

(second copy for other dental health professionals in your practice)

May 05, 2005

Dear Doctor:

We are writing to inform you of an adverse event **Osteonecrosis of the Jaw (ONJ)** observed in cancer patients receiving treatment with intravenous bisphosphonates, Aredia and Zometa, which may have an impact on the dental care of patients within your practice. **While on treatment, invasive dental procedures should be avoided, if possible.**

The prescribing information recommends that cancer patients:

- **receive a dental examination prior to initiating therapy with intravenous bisphosphonates (Aredia and Zometa);** and
- **avoid invasive dental procedures while receiving bisphosphonate treatment.** For patients who develop ONJ while on bisphosphonate therapy, **dental surgery may exacerbate the condition.** Clinical judgment by the treating physician should guide the management plan of each patient based on individual benefit/risk assessment.

Aredia is used in the treatment of hypercalcemia of malignancy, Paget's disease, osteolytic bone metastases of breast cancer and osteolytic lesions of multiple myeloma. Zometa is used in the treatment of hypercalcemia of malignancy, the treatment of patients with multiple myeloma and patients with documented bone metastases from solid tumors, in conjunction with standard antineoplastic therapy. Prostate cancer should have progressed after treatment with at least one hormonal therapy.

In the U.S. Package Insert for both Aredia and Zometa, the following information on osteonecrosis of the jaw has been added under the **Precautions** Section.

Precautions

Osteonecrosis of the jaw

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, 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.

ONJ is a complex problem with multiple risk factors. Typical signs and symptoms of ONJ include, but are not limited to: pain, swelling, or infection of the gums; loosening of the teeth; poor healing of the gums; numbness or a feeling of heaviness in the jaw; drainage and exposed bone. The seriousness of ONJ ranges from patient being asymptomatic to requiring sections of the jaw to be removed.

Dentists, oral surgeons, periodontists, prosthodontists, dental hygienists, and other dental health professionals can play a vital role in identifying ONJ and other oral complications of cancer and cancer therapy.

For more information about dental treatment for cancer patients receiving bisphosphonate therapy, please refer to the enclosed:

- “Expert Panel Recommendations for the Prevention, Diagnosis and Treatment of Osteonecrosis of the Jaws: June 2004”
- Revised package inserts on complete prescribing information for both Aredia and Zometa
- Patient brochure, “Taking Care of Yourself While Living With Cancer: Dental Health and Osteonecrosis of the Jaw,” which you can share with patients who request more information on the topic (ONC-8155-01)
- Copy of this letter, which we ask you to share with other dental health professionals in your practice, including dental hygienists

Additional copies of the patient brochure are available at no charge by calling Novartis at [1-800-521-9445] using the order number provided above.

Healthcare professionals are strongly encouraged to submit a report of any serious adverse events that occur with the use of Aredia or Zometa to Novartis Pharmaceuticals Corporation at [1-800-882-6577] or fax [1-888-299-4565] or to the FDA's MedWatch Adverse Event Reporting program online [at www.fda.gov/MedWatch/report.htm], by phone [1-800-FDA-1088], or by returning the postage-paid FDA form 3500 [which may be downloaded from www.fda.gov/MedWatch/getforms.htm] by mail [to MedWatch, 5600 Fishers Lane, Rockville, MD 20852-9787] or fax [1-800-FDA-0178].

Please contact Novartis Oncology Medical Services at [1-888-669-6682] if you have questions.

Sincerely,

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