AAP Statement on Bisphosphonates

The Food and Drug Administration and Novartis Pharmaceuticals Corporation have each issued a drug precaution for health professionals regarding a condition known as Osteonecrosis of the Jaw (ONJ). According to these precautions, this condition has been observed in cancer patients who undergo invasive dental procedures such as dental implants or tooth extractions while receiving treatment with intravenous bisphosphonates. ONJ can cause severe, irreversible and often debilitating damage to the jaw. The two intravenous bisphosphonates that were mentioned in the precautions are marketed by Novartis under the trade names Aredia and Zometa. The precautions are available on the FDA Web site as a general background docket and a Medwatch letter to dental health professionals PDF.

Bisphosphonates, also known as bone-sparing drugs, are commonly used in the treatment of osteoporosis and cancer that has spread to the bone Doctors prescribe intravenous bisphosphonate therapy, which was the subject of the precautions, for patients with cancer that has spread to the bone to help decrease associated pain and fractures. In addition, emerging research is exploring the ability of intravenous bisphosphonate therapy to inhibit the spread of some cancers to the bone.

Doctors also prescribe an oral dose of bisphosphonates for patients at risk for osteoporosis to help delay the onset of disease by slowing the natural progression of bone tissue destruction, or to reduce its complications. Orally administered bisphosphonates were not the subject of the drug precautions. However, the FDA noted that there have been anecdotal reports of ONJ in association with oral bisphosphonates administered for osteoporosis.

Osteonecrosis literally means death, or necrosis of bone. According to the National Osteonecrosis Foundation, the many risk factors for osteonecrosis can be divided into two cateogries: definite and probable. Definite risk factors include major trauma, fractures, dislocations, Caisson Disease, Sickle Cell Disease, post-irradiation, chemotherapy, Arterial Disease and Gaucher's Disease. Probable risk factors include corticosteroids, blood clotting, alcohol, lipid disturbances, connective tissue disease, pancreatitis, kidney disease, liver disease, lupus, and smoking.[1]

The FDA recognizes additional risk factors associated with the development of osteonecrosis (not limited to the jaw) in cancer patients, such as female sex, advanced age, edentulous regions, combination cancer therapy, blood dyscrasias/metastatic disease, anemia coagulopathy, surgical dental procedures, and prior infection. [2]

Of course, the decision about what treatment to provide to a patient must be made by a periodontist in the exercise of his or her best judgment. However, in light of the precautions, periodontists are advised to determine whether a patient is receiving intravenous bisphosphonate therapy. If so, invasive dental procedures should be avoided unless absolutely necessary. Conversely, if a periodontist becomes aware that a patient is going to be treated with intravenous bisphosphonates, any needed invasive dentistry should, if possible, be performed before the initiation of such treatment. Finally, periodontists should endeavor to identify ONJ and other oral complications of cancer and cancer therapy.

Any questions about ONJ associated with intravenous bisphosphonate therapy can be addressed to Novartis at 1.888.669.6682.

Footnotes

[1]The National Osteonecrosis Foundation Web Site. Accessed August 5, 2005. An introduction to osteonecrosis by the National Osteonecrosis Foundation and the Center for Osteonecrosis Research and Education.
[2]The Food and Drug Administration Web site. 03-02-2005. Accessed August 5, 2005. Expert Panel Recommendation for the Prevention, Diagnosis and Treatment of Osteonecrosis of the Jaw.

Resources

- Patients Taking Bisphosphonates: Implications for Periodontal Therapy (AAP Practice Management Article)

- The Food and Drug Administration Web site PDF. 03-02-2005. Accessed August 5, 2005. Expert Panel Recommendation for the Prevention, Diagnosis and Treatment of Osteonecrosis of the Jaw.
- Durie B GM, Katz M, Crowley J, Woo S-B, Hande K, Richardson PG, Maerevoet M, Martin C, Duck L, Tarassoff P, Hei Y-j. Osteonecrosis of the Jaw and Bisphosphonates. *N Engl J Med* 2005; 353:99-102, July 7.2005. Correspondence. (Pay per view copies available.)
- Quantities of the patient education brochure “Taking Care of Yourself While Living With Cancer: Dental Health and Osteonecrosis of the Jaw” are available at no charge by calling Novartis Pharmaceuticals 1.800.521.9455.
- Adverse events that occur with the use of Aredia or Zometa should be reported to Novartis Pharmaceuticals Corporation 1.800.882.6577, or via fax 1.888.299.4565.
- Adverse events that occur with bisphosphonate or any FDA-approved therapy should be reported to the FDA’s MedWatch Adverse Event Reporting program, by phone 1.800.FDA.1088, of by returning the postage-paid FDA form 3500 which may be downloaded from the Food and Drug Administration Web site.
- Position Paper on Bisphosphonates and Osteonecrosis of the Jaw PDFfrom the Australian and New Zealand Bone and Mineral Society, Osteoporosis Australia, Medical Oncology Group of Australia, and the Australian Dental Association