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## Osteonecrosis of the jaws associated with the use of bisphosphonates

**B**isphosphonates are widely used in the management of metastatic diseases of the bone and in the treatment of osteoporosis, Paget's disease and other illnesses. Bisphosphonates inhibit bone resorption by decreasing the activity of the cells that remove old, injured, and dying bone (osteoclasts)<sup>(1)</sup>.

Recently, bisphosphonates have been linked to Osteonecrosis of the jaw. This complication has been most frequently associated with the nitrogen containing injectable bisphosphonates, pamidronate (Aredia) and zoledronate (Zometa)<sup>(2)</sup>.

There have also been a few reported cases in patients taking the more common drug alendronate (Fosamax)<sup>(2)</sup>. Other drugs in this class are risedronate (Actonel), etidronate and ibandronate (Boniva).

The mechanism leading to bisphosphonate-associated osteonecrosis may have to do with the inhibition of bone remodeling and decreased intraosseous blood flow. The risk of developing complications appears to increase with duration of use of the medication<sup>(3)</sup>.

Typically, slight osteonecrosis occurs after injury to the jaw bone, and is most common following tooth extraction<sup>(4)</sup>.

It has been theorized that bisphosphonates suppress the cells which would normally remove this very small layer of injured bone and allow the area to heal. The healing never occurs; the dead bone affects neighboring live bone, and eventually causes necrosis which expands into neighboring bone<sup>(4)</sup>.

Sixty-three cases of bisphosphonate-induced osteonecrosis of the jaw have been documented by Ruggiero in the *Journal of Oral and Maxillofacial Surgery*. Fifty-seven of those patients had received intravenous bisphosphonates (Aredia and Zometa) for at least one year. Seven patients were on chronic oral bisphosphonate therapy (Fosamax)<sup>(1)</sup>.

Marx reported 119 patients diagnosed with bisphosphonate-induced osteonecrosis. The majority had taken Aredia and Zometa while three had taken Fosamax<sup>(2)</sup>.

Impaired wound healing may result from a compromised vascular supply caused by the antiangiogenic effects of bisphosphonates. The absence of bone problems elsewhere in the body may be due to the unique environment created by oral microflora<sup>(1)</sup>.

Patients who are taking bisphosphonates should be alert to tooth pain, swelling, numbness of the lip and chin, or pain in the jaw<sup>(1)</sup>.

Prior to initiating bisphosphonate therapy, patients should have a complete oral evaluation to eliminate any existing infection that may be present to reduce the need for invasive dental procedures in the near or intermediate future. Prophylactic antibiotic coverage for non-invasive care is not required, but recommended for any invasive dental procedures<sup>(2)</sup>.

Currently, the protocol for patients using oral bisphosphonates for three years or less is that patients may have the surgical procedure performed without delay. Patients who have taken the oral medications for a longer period, must discontinue use for at least three months prior to surgical treatment and should wait an additional three months after surgery before starting to take the medication again. No invasive procedures should be done on patients who have taken or who are presently taking the injectable bisphosphonates (Aredia or Zometa). These patients should be referred to an oral maxillofacial surgeon for evaluation and treatment.

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1. Ruggiero SL, Mehrotra B, Rosenberg TJ, Engroff SL. Related Articles, Links Osteonecrosis of the jaws associated with the use of bisphosphonates: a review of 63 cases. *J Oral Maxillofac Surg*. 2004 May;62(5):527-34.

2. Marx RE, Sawatari Y, Fortin M, Broumand V. Related Articles, Links Bisphosphonate-induced exposed bone (osteonecrosis/osteopetrosis) of the jaws: risk factors, recognition, prevention, and treatment. *J Oral Maxillofac Surg*. 2005 Nov;63(11):1567-75.

3. Migliorati CA, Casiglia J, Epstein J, Jacobsen PL, Siegel MA, Woo SB. Related Articles, Links Managing the care of patients with bisphosphonate-associated osteonecrosis: an American Academy of Oral Medicine position paper. *J Am Dent Assoc*. 2005 Dec;136(12):1658-68. Review. Erratum in: *J Am Dent Assoc*. 2006 Jan;137(1):26.

4. Brown, Stephen, Bisphosphonate-Related Osteonecrosis of the Jaws, *Periodontal Letter*. Spring 2006.