

## INTRODUCTION

Reports of osteonecrosis of the jaw associated with the use of bisphosphonates, zoledronic acid and pamidronate, began in 2003. Both drugs are intravenous bisphosphonates. They are used to reduce bone pain, hypercalcemia of malignancy and skeletal complications in patients with multiple myeloma, breast, lung and other cancers, as well as Paget's disease. Most cases of bisphosphonate related osteonecrosis of the jaw occur after dental procedures like tooth extraction.

In 2006, reports of osteonecrosis of the jaw had been reported in patients taking oral bisphosphonates, for the treatment of osteoporosis. The total number of cases of reported bisphosphonate related osteonecrosis in patients taking alendronate is about 170, 12 people taking risedronate, and 1 person taking ibandronate. These numbers were reported in 2006. At the time of this article, the limited data on reported cases did not allow for identification of other risk factors. In oncology patients receiving IV bisphosphonates, extrapolating data may suggest that using oral glucocorticoids and estrogen may increase the risk for developing bisphosphonate related osteonecrosis. In cancer patients receiving IV bisphosphonate therapy, the median time from starting the therapy to developing bisphosphonate related osteonecrosis was 25 months. Additionally, being aged 65 years or older may increase risk. The most common dental comorbidity is clinically and radiographic apparent periodontitis.

Due to the uncertainty surrounding the incidence of bisphosphonate related osteonecrosis and the risk factors, dentists have questioned how to manage the care of patients receiving oral bisphosphonate therapy. Because of this, the American Dental Association assembled an expert panel to develop guidance for dentists that are treating patients using oral bisphosphonates.

## Expert Panel

The panelists were chosen on the basis of their expertise in the subject matter and their relevant medical or dental specialty. The panelists were required to sign a disclosure statement that neither the panelists nor spouse or dependent children had significant financial interest that would appear to affect the development of the recommendations.

### Incorporating expert panel recommendations into clinical decision making:

Knowing the patient's health history and vulnerability to oral disease put the dentist in the best position to make the decisions around the patient's oral health care treatment. Because of this, the expert panel recommendations are intended to provide guidance and are not the standard of care, requirements or regulations based on scientific evidence. These recommendations are a resource for dentists to use in their clinical practice, in addition to the dentist's clinical judgment, information available in the clinical literature, and information from the patient's physician.

Through the development of these recommendations, areas where there are gaps were identified. To address these areas, topic of future research are included.

## Bisphosphonates on the market

**TABLE 1**  
Bisphosphonates on the market in the United States.

BRAND NAME	MANUFACTURER	GENERIC NAME
<b>Orally Administered</b>		
Actonel	Procter & Gamble Pharmaceuticals, Cincinnati/sanofi-aventis Group, New York	Risedronate
Boniva	Roche Pharmaceuticals, Basel, Switzerland/ GlaxoSmithKline, Philadelphia	Ibandronate
Didronel	Procter & Gamble Pharmaceuticals	Etidronate
Fosamax	Merck & Co., Whitehouse Station, N.J.	Alendronate
Fosamax Plus D	Merck & Co.	Alendronate
Skelid	sanofi-aventis Group	Tiludronate
<b>Intravenously Administered</b>		
Aredia	Novartis, East Hanover, N.J.	Pamidronate
Bonefos	Schering AG, Montville, N.J.	Clodronate
Zometa	Novartis	Zoledronic acid

## Antibiotics

**TABLE 2**  
Antibiotics that may be used to treat unexpected pain, purulence or active sequestration after a dental procedure.

PATIENT TYPE	SUGGESTED DRUG	ORAL REGIMEN
Patients Not Allergic to Penicillin	Amoxicillin	500 milligrams three times per day for 14 days
	may be combined with* Metronidazole	250 mg three times per day for 14 days
Patients Allergic to Penicillin	Clindamycin	300 mg three times per day for 14 days
	or Azithromycin	250 mg one time per day for 10 days

\* Amoxicillin may be combined with metronidazole for maximum coverage of periodontal microflora.

## Osteoporosis and Bisphosphonates

The risk of developing bisphosphonate related osteonecrosis is much higher for cancer patients receiving IV bisphosphonates than for patients taking oral bisphosphonates. The bone anti-resorptive property of the drug contributes may play an important role. Less than 1 percent of the drug taken orally is absorbed by the gastrointestinal tract, whereas over than 50 percent of bisphosphonate given intravenously is bioavailable.

The risk of developing bisphosphonate related osteonecrosis is low if the patient is taking oral bisphosphonates, however because there were over 22 million prescriptions for Fosamax between May 2003 and April 2004, these individuals still require routine dental treatment and guidelines need to be established in order to assist dentists.

Osteoporosis is a major cause of morbidity in older adults. 1 in every 2 women will sustain an osteoporosis related fracture in her lifetime. Bisphosphonates are analogs of inorganic pyrophosphate and are used to treat bone loss associated with osteoporosis and Paget's disease. Bisphosphonates inhibit osteoclast differentiation and induce osteoclast apoptosis. This results in an imbalance in the bone-remodeling process and promote an increase in bone trabecular thickness and bone mass. Because of this, bisphosphonates affect bone turnover and may inhibit some of bone's biomechanical and reparative properties. There is a reduction in bone toughness, without a reduction in bone strength.

## Clinical Presentation

The clinical presentation of bisphosphonate related osteonecrosis includes pain, soft tissue swelling and infection, loosening of teeth, drainage, and exposed bone. Symptoms may occur spontaneously in bone, however occur more commonly at the site of a tooth extraction. Patients may present complaining of pain that mimics a dental problem. It may also remain asymptomatic and only present with exposed bone during an examination. Bisphosphonate related osteonecrosis can also mimic dental or periodontal disease. In any case, routine dental treatment will not resolve the issue. Bisphosphonate related osteonecrosis can occur spontaneously but is more commonly associated with dental procedures that traumatize bone.

## Clinical Recommendations

These panel recommendations focus on conservative surgical procedures, proper sterile technique, appropriate use of oral disinfectants and the principles of effective antibiotic therapy.

### General Recommendations:

- A comprehensive oral examination should be done for any patient prior to commencing oral bisphosphonate therapy
- The dentist should inform the patient of the low risk of developing bisphosphonate related osteonecrosis
- That there are ways to minimize risk, but not eliminate risk
- The best way to to lower risk is to maintain good oral hygiene along with regular dental care
- There are no diagnostic tests to identify those at increased risk of developing bisphosphonate related osteonecrosis
- The patient should be aware of dental treatments needed, alternative treatments, and how these treatment relate to bisphosphonate related osteonecrosis.

When the treatment plan dictates exposure of bone or periosteum, treatment should be done in sextants, and allow for 2. months in between sextants for follow-up and monitoring of disease.

Periapical pathosis, sinus tracts, purulent periodontal pockets, and active abscesses may induce disease due to their involvement in the medullary bone.

### Management of Periodontal disease:

Patients should receive appropriate for of non-surgical therapy, which should be combine with a prolonged initial phase of therapy for observation. Surgical treatment should minimize bone exposure and focus only on gaining access to root structure.

### Implant placement and management:

The patient may be at increased risk of developing bisphosphonate related osteonecrosis with extensive implant placement or guided bone regeneration. Maintenance of implants should follow acceptable methods to prevent peri-implantitis.

### Oral and Maxillofacial Surgery:

Patients should be aware of the small risk of disease. Alternative treatment plans should be considered. If surgery is necessary, conservative technique with primary closure should be performed. Chlorhexidine rinse and antibiotics should be considered.

### Endodontics:

Endodontic treatment is preferable to surgical manipulation if the tooth is salvageable.

### Restorative Dentistry and Prosthodontics:

All routine restorative dentistry may be done with no precautions. Prosthodontic appliances should be adjusted for good fit.

## Resources

Dental management of patients receiving oral bisphosphonate therapy. (2006). *The Journal of the American Dental Association*, 137(8), 1144–1150.  
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