

# Diagnosis, Prevention & Management for *Medication Related Osteonecrosis of the Jaw [MRONJ]*

## *What is MRONJ?*

In 2014, a special committee of AAOMS recognized that Jaw Necrosis was not only a complication from the use of IV bisphosphonates but also from Denosumab and antiangiogenic agents. The term "medication related osteonecrosis of the jaw" {MRONJ} was recommended as were revisions to diagnosis and management.

## *Diagnosis*

1. Current or previous treatment with antiresorptive or antiangiogenic agents;
2. Exposed bone or bone that can be probed through an intraoral or extraoral fistula(e) in the maxillofacial region that has persisted for more than eight weeks; and
3. No history of radiation therapy to the jaws or obvious metastatic disease to the jaws.

## *Pathophysiology*

Proposed hypotheses that attempt to explain the unique localization of MRONJ exclusively to the jaws include altered bone remodeling or over suppression of bone resorption, angiogenesis inhibition, constant microtrauma, suppression of innate or acquired immunity, vitamin D deficiency, soft tissue BP toxicity, and inflammation or infection.

## *Management*

When exposed bone in the jaw is identified by the dentist or oncologist, a multi-disciplinary approach to patient care should be taken. This would included consultation between oncologist, general dentist, oral surgeon and patient, over the risks, benefits and timing for dental treatment and initiation of antiresorptive and antiangiogenic therapy. A clinical staging system was developed in 2007 and modified in the 2014 Update. It categorizes patients according to severity and directs rational treatment based on the staging of the disease.

*Q. Did you know that MRONJ is associated with comorbid risk factors such as rheumatoid arthritis, prior or current glucocorticoid exposure, diabetes and smoking?*



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Tyman P. Loveless DMD, MD



## Prevention

- **Asymptomatic patients receiving intravenous bisphosphonates or antiangiogenic drugs for cancer:** Procedures that involve direct osseous injury should be avoided. Non-restorable teeth may be treated by removal of the crown and endodontic treatment of the remaining roots.
- **Asymptomatic patients receiving antiresorptive therapy for osteoporosis:** Elective dentoalveolar surgery does not appear to be contraindicated in this group. Patients should be informed of the small risk (<1%) of compromised bone healing. The risk of developing MRONJ associated with oral bisphosphonates, while exceedingly small, appears to increase when the duration of therapy exceeds 4 years.
  1. For individuals who have taken an oral bisphosphonate for **less than four years** and have no clinical risk factors, no alteration or delay in the planned surgery is necessary.
  2. For those patients who have taken an oral bisphosphonate, for **less than four years** and have **also taken corticosteroids or antiangiogenic medications concomitantly**, the prescribing provider should be contacted to consider discontinuation of the oral bisphosphonate (drug holiday) for at least two months prior to oral surgery, if systemic conditions permit.
  3. For those patients who have taken an oral bisphosphonate for **more than four years with or without any concomitant medical therapy**, the prescribing provider should be contacted to consider discontinuation of the antiresorptive for two months prior to oral surgery if systemic conditions permit.
- **Patients with established MRONJ:** Treatment objectives for patients with an established diagnosis of MRONJ are to eliminate pain, control infection of the soft and hard tissue, and minimize the progression or occurrence of bone necrosis. Patients with established MRONJ should avoid elective dentoalveolar surgical procedures, since these surgical sites may result in additional areas of exposed necrotic bone.

### Antiresorptive and Antiangiogenic Preparations Commonly Used in the U.S.

|              |                 |                         |          |
|--------------|-----------------|-------------------------|----------|
| Alendronate  | Fosamax         | Osteoporosis            | Oral     |
| Risendronate | Actonel         | Osteoporosis            | Oral     |
| Ibandronate  | Boniva          | Osteoporosis            | Oral, IV |
| Pamidronate  | Aredia          | Bone Metastasis         | IV       |
| Zoledronate  | Zometa, Reclast | Bone Mets, Osteoporosis | IV       |
| Denosumab    | Xgeva, Prolia   | Bone Mets, Osteoporosis | SQ       |
| Sunitinib    | Sutent          | Cancer                  | Oral     |
| Sorafenib    | Nexavar         | Cancer                  | Oral     |
| Bevacizumab  | Avastin         | Cancer                  | IV       |
| Sirolimus    | Rapamune        | Organ rejection         | Oral     |