

Bisphosphonate Preparations Currently Available in the US

	Primary Indication	Nitrogen Containing	Dose	Route	Relative Potency**
Etidronate (Didronel)	Paget's Disease	No	300-750 mg daily for 6 months	Oral	1
Tiludronate (Skelid)	Paget's Disease	No	400 mg daily for 3 months	Oral	50
Alendronate (Fosamax)	Osteoporosis	Yes	10 mg/day 70 mg/week	Oral	1,000
Risedronate (Actonel)	Osteoporosis	Yes	5 mg/day 35 mg/week	Oral	1,000
Ibandronate (Boniva)	Osteoporosis	Yes	2.5 mg/day 150 mg/month	Oral	1,000
Pamidronate (Aredia)	Bone Metastasis	Yes	90 mg/3 weeks	IV	1,000 – 5,000
Zoledronate (Zometa)	Bone Metastasis	Yes	4 mg/3 weeks	IV	10,000 +

*A once-yearly infusion of zoledronic acid for the treatment of postmenopausal osteoporosis is under FDA review.

**Relative to etidronate

LETTER TO DENTISTS

Dear Dr. _____

As we all know, a number of patients have developed osteonecrosis of the jaws after taking bisphosphonates, particularly IV bisphosphonates. We also see attorneys advertising for patients with osteonecrosis of the jaw (ONJ) to contact them for legal help to “get the settlement that they deserve”.

While initially dentists saw the bisphosphonate issue as “someone else’s problem”, unfortunately it appears that dentists will also have malpractice claims as plaintiff’s attorneys start looking for someone to “blame” for their client’s misfortunes. Patients who are on IV bisphosphonates are usually being treated for multiple myeloma , metastatic breast, lung or prostate cancer. Many of these patients will likely die because of their disease, but have been spared several years of debilitating bone pain that many times goes along with these diseases. Unfortunately, a small percentage of these patients will be trading off the bone destruction and pain associated with their disease for ONJ. Oncologists appear to be continuing to use IV bisphosphonates in spite of the potential for the development of ONJ saying that the benefits outweigh the risks.

While it is obvious that ONJ is NOT a condition that dentists are responsible for creating, it is important that dentists look at every patient who walks into their office with metastatic bone cancer as a potential “claim”. We have seen that many patients on IV bisphosphonates DO NOT DISCLOSE to the dentist that they are on them. Rather, they will disclose that they are on “chemotherapy”, NOT LISTING which specific drugs they are taking. It is important for the dentist to be suspicious that patients with metastatic disease MAY be on bisphosphonates, and question the patient and their oncologist as to which specific drugs they are taking.

As always, claims defense is much easier if the cardinal principles of risk management are followed:

1. Disclose ...patients need to be advised of potential bad outcomes from surgical treatment while on bisphosphonates
2. Document ...a documented informed consent discussion, along with the use of a consent form for patients on oral or IV bisphosphonates really helps with claims defense. We have copies of consent forms for patients taking both forms of the drug, oral and intravenous. If you would like a copy of these forms, please contact our office.
3. Follow Guidelines for Treatment as announced by the company producing IV bisphosphonates (Novartis). In the letter to dentists on May 05, 2005, Novartis indicates that “prescribing information recommends that cancer patients:
 - receive a dental examination prior to initiating therapy with intravenous bisphosphonates; 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.”
4. The American Dental Association convened an Expert Panel and developed recommendations for dental management of patients on bisphosphonates and published them in June, 2006. The recommendations can be found at <http://www.ada.org/prof/resources/topics/osteonecrosis>.
 5. The American Association of Oral and Maxillofacial Surgeons has recently issued a “Position Paper on Bisphosphonate-Related Osteonecrosis of the Jaws (September 25, 2006) available at http://www.aaoms.org/docs/position_papers/osteonecrosis.pdf. This paper defines Bisphosphonate-Related Osteonecrosis of the Jaws (“BRON”) and provides current management/treatment strategies for patients undergoing either oral or IV bisphosphonate therapy. These recommendations are somewhat more involved than the recommendations issued by the ADA. For patients taking oral bisphosphonates for longer than three years prior to any invasive surgery, the current recommendation is a “drug holiday” of three months before surgery and three months after surgery. These recommendations are based on anecdotal evidence that may be of benefit, not on any long-term clinical studies. We have enclosed a summary of the AAOMS “Treatment” and “Management” recommendations for you to use as a guide for treatment if you want. These summaries can be kept in your desk for reference. In addition, we have included a current listing of all bisphosphonate drugs currently available, both oral and intravenous.

It is important that we as a dental community do what is best for our patients. With regard to treatment of those patients on bisphosphonates, it is important to keep current with the latest information and suggestions. A little bit of additional time on the initial consultation will be beneficial in allowing the doctor to provide excellent care to patients taking bisphosphonates.

Cordially,

DDS
Oral and Maxillofacial Surgery

CONSENT FOR ORAL SURGICAL TREATMENT IN PATIENTS WHO HAVE RECEIVED INTRAVENOUS BIPHOSPHONATE DRUGS

Page 1 of 2

Patient's Name

Date

Please initial each paragraph after reading. If you have any questions, please ask your doctor BEFORE initialing.

Having been treated previously with IV Bisphosphonate drugs you should know that there is a significant risk of future severe complications associated with oral surgical treatment. IV Bisphosphonate drugs appear to adversely affect the ability for jaw bones to break down or remodel itself, thereby reducing or eliminating its ordinary excellent healing capacity and the ability to maintain normal health. This risk is increased after surgery, especially from extraction; gum surgery, implant placement or other "invasive" procedures that might cause even mild trauma to bone. Necrosis or exposure of the bone (Osteonecrosis) and subsequent soft tissue and/or bone infection may result. This is a smoldering, long-term, destructive process in the jawbone that is often very difficult or impossible to eliminate.

Your medical/dental history is very important. We must know the medications and drugs that you have received or taken or are currently receiving or taking. An accurate medical history, including names of physicians is important.

The decision to discontinue IV Bisphosphonate drug therapy before dental treatment will not decrease the risk of developing Osteonecrosis.

- ___ 1. Antibiotic therapy may be used to help control possible post-operative infection. For some patients, such therapy may cause allergic responses or have undesirable side effects such as gastric discomfort, diarrhea, colitis, etc.
- ___ 2. Despite all precautions, there may be delayed healing, necrosis of the jaw bone, loss of bone and soft tissues, infection, pathologic fracture of the jaw, oral-cutaneous fistula (open draining wounds), or other significant complications.
- ___ 3. If osteonecrosis should occur, treatment may be prolonged and difficult, involving ongoing intensive therapy including hospitalization, long-term antibiotics, and debridement to remove non-vital bone. Reconstructive surgery may be required, including bone grafting, metal plates and screws, and/or skin flaps and grafts.
- ___ 4. Even if there are no immediate complications from the proposed dental treatment, the area is always subject to spontaneous breakdown and infection due to the precarious condition of the bone. Even minimal trauma from a toothbrush, chewing hard food, or denture sores may trigger a complication.

CONSENT FOR ORAL SURGICAL TREATMENT IN PATIENTS WHO HAVE RECEIVED INTRAVENOUS BISPHOSPHONATE DRUGS

Page 2 of 2

____ 5. Long-term post-operative monitoring may be required and cooperation in keeping scheduled appointments is important. Regular and frequent dental check-ups with your dentist are important to monitor and attempt to prevent breakdown in your oral health.

____ 6. I have read the above paragraphs and understand the possible risks of undergoing my planned treatment. I understand and agree to the following treatment plan:

____ 7. I understand the importance of my health history and affirm that I have given any and all information that may impact my care. I understand that failure to give true health information may adversely affect my care and lead to unwanted complications.

____ 8. I realize that, despite all precautions that may be taken to avoid complications; there can be no guarantee as to the result of the proposed treatment.

CONSENT

I certify that I speak, read and write English and have read and fully understand this consent for surgery, have had my questions answered and that all blanks were filled in prior to my initials or signature.

Patient's (or Legal Guardian's) Signature Date

Doctor's Signature Date

Witness' Signature Date

BISPHOSPHONATES - MANAGEMENT STRATEGIES

- A. Patients who have taken **oral bisphosphonates for less than three years** and have no clinical risk factors (corticosteroid therapy, diabetes, smoking, alcohol use, poor oral hygiene, and chemotherapeutic drugs)
- No alteration or delay in the planned surgery is necessary.
 - If implants are placed, informed consent should be provided related to possible implant failure and possible osteonecrosis of the jaws if the patient continues taking oral bisphosphonates.
 - It is advisable to contact the practitioner who initially prescribed the oral bisphosphonate and suggest monitoring such patients and considering either alternate dosing of the bisphosphonate, drug holidays, or an alternative to bisphosphonate therapy.
 - Implant patients should be on a regular recall schedule
- B. Patients who have taken **oral bisphosphonates for less than three years and have also taken corticosteroids concomitantly or have any of the other risk factors listed above**
- The prescribing provider should be contacted to consider discontinuation of the oral bisphosphonate (drug holiday) for at least three months prior to oral surgery (if systemic conditions permit).
 - The bisphosphonate should not be restarted until osseous healing has occurred.
- C. Patients who have taken **oral bisphosphonates for more than three years** with or without concomitant steroid medication or other risk factors
- The prescribing provider should be contacted to consider discontinuation of the oral bisphosphonate for three months prior to oral surgery, if systemic conditions permit.
 - The bisphosphonate should not be restarted until osseous healing has occurred.
- D. Patients with **an established diagnosis of Bisphosphonate-Related Osteonecrosis of the Jaws (BRON)**
- Treatment objectives are to eliminate pain, control infection of the hard and soft tissues, and minimize the progression or occurrence of bone necrosis
 - Surgical treatment is less predictable than with the established surgical algorithms for osteomyelitis or osteoradionecrosis; therefore, surgery should be delayed if possible
 - Areas of necrotic bone that are a constant source of irritation should be removed or recontoured without exposure of additional bone.
 - Loose segments of bony sequestrum should be removed with exposed/necrotic bone in patients with pain,
 - Patients should avoid elective dentoalveolar surgical procedures.
 - The extraction of symptomatic teeth within exposed, necrotic bone should be considered since it is unlikely that the extraction will exacerbate the established necrotic process.

Dear Dr.

Date _____

Re: _____

I am currently seeing your patient, _____. Your patient informs me that she/he has been taking (Fosamax, Actonel, Boniva, Didronel, or Skelid). As you know, a number of patients have developed osteonecrosis of the jaws (ONJ) after taking bisphosphonates, particularly IV bisphosphonates (Zometa or Aredia).

The American Association of Oral and Maxillofacial Surgeons (AAOMS) has recently issued a **Position Paper** on Bisphosphonate-Related Osteonecrosis of the Jaws. While oral bisphosphonates are associated with only a small number of osteonecrosis cases, it appears that the risk of developing Bisphosphonate-Related Osteonecrosis of the Jaws (BRON) is increased when duration of therapy exceeds three (3) years, or when oral bisphosphonates are given with long-term corticosteroids or chemotherapy, the patient has diabetes, smokes, uses excessive alcohol, or has poor oral hygiene. Your patient meets one of these criteria.

For patients who have been on oral bisphosphonates more than 3 years, or have taken oral bisphosphonates and have one of the additional risk factors listed above, the AAOMS Position Paper recommends the following prior to any elective dentoalveolar surgery:

“ ...the prescribing provider should be contacted to consider discontinuation of the oral bisphosphonate (drug holiday) for at least three months prior to oral surgery, if systemic conditions permit. The bisphosphonate should not be restarted until osseous healing has occurred (approximately three more months).”

Please advise our office by return fax (828-324-5877) or phone (828-322-1667) if you would:

- | | |
|---|-----------|
| 1. recommend a drug holiday as described above | YES _____ |
| 2. NOT recommend a drug holiday as discussed above | YES _____ |

Signature _____ Date _____

Once we have your response, we will contact your patient with your recommendation and schedule our surgery in compliance with it. Thank you in advance for your help and assistance with this patient. Working together, we can provide the best care for your patient.

Best Regards,

CONSENT FOR ORAL SURGICAL TREATMENT IN PATIENTS WHO HAVE RECEIVED ORAL BISPHOSPHONATE DRUGS

Page 1 of 2

Patient's Name

Date

Please initial each paragraph after reading. If you have any questions, please ask your doctor BEFORE initialing.

Having been treated previously with oral Bisphosphonate drugs you should know that there is a very small, but real risk of future complications associated with dental treatment. This risk is currently estimated to be less than 1/10 of one percent. Bisphosphonate drugs appear to adversely affect the health of jaw bones, thereby reducing or eliminating the jaw bones ordinary excellent healing capacity. This risk is increased after surgery, especially from extraction; implant placement or other "invasive" procedures that might cause even mild trauma to the bone. Spontaneous exposure of the jaw bone (Osteonecrosis) may result. This is a smoldering, long-term, destructive process in the jawbone that is often very difficult or impossible to eliminate.

Your medical/dental history is very important. We must know the medications and drugs that you have received or taken or are currently receiving or taking. An accurate medical history, including names of physicians is important.

The decision to discontinue oral Bisphosphonate drug therapy before dental treatment should be made by you in consultation with your medical doctor.

- ___ 1. If a complication occurs, antibiotic therapy may be used to help control infection. For some patients, such therapy may cause allergic responses or have undesirable side effects such as gastric discomfort, diarrhea, colitis, etc.
- ___ 2. Despite all precautions, there may be delayed healing, osteonecrosis, loss of bone and soft tissues, pathologic fracture of the jaw, oral-cutaneous fistula (open draining wound), or other significant complications.
- ___ 3. If osteonecrosis should occur, treatment may be prolonged and difficult, involving ongoing intensive therapy including hospitalization, long-term antibiotics, and debridement to remove non-vital bone. Reconstructive surgery may be required, including bone grafting, metal plates and screws, and/or skin flaps and grafts.
- ___ 4. Even if there are no immediate complications from the proposed dental treatment, the area is always subject to spontaneous breakdown and infection due to the condition of the bone. Even minimal trauma from a toothbrush, chewing hard food, or denture sores may trigger a complication.

CONSENT FOR ORAL SURGICAL TREATMENT IN PATIENTS WHO HAVE RECEIVED ORAL BISPHOSPHONATE DRUGS

Page 2 of 2

____ 5. Long-term post-operative monitoring may be required and cooperation in keeping scheduled appointments is important. Regular and frequent dental check-ups with your dentist are important to monitor and attempt to prevent breakdown in your oral health.

____ 6. I have read the above paragraphs and understand the possible risks of undergoing my planned treatment. I understand and agree to the following treatment plan:

____ 7. I understand the importance of my health history and affirm that I have given any and all information that may impact my care. I understand that failure to give true health information may adversely affect my care and lead to unwanted complications.

____ 8. I realize that, despite all precautions that may be taken to avoid complications; there can be no guarantee as to the result of the proposed treatment.

CONSENT

I certify that I speak, read and write English and have read and fully understand this consent for surgery, have had my questions answered and that all blanks were filled in prior to my initials or signature.

Patient's (or Legal Guardian's) Signature Date

Doctor's Signature Date

Witness' Signature Date

Dear Dr. _____

Date _____

Re: _____

I am currently seeing your patient, _____. Your patient informs me that she/he has been taking an oral bisphosphonate (Fosamax, Actonel, Boniva, Didronel, or Skelid). As you know, a number of patients have developed osteonecrosis of the jaws (ONJ) after taking bisphosphonates, particularly IV bisphosphonates (Zometa or Aredia).

The American Association of Oral and Maxillofacial Surgeons has recently issued a "Position Paper" on "Bisphosphonate-Related Osteonecrosis of the Jaws". While oral bisphosphonates are associated with only a small number of osteonecrosis cases at this time, it appears that the risk of developing Bisphosphonate-Related Osteonecrosis of the Jaws (BRON) associated with oral bisphosphonates may be increased when duration of therapy exceeds three years, or when oral bisphosphonates are given concomitantly with long-term corticosteroids or chemotherapy, the patient has diabetes, smokes, uses excessive alcohol, or has poor oral hygiene. Your patient meets one of these criteria.

For patients who have been on oral bisphosphonates more than 3 years, or have taken oral bisphosphonates and have one of the additional risk factors listed above, the AAOMS Position Paper recommends the following for patient management prior to any elective dentoalveolar surgery:

"...the prescribing provider should be contacted to consider discontinuation of the oral bisphosphonate (drug holiday) for at least three months prior to oral surgery, *if systemic conditions permit*. The bisphosphonate should not be restarted until osseous healing has occurred (approximately three more months)."

Please advise our office by return fax (_____) or phone (_____) if you would:

1. recommend a drug holiday as described above YES _____
2. not recommend a drug holiday as discussed above YES _____

Signature _____

Once we have your recommendation, we will contact your patient with your recommendation and schedule our surgery in compliance with it. Thank you for your help with this patient. Working together, we can provide the best care for your patient.

Cordially,

STAGING AND TREATMENT STRATEGIES FOR Bisphosphonate-Related Osteonecrosis of the Jaws (BRON)

- A. At risk category:** no apparent exposed/necrotic bone, in patients who have been treated with either oral or IV bisphosphonates
- No treatment indicated
 - Patient education
- B. BRON Stage 1:** Exposed/necrotic bone in patients who are asymptomatic and have no evidence of infection
- Oral antibacterial mouth rinse
 - Clinical follow-up on a monthly basis
 - Patient education and review of indications for continued bisphosphonate therapy
- C. BRON Stage 2:** Exposed/necrotic bone associated with infection as evidenced by pain and erythema in the region of the exposed bone with or without purulent drainage
- Symptomatic treatment with broad-spectrum oral antibiotics, e.g., penicillin, cephalexin, or 1st generation fluoroquinolone
 - Oral antibacterial mouth rinse
 - Pain control
 - Only superficial debridement to relieve soft tissue irritation
- D. BRON Stage 3:** Exposed/necrotic bone in patients with pain, infection, and one or more of the following: pathologic fracture, extra-oral fistula, or osteolysis extending to the inferior border of the mandible
- Oral antibacterial mouth rinse
 - Antibiotic therapy and pain control
 - Surgical debridement/resection for longer term palliation of infection and pain

BISPHOSPHONATES -TREATMENT STRATEGIES

A. Patients about to initiate intravenous bisphosphonate therapy

- If systemic conditions permit, initiation of IV bisphosphonate therapy should be delayed until dental health is optimized.
- Non-restorable teeth and those with a poor prognosis should be extracted. Other elective dentoalveolar surgery necessary should be done at this time.
- Patients with full or partial dentures should be examined for areas of mucosal trauma (lingual flange, palatal or mandibular tori, or other exostoses). These areas should be treated if necessary prior to bisphosphonate therapy.
- If systemic conditions permit, bisphosphonate therapy should be delayed until the extraction site has mucosalized (14-21 days) or until there is adequate osseous healing. Dental prophylaxis, caries control, and conservative restorative dentistry on an ongoing basis are necessary to maintain functionally sound teeth.

B. Asymptomatic patients receiving intravenous bisphosphonate treatment

- Procedures that involve direct osseous injury should be avoided. Non-restorable teeth may be treated by crown removal and endodontic treatment of the remaining roots.
- Placement of dental implants should be avoided in patients exposed to the more potent IV bisphosphonates (zoledronate “Zometa” and pamidronate “Aredia” on a frequent dosing schedule [4-12 times per year]).

C. Asymptomatic patients receiving oral bisphosphonate therapy

- Appear to be at risk of developing Bisphosphonate-Related Osteonecrosis of the Jaws (BRON) to a much lesser degree than those people treated with IV bisphosphonates
- BRON can develop spontaneously or after minor trauma
- These patients seem to have less severe manifestations of necrosis, and respond more readily to stage specific treatment regimens
- Elective dentoalveolar surgery does not seem to be contraindicated in this group
- Patients should be informed of the small risk of compromised bone healing. The risk of BRON may be associated with increased duration of treatment with oral bisphosphonates, i.e., greater than three years, and other risk factors including concomitant use of corticosteroids, chemotherapy, diabetes, smoking, excessive alcohol use, and poor oral hygiene