

**Fact sheet****12 December 2007**

## **Incidence and avoidance of osteonecrosis of the jaw associated with use of bisphosphonates**

*This information has been prepared to provide doctors and pharmacists with information on the incidence of osteonecrosis of the jaw associated with use of bisphosphonates. This is provided following requests for information sources resulting from a television report on Tuesday 11 December 2007.*

The incidence and strategies to reduce risk of osteonecrosis of the jaw associated with use of bisphosphonates has been discussed in several recent NPS publications as below:

NPS News 53: See *Preventing osteonecrosis of the jaw* (page 3)  
[www.nps.org.au/news\\_53](http://www.nps.org.au/news_53)

NPS Prescribing Practice Review 39: (page 6)  
[www.nps.org.au/ppr\\_39](http://www.nps.org.au/ppr_39)

NPS Radar: Alendronate  
[www.nps.org.au/health\\_professionals/publications/nps\\_radar/issues/current/april\\_2007/alendronate](http://www.nps.org.au/health_professionals/publications/nps_radar/issues/current/april_2007/alendronate)

### **Summary of evidence**

Osteonecrosis of the jaw is the breakdown of bone in the jaw. It occurs rarely with bisphosphonate therapy, but it is difficult to treat and may not resolve.<sup>1,2</sup> Assessing the patient's risk, and referring them for a dental check-up before starting a bisphosphonate, may help to minimise the likelihood of this adverse effect.<sup>3</sup> Patients who are taking a bisphosphonate need to be aware of the signs and symptoms of osteonecrosis of the jaw which can vary and include exposed bone, severe jaw pain, numbness, loose teeth, oral odour, infection, impaired healing and denture sore spots.<sup>4,5</sup>

The cause of bisphosphonate-induced osteonecrosis of the jaw is unknown, however the risk increases after dental surgery.<sup>3,4</sup> A systematic review of 368 published case reports found that 60% of cases occurred after a tooth extraction or other dental surgery.<sup>5</sup> Infection or local trauma, such as that caused by poorly fitted dentures, may also precipitate osteonecrosis of the jaw.<sup>3,5</sup>

Most reports of osteonecrosis of the jaw are associated with intravenous bisphosphonates (such as zoledronic acid or pamidronate) in people with multiple myeloma or metastatic breast cancer who underwent dental surgery during treatment.<sup>1-6</sup> An Australian study estimated the incidence in people with osteoporosis taking bisphosphonates to be about 0.01% to 0.04%, and in people with malignancy using bisphosphonates to be about 0.88% to 1.15%.<sup>3</sup> While the incidence is lower among people taking oral bisphosphonates for osteoporosis, a dental extraction can increase the risk in any patient taking a bisphosphonate by about a factor of 8.<sup>3,5</sup>

### Risk of osteonecrosis of the jaw in patients taking bisphosphonates\*<sup>3</sup>

	Absolute risk <sup>†</sup>	Risk if having a dental extraction <sup>†</sup>
All patients taking bisphosphonates	0.05% to 0.10%	0.37% to 0.80%
Patients with osteoporosis	0.01% to 0.04%	0.09% to 0.34%
Patients with Paget's disease	0.26% to 1.8%	2.1% to 13.5%
Patients with malignancy	0.88% to 1.15%	6.67% to 9.1%

\* Table has been adapted with permission from: Oral and Dental Expert Group. Therapeutic Guidelines: Oral and Dental. Version 1. Melbourne: Therapeutic Guidelines Ltd, 2007: p.77.

† Risk increases with increasing age of patient, increasing duration of bisphosphonate use, and increasing potency of the bisphosphonate. Risk is higher in patients with immunological compromise (e.g. corticosteroid use, type 1 diabetes).

Avoiding dental surgery during bisphosphonate therapy is especially important for people at risk of osteonecrosis of the jaw, such as those receiving large intravenous doses for malignancy. Other risk factors to consider include advanced age, long-term therapy, immunosuppression and co-morbidities (e.g. diabetes).<sup>1-5</sup>

A dental assessment may be needed before starting a bisphosphonate (including people with dentures).<sup>3,4</sup> People already receiving a bisphosphonate should not undergo dental surgery until their risk of osteonecrosis of the jaw has been assessed.<sup>3</sup> There is no evidence as to whether bisphosphonates should or should not be stopped before dental surgery or after the onset of a reaction.<sup>4,5</sup>

#### For more information see:

TGA ADRAC Bulletin Volume 25, Number 4 (August 2006)  
Osteonecrosis of the jaw with bisphosphonates  
<http://www.tga.gov.au/adr/aadrb/aadr0608.htm#a1>

OR

Call the NPS Therapeutic Advice and Information Service (TAIS) on 1300 138 677

#### References

1. Carter G, Goss AN, Doecke C. Bisphosphonates and avascular necrosis of the jaw: a possible association. *Med J Aust* 2005;182:413–5.
2. Purcell PM, Boyd IW. Bisphosphonates and osteonecrosis of the jaw. *Med J Aust* 2005;182:417–8.
3. Oral and Dental Expert Group. Therapeutic Guidelines: Oral and dental. In eTG complete[CD-ROM] (accessed December 2007). Melbourne: Therapeutic Guidelines Limited, 2007.
4. Sambrook P, Olver I, Goss A. Bisphosphonates and osteonecrosis of the jaw. *Aust Fam Physic* 2006;35:801–3.
5. Woo SB, Hellstein JW, Kalmar JR. Systematic review: bisphosphonates and osteonecrosis of the jaws. *Ann Intern Med* 2006;144:753–61.
6. Cheng A, Mavrokokki A, Carter G, et al. The dental implications of bisphosphonates and bone disease. *Aust Dental J* 2005;50:S4–13.

The information contained in this material is derived from a critical analysis of a wide range of authoritative evidence. Any treatment decision based on this information should be made in the context of the clinical circumstances of each patient.