

# Coventry & Warwickshire Area Prescribing Committee



## Clinical Guideline CG007

### **Bisphosphonates and Jaw Necrosis**

#### **Introduction**

There is growing evidence that bisphosphonate therapy is associated with osteonecrosis of both the upper and lower jaws. The first reports describing osteonecrosis of the jaw were published in 2003 and whilst the majority of reported cases have been in patients receiving intravenous bisphosphonates, some cases have been reported in patients taking oral preparations.

Bisphosphonate-related osteonecrosis of the jaw is associated with significant morbidity and reduced quality of life. It is defined as an area of exposed necrotic bone in the maxillofacial region that has not healed within 8 weeks after identification by a healthcare provider in a patient who was receiving or had been exposed to bisphosphonate therapy and had no history of previous radiation therapy to the craniofacial region<sup>1</sup>.

#### **Bisphosphonate therapy**

Bisphosphonates are routinely used in the management of osteoporosis and metastatic bone disease. They are adsorbed onto hydroxyapatite crystals in bone, slowing both their rate of growth and dissolution, and therefore reducing the rate of bone turnover.

Oral bisphosphonates are mainly used in the treatment of osteoporosis and some less common conditions such as Paget's Disease and osteogenesis imperfecta of childhood. Examples include alendronate (Fosamax®, Merck) and risedronate (Actonel®, Aventis).

Intravenous bisphosphonates are primarily used in the management of cancer-related conditions such as hypercalcaemia of malignancy, lytic lesions in multiple myeloma, bone metastases from malignancies such as breast cancer, prostate and lung cancer. They are more potent than the oral forms and include pamidronate (Aredia®, Novartis) and zoledronate (Zometa®, Novartis).

All forms of bisphosphonates may potentially increase the risk of jaw necrosis but the intravenous drugs are more associated with complications, although cases have also been reported with long-term oral therapy. Management of bisphosphonate-associated osteonecrosis [BON] is difficult and can leave significant deformity in afflicted patients.

The European Medicines Agency recently conducted a review on the risk of jaw osteonecrosis linked to use of bisphosphonates<sup>2</sup>. The Agency's Committee for Medicinal Products for Human Use (CHMP) concluded that "there is an increased risk of osteonecrosis of the jaw in patients using these medicines. However, further studies should be carried out to better identify the factors that increase the risk and the measures needed to minimise it."

The following recommendations are based upon best practice guidelines from a number of recent publications.

### **Management of patients on or due to receive bisphosphonate therapy**

Before taking any decisions concerning treatment with bisphosphonates, prescribers should take the risks and benefits for each individual patient into account.

Patients **scheduled for bisphosphonates**, especially intravenous preparations, should be advised to see their dentist for a thorough dental examination before the bisphosphonates are started. Any dental work that is necessary should be completed and time allowed for full healing before the

drugs are started. See below for advice once drug treatment has commenced.

Patients **already on either intravenous or oral bisphosphonates** should be advised to have regular dental check ups and to report any signs of infection and trauma or any unusual symptoms in their mouth such as loose teeth, pain or swelling to their dentist.

A high level of oral hygiene is essential and patients should be taught how to do this by their usual dentist. Patients should be advised to attend their dentist regularly for check-ups and control of dental disease in early stages. Patients should be told about the risk of BON and what the warning symptoms are: localised pain, numbness and altered sensation, loosening of teeth, soft tissue infection and swelling.

If patients don't have access to a dentist, they can contact their local Primary Care Trust for help with getting a NHS dentist.

It is essential that prescribers, dentists and patients work together to manage the risk of osteonecrosis of the jaw.

**Jonathan Iloya**  
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<sup>1</sup> Khosla S et al. Bisphosphonate-Associated Osteonecrosis of the Jaw: Report of a Task Force of the American Society for Bone and Mineral Research. *J Bone Miner Res* 2007; 22: 1479 -1491

<sup>2</sup> European Medicines Agency. European review of bisphosphonates and risk of jaw osteonecrosis. 30 September 2009.