



IRISH MEDICINES BOARD

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# **BISPHOSPHONATES AND OSTEONECROSIS OF THE JAW: UPDATE ON RISK MINIMISATION INCLUDING NEW RECOMMENDATIONS ON PREVENTATIVE DENTAL MEASURES**

Bisphosphonates are a class of medicines approved for various indications related to their inhibitory effect on bone resorption in certain malignant and benign diseases, including prophylaxis and treatment of osteoporosis; treatment of Paget's disease; and as part of some cancer regimens, particularly for metastatic bone cancer and multiple myeloma. Detailed information on the approved indications for use, warnings and precautions etc. is described in the product information for the individual products concerned (alendronic acid, clodronic acid, etidronic acid, ibandronic acid, neridronic acid, pamidronic acid, risedronic acid, tiludronic acid, zoledronic acid). The risk of osteonecrosis of the jaw (ONJ) in association with the use of bisphosphonates has been closely monitored and reviewed at EU level on several occasions, with a number of risk minimisation measures taken, including updates to the product information and communication to healthcare professionals. The most recent review of information on the risk of bisphosphonate associated ONJ included assessment of the currently available published literature and data provided by the Marketing Authorisation Holders (including data from experimental and preclinical studies, clinical trials, and post-marketing reports),

together with current guidelines produced by learned societies. The review also incorporated advice from a group of experts representing all areas of medicine where bisphosphonates are used, dentistry and bone surgery, and representatives of patients' organisations. Whilst it is recognised that risk factors for ONJ are multiple and currently not fully elucidated, the most significant risk factors for the development of ONJ in association with bisphosphonates are considered to be bisphosphonate potency, route of administration and cumulative dose of bisphosphonate exposure. A history of dental disease, including invasive dental procedures, dental trauma, periodontal disease, and poorly fitting dentures is associated with an increased risk of ONJ. Further research is needed to increase knowledge about the underlying mechanisms and risk factors for ONJ, and about how best to minimise these risks. The EU regulatory authorities will explore strategies to promote this research and the European Medicines Agency (EMA) has adopted a definition of ONJ related to bisphosphonates to facilitate future case reporting and research. However, healthcare professionals should consider these risk factors when evaluating an individual's risk of developing ONJ.

### **Advice for Healthcare Professionals**

- *The risk of developing ONJ in association with oral bisphosphonates seems to be low. The risk of ONJ is substantially greater for patients receiving intravenously bisphosphonates for cancer indications than for patients receiving oral bisphosphonates for osteoporosis or Paget's disease.*
- *There is clear evidence to suggest bisphosphonate-specific and indication-specific risk factors for the development of ONJ, such as potency (highest for zoledronic acid), route of administration (e.g. intravenous ibandronic acid, pamidronic acid and zoledronic acid); and cumulative dose. The evidence base is less robust for other proposed risk factors (e.g. duration and type of malignant disease, concomitant treatment, smoking, and comorbid conditions). However, healthcare professionals should consider these risk factors when evaluating an individual's risk of developing ONJ.*
- *A history of dental disease – including invasive dental procedures, dental trauma, periodontal disease, and poorly fitting dentures is associated with an increased risk of ONJ.*

### **Risk Minimisation – Recommendations for preventative dental measures (baseline assessment and ongoing monitoring)**

#### **For patients receiving bisphosphonates for CANCER indications; the recommendations are as follows:**

Before starting treatment with bisphosphonates:

- An oral and dental assessment should be performed by a dentist or oral surgeon to optimise dental health. If dental treatment is required, this should take place as quickly as possible before start of bisphosphonate treatment. If urgent treatment with a bisphosphonate is necessary, this treatment should not be delayed and the patient should be referred in an expedited manner for a dental examination.

During treatment with bisphosphonates:

- Patients should be advised of the importance of

maintaining good oral hygiene in preventing dental disease.

- There is a need to ensure oral and dental follow-up performed by a dentist.
- Dental examination is recommended as soon as the patient develops oral symptoms, such as pain or swelling.
- Dental interventions should be as conservative and preservative as possible (preservation of tooth). The dentist should refer the patient to specialist centres if extractions or invasive procedures are contemplated.

#### **For patients receiving bisphosphonates for NON-CANCER indications, the recommendations are as follows:**

Before starting treatment with bisphosphonates:

- A dental examination should be performed if the dental status of the patient is poor. Since the start of bisphosphonate treatment may not be urgent in this setting, oral and dental assessment may be followed by dental care if necessary.

During treatment with bisphosphonates:

- Patients should be advised of the importance of maintaining good oral hygiene to prevent dental disease.
- Routine dental checkups by a regular dentist are recommended. Dental examination is recommended as soon as the patient develops dental problems whilst on treatment. Dental interventions should be as conservative and preservative as possible.

**Key message: All patients with cancer should have a dental check-up before bisphosphonate treatment. All other patients who start bisphosphonates should have a dental examination if they have poor dental status. During bisphosphonate treatment, patients should be advised to maintain good oral hygiene, receive routine dental check-ups, and report any oral symptoms such as dental mobility, pain or swelling.**