

<p style="text-align: center;"><b>Bisphosphonates – osteonecrosis of jaw</b> <b>As agreed by the PhVWP in February 2006</b></p>
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## **Pamidronic acid and for zoledronic acid:**

### **Section 4.4**

*Osteonecrosis of the jaw has been reported in patients with cancer receiving treatment regimens including bisphosphonates. Many of these patients were also receiving chemotherapy and corticosteroids. The majority of reported cases have been associated with dental procedures such as tooth extraction. Many had signs of local infection including osteomyelitis.*

*A dental examination with appropriate preventive dentistry should be considered prior to treatment with bisphosphonates in patients with concomitant risk factors (e.g. cancer, chemotherapy, corticosteroids, poor oral hygiene).*

*While on treatment, these patients should avoid invasive dental procedures if possible. For patients who develop osteonecrosis of the jaw while on bisphosphonate therapy, dental surgery may exacerbate the condition. For patients requiring dental procedures, there are no data available to suggest whether discontinuation of bisphosphonate treatment reduces the risk of osteonecrosis of the jaw. Clinical judgement of the treating physician should guide the management plan of each patient based on individual benefit/risk assessment.*

## **Remaining bisphosphonates:**

### **Section 4.4.**

*Osteonecrosis of the jaw, generally associated with tooth extraction and/or local infection (including osteomyelitis) has been reported in patients with cancer receiving treatment regimens including primarily intravenously administered bisphosphonates. Many of these patients were also receiving chemotherapy and corticosteroids. Osteonecrosis of the jaw has also been reported in patients with osteoporosis receiving oral bisphosphonates.*

*A dental examination with appropriate preventive dentistry should be considered prior to treatment with bisphosphonates in patients with concomitant risk factors (e.g. cancer, chemotherapy, radiotherapy, corticosteroids, poor oral hygiene).*

*While on treatment, these patients should avoid invasive dental procedures if possible. For patients who develop osteonecrosis of the jaw while on bisphosphonate therapy, dental surgery may exacerbate the condition. For patients requiring dental procedures, there are no data available to suggest whether discontinuation of bisphosphonate treatment reduces the risk of osteonecrosis of the jaw.*

*Clinical judgement of the treating physician should guide the management plan of each patient based on individual benefit/risk assessment.*

The following wording has been implemented in Section 4.8 for zoledronic acid and pamidronic acid. The PhVWP proposes to implement the same wording also for ACLASTA® (zoledronic acid).

### **Section 4.8**

*Post-marketing: Very rare cases of osteonecrosis (primarily of the jaw) have been reported in patients treated with bisphosphonates. Many had signs of local infection including osteomyelitis. The majority of the reports refer to cancer patients following tooth extractions or other dental surgeries. Osteonecrosis of the jaw has multiple well-documented risk factors including a diagnosis of cancer,*

*concomitant therapies (e.g. chemotherapy, radiotherapy, corticosteroids) and co-morbid conditions (e.g. anaemia, coagulopathies, infection, pre-existing oral disease). Although causality cannot be determined, it is prudent to avoid dental surgery as recovery may be prolonged (see section 4.4 Special warnings and special precautions for use).*

The following wording is proposed for implementation for alendronic and ibandronic acid:

**Section 4.8 for alendronic acid and ibandronic acid**

*Osteonecrosis of the jaw has been reported in patients treated by bisphosphonates. The majority of the reports refer to cancer patients, but such cases have also been reported in patients treated for osteoporosis. Osteonecrosis of the jaw is generally associated with tooth extraction and / or local infection (including osteomyelitis). Diagnosis of cancer, chemotherapy, radiotherapy, corticosteroids and poor oral hygiene are also deemed as risk factors (see section 4.4).*

*A wording for Section 4.8 is not considered necessary for the remaining bisphosphonates.*