IRISH MEDICINES BOARD

Notice Information: Human Medicines - Advisory 14 January 2008

Part 1. Product Information

a)	Title:	Bisphosphonates and Osteonecrosis of the Jaw - Further Class Review by the Pharmacovigilance Working Party (PhVWP)
b)	Product Name/Type:	Fosamax, Fosavance, Osteomel, Bonefos, Didronel, Bonviva, Bondenza, Bondronat, Aredia, Actonel, Zometa & Aclasta

Part 2. Problem/Issue

a) Problem/Issue:

Bisphosphonates[1] are a class of medicinal substances approved for various indications related to their inhibitory effect on bone resorption in certain malignant and benign diseases, including osteoporosis. For detailed information on the approved indications for use, warning and precautions for use etc. please refer to the product information for the individual products concerned (Fosamax, Fosavance, Osteomel, Bonefos, Didronel, Bonviva, Bondenza, Bondronat, Aredia, Actonel, Zometa & Aclasta). In 2005, the European scientific committee responsible for medicines safety, the Pharmacovigilance Working Party (PhVWP), initiated a class review following reports of a serious suspected adverse reaction of osteonecrosis of the jaw associated with bisphosphonates. This review concluded that the occurrences of osteonecrosis of the jaw were positively associated with the potency of the bisphosphonate used and were strongly related with use in malignant diseases and with intravenous administration forms. However, there was also concern regarding orally administered bisphosphonates and usage in non-malignant indications. The aetiology is unknown and a pathophysiological mechanism has not been established, however, a number of risk factors have been identified, e.g. malignant disease per se, chemo- and radiotherapy, concomitant treatment with corticosteroids, female gender, advanced age, malnutrition, vascular disorders and dental procedures. Location to the mandible is a prevailing characteristic. The 2005 review resulted in the introduction of risk minimization measures; in particular the product information for all bisphosphonate-containing products was updated to include additional information and advice regarding osteonecrosis of the jaw and bisphosphonate use. In addition the IMB, as well as some professional societies, communicated the updated information to healthcare professionals with the aim of improving the safe use of bisphosphonates (link to IMB bisphosphonate MIMS article August 2006). (IMB Drug Safety Newsletter October 2006) Nevertheless, osteonecrosis of the jaw continues to be reported as a suspected adverse reaction associated with bisphosphonates and the numbers of reports appear to be increasing, particularly for the most potent bisphosphonates. The PhVWP considers that a further class review at a European level is warranted and letters have been sent to the relevant companies requesting an in-depth analysis of this safety issue. The PhVWP will review the data provided at their meetings in spring 2008 and any further information/recommendations will be communicated, when available. For further information please contact the Pharmacovigilance Section of the Irish Medicines Board at (01) 6764971 or imbpharmacovigilance@imb.ie .

Part 3. Enquiries

a) All enquiries should be made to:

[1] Bisphosphonates included in the class review: alendronic acid, clodronic acid, etidronic acid, ibandronic acid, neridronic acid, pamidronic acid, risedronic acid, tiludronic acid, zoledronic acid and associated salt forms.

Part 4. Keywords

a) Keywords: bisphosphonates