IRISH MEDICINES BOARD

Bisphosphonates – risk of atypical femoral fracture

Bisphosphonates* are a class of medicines which inhibit osteoclast mediated bone resorption and are indicated in certain malignant and benign diseases, including prophylaxis and treatment of osteoporosis.

In 2008, a European review concluded that the available data supported an association between alendronate and atypical stress fractures of the femur and the product information for alendronate was updated to include a warning about this risk. A class effect could not be ruled out however and the issue was kept under close review.

As part of this ongoing monitoring, a recent evaluation of new data from published literature, case reports and epidemiological studies was conducted by the Pharmacovigilance Working Party (PhVWP) of the European Medicines Agency. The PhVWP concluded that the risk of atypical femoral fractures is likely to be a class effect of bisphosphonates, but that such fractures occur only rarely.

The precise mechanism is unknown, however it is possible that the effect of bisphosphonates on the suppression of bone turnover may lead indirectly to the delay or prevention of repair of naturally occurring stress fractures. Atypical femoral fractures can occur after minimal or no trauma. Some patients experience thigh or groin pain, often associated with features of stress fractures on x-ray, weeks to months before presenting with a completed femoral fracture. Poor healing of these fractures has been reported.

The product information for these medicines will be updated to inform healthcare professionals and patients that atypical femoral fractures have been reported rarely with bisphosphonates, primarily in patients receiving long-term treatment for osteoporosis. For bisphosphonates used in osteoporosis, the product information will also advise periodic review of therapy, in particular after five or more years of treatment.

The IMB has previously highlighted potential and evolving concerns related to the safety of bisphosphonates, most recently in the November 2010 issue of its Drug Safety Newsletter and in the December 2010 issue of MIMS Ireland. Please also see the Summaries of Product Characteristics for the individual products for full details of the specific prescribing information applicable, including details of potential adverse reactions and risk minimisation measures.

Advice for Healthcare Professionals

- During bisphosphonate treatment patients should be advised to report any thigh, hip or groin pain. Any patient presenting with such symptoms should be evaluated for an incomplete fracture of the femur.
- Fractures are often bilateral; therefore the contralateral femur should be examined in bisphosphonate-treated patients who have sustained a femoral shaft fracture.
- Discontinuation of bisphosphonate therapy in patients suspected to have an atypical fracture of the femur should be considered pending evaluation of the patient, based on an individual benefit risk assessment.
- The optimal duration of bisphosphonate treatment for osteoporosis has not been established. The need for continued treatment should be re-evaluated periodically based on the benefits and potential risks of bisphosphonate therapy on an individual patient basis, particularly after 5 or more years of use.
- Any cases of atypical femoral fractures or atypical fractures at other sites associated with bisphosphonate treatment should be reported to the IMB.

Key Message:

Atypical femoral fractures have been reported rarely with bisphosphonate therapy, primarily in patients receiving long-term treatment for osteoporosis. The need for continued treatment should be re-evaluated periodically based on the benefits and potential risks of bisphosphonate therapy on an individual patient basis, particularly after 5 or more years of use.
The overall balance of risks and benefits of individual bisphosphonates in their authorised indications remain favourable.

*Bisphosphonates currently authorised in Ireland include: alendronate, clodronate, etidronate, ibandronate, pamidronate, risedronate and zoledronate.