

# RGH Pharmacy E-Bulletin

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A joint initiative of the Patient Services Section and the Drug and Therapeutics Information Service of the Pharmacy Department, Repatriation General Hospital, Daw Park, South Australia. The RGH Pharmacy E-Bulletin is distributed in electronic format on a weekly basis, and aims to present concise, factual information on issues of current interest in therapeutics, drug safety and cost-effective use of medications.

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## Use of bisphosphonates in osteoporosis

### *Revised PBS restrictions for alendronate*

Prior to April 2007 alendronate was listed on the Australian Pharmaceutical Benefits Scheme (PBS) for the treatment of established osteoporosis in people with fracture due to minimal trauma. Due to this restriction many patients without a fracture but who were considered to be at high risk (for example those with a low bone mineral density (BMD) and at risk of falls) were ineligible for treatment. The PBS listing has now been extended to cover the treatment of osteoporosis without fracture, in people aged 70 years or older who have a BMD T-score of  $-3.0$  or less. This change will benefit many of the patients considered to be at high risk of fracture who were previously unable to access subsidised treatment.

### *Duration of therapy*

The optimum duration of oral bisphosphonate therapy in osteoporosis has been the subject of considerable debate. No significant differences in fracture outcomes have been shown between 5-year and 10-year treatment, but this result is inconclusive, as studies were only powered to detect differences in BMD. There is some evidence to suggest that patients with a high risk of fracture have fewer clinically diagnosed vertebral fractures with longer treatment. Further studies are needed, but at the current time consideration can be given to ceasing oral bisphosphonates after 5 years in those who have increased their BMD by at least 5% and who have not had a fracture during treatment. Longer treatment may be needed for high risk patients, such as those with multiple vertebral fractures.

### *Once yearly IV Zoledronate*

The risk of oesophagitis with oral bisphosphonates is well-recognised and patients with moderate–severe gastroesophageal reflux disease or swallowing problems are at increased risk. For some of these patients intravenous bisphosphonate therapy has been used as an alternative therapy, with annual IV zoledronate infusions being an attractive option due to the simplicity of the dosing regimen. This treatment approach may also benefit those patients with poor adherence to oral bisphosphonate therapy.

Additional evidence for IV zoledronate in postmenopausal osteoporosis has recently been published. In the HORIZON Pivotal Fracture Trial 7765 patients (mean age 73 years) were randomised to receive either a single 15 minutes IV infusion of zoledronate 5mg, or placebo, at baseline and again after 12 and 24 months. A significant reduction in vertebral, hip and other fractures was observed over a 3-year follow-up period

### *Adverse effects*

Osteonecrosis of the jaw is a rare but serious adverse effect of bisphosphonates, with most case reports occurring in cancer patients receiving frequent doses of IV bisphosphonates. In the HORIZON study there was one possible case of osteonecrosis of the jaw in each of the zoledronate and placebo groups. However an unexpected finding in the trial was the increased incidence of serious atrial fibrillation in the zoledronate group (1.3% vs 0.5%,  $p < 0.001$ ). A similar non-significant trend was also observed with oral alendronate in postmenopausal women enrolled in the Fracture Intervention Trial. The possibility of an increased risk of atrial fibrillation with bisphosphonate therapy requires further study.

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