A recent systematic review of 315 studies looked at the effectiveness and adverse events of a range of treatments to prevent fractures.\(^1\) Their findings indicate strong evidence for the efficacy of a number of bisphosphonates. The magnitude of the effect indicated a NNT of between 40 and 89 over 1-3 years of treatment to prevent one fracture in women.\(^1\)

The FLEX trial looked at the legacy effect of alendronate for patients who had been treated in the FIT trial for 5 years.\(^2\) They found that there was no difference in non-vertebral fracture risk in patients who continued alendronate for a further 5 years, compared to those that took a placebo for the five years. There was however an increase in the number of clinical vertebral fractures in patients who took placebo instead of alendronate (23/437; 5.3% vs 16/662; 2.4% respectively; NNT 34 for one vertebral fracture over 5 years.

The same authors reanalysed the data at a later date to look more closely at those patients with nonvertebral fractures.\(^3\) They clarified that in those patients without a previous vertebral fracture and a T score of -2.5 or less (when they had completed 5 years of alendronate treatment) that there was a benefit in fracture risk reduction (14.7% vs 28%, NNT -7 over 5 years) compared to no benefit in those patients with a T score of -2.5 or above.\(^3\)

### BISPHOSPHONATES

#### KEY POINTS

- Oral bisphosphonates are effective in the prevention of secondary fractures with one fracture avoided for every 40-90 patients treated for 1-3 years.
- Many patients who have had 5 years of continuous treatment with an oral bisphosphonate will have ongoing benefit for a further 5 years after cessation of the bisphosphonate.
- Where ongoing treatment for osteoporosis is required, options other than bisphosphonates may be safer.

#### CONTEXT

This guide considers the deprescribing of oral bisphosphonates in the treatment of osteoporosis.

#### RECOMMENDED DEPRESCRIBING STRATEGY

1. Patients with a history of osteoporosis who have had 5 years of bisphosphonate treatment and whose risk of fracture is now low should have their bisphosphonate ceased for 5 years.
2. A plan for regular (eg. biennial) monitoring of bone mineral density may be of benefit to monitor for any decline.
3. Bisphosphonates can usually be ceased without the need for tapering.

#### Efficacy

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#### Adverse Effects

Bisphosphonates are poorly absorbed (less than 5% bioavailable) and as such require relatively strict administration procedures. It is recommended that patients do not lie down for 30min after taking the agent and that it be taken at least an hour before the first food or beverage of the day.

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\(^3\) Bisphosphonates can usually be ceased without the need for tapering.
**ADVERSE EFFECTS continued from page 1**

They are highly irritant to the oesophageal mucosa and can cause a range of upper abdominal and gastrointestinal symptoms (abdominal pain ~ 7%, acid dyspepsia, regurgitation and nausea (all ~ 4%).

Long term use has been associated with an increased risk of atypical fractures. A report of a Nationwide study of bisphosphonate use in Sweden indicated a markedly increased relative risk of fracture of the femoral shaft in both women (RR 55; 95% CI 59-79) and men (RR 54; 95% CI 15-192). The risk increases with duration of use. The absolute risk remained low (1/100,000 patients (0.0007%) for oral therapy. Estimates of 0.001% to 0.01% have been proposed by other authors (NNH of 1000-10,000). Bisphosphonate-associated osteonecrosis of the jaw (ONJ) is a rare, but serious clinical condition caused by anti-osteoclastic, antiangiogenic and anti-human endothelial cell proliferation effects of bisphosphonates, which inhibit bone turnover.

Bisphosphonate-associated osteonecrosis of the jaw (ONJ) is a rare, but serious clinical condition caused by anti-osteoclastic, antiangiogenic and anti-human endothelial cell proliferation effects of bisphosphonates, which inhibit bone turnover. ONJ more often develops in those patients who are receiving either long term nitrogen-containing IV bisphosphonate therapy alone or have associated invasive dental procedures. Incidence is difficult to ascertain with one of the major drug companies estimating an incidence rate of 0.7 per 10,000 years of patient use; NNH 909) and the risk decreased rapidly (by 70% per year) after cessation of bisphosphonate.

**REFERENCES**


