UKMi UK Medicines Information MIDLANDS

TRENT MEDICINES INFORMATION SERVICE

NHS

QIPP Detail Aid

Providing support for quality in prescribing

BISPHOSPHONATES- is a holiday necessary?

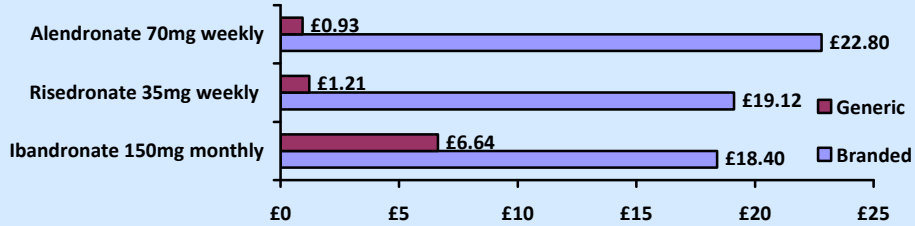
WHAT IS THE PROBLEM?

- Bisphosphonates such as alendronate or risedronate have become the mainstay of treatment and prevention of osteoporosis, particularly since the use of HRT has declined.
- Their long-term use has been associated with several problems, including osteonecrosis of the jaw and atypical femoral fractures. The suggestion of stopping therapy or a drug 'holiday' after 5 years treatment has been made in the literature.

KEY MESSAGES

- **Long-term bisphosphonate use has been associated with atypical femoral fractures. The suggestion of stopping therapy or a drug 'holiday' after 5 years treatment has been made in the literature.**
- **National guidance is not available on whether a drug holiday is required, which patients would be suitable or for how long the holiday should be.**
- **The absolute risk of femoral fractures due to bisphosphonates is far lower than the number of osteoporotic fractures prevented.**
- **Some areas have local guidance which should be followed. Otherwise, the following is suggested, after a full discussion of the risks and benefits with the patient.**
- **Patients at continued high risk of an osteoporotic fracture should continue therapy with bisphosphonate. Re-assess at regular intervals and advise patients to report any thigh, hip or groin pain which may be indicative of an atypical femoral fracture. Some local guidance suggests stopping therapy in all patients after 10 years of treatment.**
- **Patients at moderate risk could consider a drug holiday after 5 years of alendronate or 3-5 years of zoledronic acid after discussion. There is limited information about risedronate and no information about ibandronate and drug holidays. Patients should be assessed regularly (at least annually) using tools such as bone markers (eg P1NP) or the FRAX® online tool. Consider restarting therapy after 1-3 years. Alternative non-bisphosphonate therapies may also be an option.**
- **Patients at low risk – consider discontinuing therapy. Re-start when indications for therapy are met.**
- **Ensure adequate intake of calcium and vitamin D in all patients including those who discontinue bisphosphonates.**

WHAT ARE THE COSTS?



Costs for 28 days supply. Taken from MIMS/ Drug Tariff July 2013
Most bisphosphonates are now off patent, however branded prescribing still occurs. For risedronate 5% of prescriptions are for the branded product but these make up 37% of the cost. £180,000 could have been saved in 2012-13 in the East Midlands just by prescribing bisphosphonates generically.

WHAT IS THE EVIDENCE?

- In 2011, the MHRA warned of the risk of atypical femoral fractures with bisphosphonates, particularly after long-term use. All bisphosphonates' Summaries of Product Characteristics (SPCs) now contain the advice that '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 on an individual patient basis, particularly after 5 or more years of use.'
- The absolute number of atypical fractures reported is far lower than the number of osteoporotic fractures prevented. Best available data suggest that, if 150 patients were treated for 8 years with a bisphosphonate, depending on severity of disease, 6-50 vertebral and 6-21 non-vertebral fractures would be prevented; 0.1-1 femoral fracture and 0.0015-0.15 cases of osteonecrosis of the jaw may occur as adverse events.
- The suggestion of a 'holiday' from bisphosphonate therapy has been made, based on the risks of long term therapy and the fact that bisphosphonate remain in the bone for up to several years after therapy is stopped.
- No clear UK guidelines are available advising whether a drug holiday is required, which patients would be suitable or how long the holiday should be for.
- In the absence of clear guidance US specialists have suggested patients still at high risk of osteoporotic fracture should continue therapy with bisphosphonate. Patients should be re-assessed at regular Intervals for the need for continued therapy and advised to report any thigh, hip or groin pain which may indicate an atypical fracture. Those at moderate risk should consider a drug holiday after 3-5 years of therapy after informed discussion. Data on duration of holiday are not available but reassessment after 2 years has been suggested. Those at low risk could discontinue therapy; re-start when indications for therapy are met.

References: **Date of Preparation: July 2013**

1. MHRA Drug Safety Update June 2011, vol 4, issue 4: (http://www.mhra.gov.uk/Safetyinformation/)
2. Am J Med (2013) 126, 13-20
3. FRAX ® WHO Fracture Risk Assessment Tool (http://www.shef.ac.uk/FRAX/)