

Bisphosphonates: Guidance on length of treatment (Treatment Holiday)

WHAT IS THE PROBLEM?

- Bisphosphonates are widely used for the treatment and prevention of osteoporosis
- Due to concerns of possible adverse effects of long-term treatment, the need for continuation of treatment should be reviewed at regular intervals – 3 to 5 years, and a treatment break (drug holiday) considered.

POTENTIAL SIDE EFFECTS

Gastrointestinal

GI side-effects such as oesophageal irritation, dysphagia and heartburn are well known and represent a potential barrier to tolerance and adherence. Tablets should be taken with plenty of water and patient should remain upright for 30-60 minutes after dose.

Nephrotoxicity

To avoid renal injury, do not use risedronate if eGFR less than 30ml/min, or alendronate if eGFR is less than 35ml/min.

Osteonecrosis of the jaw

This is a rare complication and can be associated with substantial morbidity. The risk is greatest with intravenous bisphosphonate but can occur with oral bisphosphonates; and seems to increase when treatment is longer than three years.

For patients with poor oral hygiene, please recommend a dental check before commencing treatment, or as soon as possible after starting. Advise all patients to maintain good oral hygiene and report any oral symptoms such as pain, swelling, non-healing sores to doctor or dentist.

Atypical femoral fractures

These have been reported rarely with bisphosphonates, mainly in patients on long-term treatment, and can occur after minimal or no trauma. One study showed a 100 fold increase in risk, from 0.00178% when on treatment for less than two years to 0.1% when on treatment for eight years.

Patients should be advised to report any thigh, hip or groin pain during treatment, and treatment reviewed/discontinued if suspected to have an atypical femoral fracture.

Osteonecrosis of external auditory canal

Very rarely reported with bisphosphonate treatment (fewer than 1 in 10 000 patients), and mainly in patients on long-term treatment (2 years or longer)

Patients should report any ear pain, discharge from the ear, or are infection during treatment.

KEY MESSAGES

- Review indication for all patients prescribed bisphosphonates & ensure product/dose is appropriate and patient is adherent to therapy.
- Re-assess patients fracture risk at least every five years, and consider treatment holiday if appropriate
- Ensure adequate intake of calcium and vitamin D in all patients including those who discontinue bisphosphonates

WHO SHOULD HAVE A TREATMENT HOLIDAY?

Bisphosphonates are widely used for treatment/prevention of osteoporosis. They bind strongly to bone mineral and inhibit bone turnover, remaining in the bone with a half-life of at least ten years. As these agents accumulate in the bone with some persistent anti-fracture efficacy after treatment is stopped, it is reasonable to consider a treatment break (drug holiday) from oral bisphosphonates for patients with a low fracture risk after 5 years.

Use FRAX too / DEXA scan to assess fracture risk: <http://www.shef.ac.uk/FRAX/tool.jsp>

- High risk patients (age >75, >7.5mg/day oral prednisolone or equivalent, history of fractures or fracture whilst on treatment, T score < -2.5) should continue treatment for a further 5 years
- Low risk patients (age <75, no fractures, T score > -2.5) should be considered for a treatment break (2-3 year 'holiday' for alendronate; 1 year 'holiday' for risedronate)

For patients who fracture whilst on treatment:

- Fragility fracture sustained during the first 2 years of bisphosphonate therapy-continue the same treatment.
- Fragility fracture sustained beyond 2 years of bisphosphonate therapy (or multiple fragility fractures)- refer for a DEXA.

References:

1. BMJ state of the art review: Bisphosphonates for the prevention and treatment of osteoporosis. BMJ 2015;351:h3783
2. MHRA Drug Safety Update Nov 2009, vol 3 issue 4: 2. www.gov.uk/drug-safety-update/bisphosphonates-osteonecrosis-of-the-jaw. Accessed Dec 2016
3. MHRA Drug Safety Update June 2011, vol 4 issue 11: A1. www.gov.uk/drug-safety-update/bisphosphonates-atypical-femoral-fractures. Accessed Dec 2016
4. MHRA Drug Safety Update volume 9 issue 5 December 2015: 3. www.gov.uk/drug-safety-update/bisphosphonates-very-rare-reports-of-osteonecrosis-of-the-external-auditory-canal. Accessed Dec 2016
5. NOGG 2016. Osteoporosis – Clinical Guideline for Prevention and Treatment. https://www.shef.ac.uk/NOGG/NOGG_Executive_Summary.pdf
6. Derbyshire Joint Area Prescribing Committee February 2016 – Bisphosphonate length of treatment guidelines

Treatment algorithm

