

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, treatment should be reviewed at regular intervals – 5 years*, and a treatment break (drug holiday) considered. (*3yrs for zoledronic acid)

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 the incidence is substantially greater with the higher doses used to treat skeletal metastases. 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. 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, 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 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.

Continuation of treatment is recommended in high risk pts:

- Age > 75ys
- Previous hip or vertebral fracture
- Low trauma fracture whilst on treatment (if poor adherence and causes of secondary osteoporosis have been excluded)
- Taking >7.5mg/day oral prednisolone or equivalent

For other patients, re-assess fracture risk using FRAX and BMD

<http://www.shef.ac.uk/FRAX/tool.jsp>

- If FRAX score above NOGG intervention threshold or hip BMD T-score is ≤ -2.5 , treatment should be continued.
- Otherwise, consider drug holiday and repeat FRAX + BMD in 1.5 – 3yrs time.

NOTE: There is no evidence base to guide decision about treatment beyond 10yrs and management of such patients should be considered on an individual basis.

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 2017. Clinical guideline for the prevention and treatment of osteoporosis. <https://www.sheffield.ac.uk/NOGG/NOGG%20Guideline%202017.pdf>
6. Derbyshire Joint Area Prescribing Committee Reviewed April 2017 – Bisphosphonate length of treatment guideline in osteoporosis

Bisphosphonates: Guidance on length of treatment (Treatment Holiday)

Date: June 2018

Treatment algorithm

