Osteoporosis Drug Holiday Guidelines for GPs

Bisphosphonates have been widely used in the treatment of osteoporosis with robust data demonstrating efficacy in fracture risk reduction over three to five years of treatment. They bind strongly to bone mineral and inhibit bone turnover, remaining within the bone with a half-life of at least ten years. This has led to the concern that long term treatment may increase bone fragility by suppressing normal bone remodelling, essential for repair of skeletal micro-damage. Links have emerged with the rare but serious complications of osteonecrosis of the jaw (1 case per 100 000 person-years for osteoporosis bisphosphonate treatment) and atypical subtrochanteric fracture (2-78 cases per 100 000 person-years)

As these agents accumulate in bone with some persistent anti-fracture efficacy after therapy is stopped, it is reasonable to consider a treatment break (drug holiday). Based on the available data, it is recommended that treatment review should be performed after 5 years for Alendronic acid, Risedronic acid or Ibandronic acid and after 3 years for Zoledronic acid.

The effects of other anti-resorptive treatments (Denosumab, Raloxifene, Strontium ranelate, Teriparatide) wear off more rapidly when treatment is stopped and there is no clear case for drug holidays in patients receiving these drugs.

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<th>Recommendations</th>
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<td>• Review indication for all patients prescribed bisphosphonates.</td>
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<td>• Check treatment adherence after 3 months of initiating treatment.</td>
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<td>• Re-assess patients at high risk of osteoporotic fracture every 5 years.</td>
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<td>• Consider a treatment break (Drug holiday) for patients who have been on oral bisphosphonates for 5 years or in 3 years for Zoledronic acid (Patients should continue calcium &amp; vitamin D supplementation).</td>
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<td>• Drug holiday duration –</td>
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<td>• Risedronic acid, Ibandronic acid - 2 years</td>
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<td>• Alendronic acid, Zoledronic acid - 3 years</td>
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<td>• Consider discontinuation of therapy for low risk patients.</td>
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<td>• Reassess fracture risk after a new fracture regardless of when this occurs or at the end of drug holiday and re-continue treatment if indicated.</td>
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The duration of treatment and the length of the ‘holiday’ should be tailored to individual patient circumstances and based on individual assessments of risk and benefit based on BMD monitoring and fracture risk (FRAX [https://www.shef.ac.uk/FRAX](https://www.shef.ac.uk/FRAX)). But, ultimately the duration of the holiday should be based on clinical judgment.

Conditions that might increase fracture risk, such as initiation of glucocorticoid therapy or increased risk of falls, necessitate re-evaluation of the appropriateness of the drug holiday.

References
Bisphosphonate treatment break. NHS PrescQIPP, Bulletin 110; December 2015
Osteoporosis: clinical guideline for prevention and treatment, NOGG Executive summary. Updated Nov 2014
**Treatment Algorithm**

**Treat with oral bisphosphonate for 5 years in line with local guidance**  
1st line: Alendronic acid  
2nd line: Risedronic acid or Ibandronic acid  
3 years for intravenous Zoledronic acid

Check treatment adherence, reassess BMD (DXA) and fracture risk (FRAX)

**If NO fracture on treatment:**  
- Risk assess and consider bisphosphonate holiday

**Mild risk:**  
- Treatment was not indicated in the first place as per local guidance  
- Post treatment BMD T score > -2  
- No history of previous fragility fractures  
- No fracture during treatment

If a bisphosphonate has been prescribed, it should be **discontinued** and not restarted unless/until the patient meets treatment guidelines.

**Moderate risk:**  
- Age<75  
- Post treatment T score BMD > -2.5 (but <2)  
- Stable or improved BMD  
- No history of hip/vertebral/ multiple fragility fractures  
- No fracture during treatment

Treat with bisphosphonate for 5–10 years, offer a ‘drug holiday’ of 2-3 years or until there is >4% BMD loss or the patient has a fracture, whichever comes first.  
Drug holiday can be extended up to 3-5 years based on individual patient’s treatment response.

**High risk:**  
- History of hip/vertebral/ or multiple fragility fractures after age 50 years  
- Post treatment T ≤ -2.5 (T ≤ -2 with history of vertebral fracture)  
- Continuing oral glucocorticoid therapy  
- Continuing high risk patients (frailty, frequent falls, age >75)  
- 10 years fracture risk >20%

Continue to treat with bisphosphonate for 10 years, offer a ‘drug holiday’ of 1-2 years, until there is >4% BMD loss or the patient has a fracture, whichever comes first.  
A non bisphosphonate treatment (e.g. raloxifene or strontium) may be offered during the ‘holiday’ from the bisphosphonate.

**For patients who fracture whilst on treatment:**  
- If patient sustains a fragility fracture during the first 2 years of bisphosphonate therapy, continue the same treatment.  
- If patient has sustained fragility fracture beyond 2 years of bisphosphonate therapy (or multiple fragility fractures), Refer to the Bone Clinic at Mount Vernon Hospital for a treatment review.

Reassess fracture risk after a new fracture regardless of when this occurs or at the end of drug holiday and re-continue treatment if indicated.

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