City and Hackney Clinical Commissioning Group
Homerton University Hospital Foundation Trust

Guidance for bisphosphonate drug holidays

Background

Bisphosphonate are routinely used in treating osteoporosis in primary and secondary care. Alendronic acid (alendronate) is the most commonly prescribed bisphosphonate. Concern over the rare side effect of long-term use of bisphosphonate therapy such as osteonecrosis of the jaw or atypical fractures have raised the question of the optimal duration of therapy. It was thought that the beneficial effect of bisphosphonate may persist for some time after cessation of treatment and this led to the suggestion of drug holidays. Hence, optimal duration of bisphosphonate treatment is important to balance the risks and benefits of these medicines.

This guidance incorporates advice from the National Osteoporosis Guideline Group (NOGG).

Recommendations

- Adults who have been prescribed zoledronic acid for **3 years** and alendronate, ibandronate or risedronate for **5 years** should have a drug holiday unless they have a high fracture risk as defined below:
    - Age ≥ 75 years.
    - Previous history of a hip or vertebral fracture.
    - Post treatment T score ≤ -2.5 with history of fragility fracture.
    - Occurrence of one or more low trauma fractures during treatment, after exclusion of poor adherence to treatment (e.g. less than 80% of treatment has been taken) and after causes of secondary osteoporosis have been excluded.
    - Current treatment with oral glucocorticoids ≥ 7.5 mg prednisolone/day or equivalent.

- Any patients continuing treatment with a bisphosphonate after 5 years should be aware of the features of atypical fractures.

- If fracture risk is not high, as defined above, then a drug holiday is indicated. A drug holiday should be viewed as **temporary** suspension of active treatment. Due to the long half-life of bisphosphonates, the anti-resorptive effect persists for a long period of time. The recommended duration of the drug holiday is dependent on the drug; recommence alendronate after 2 years, risedronate and ibandronate after 1 year and after 3 years for patients on zoledronic acid infusion.

- Ensure adequate intake of calcium and vitamin D in all patients including those who discontinue bisphosphonates. Patients should remain vitamin D replete when treatment with bisphosphonate has been discontinued.

- Reassess fracture risk using FRAX with femoral bone mineral density (BMD). The NOGG intervention threshold can be used to guide the decision as to whether treatment can be stopped for a period of time (see NOGG guideline for intervention thresholds).

- There is no evidence base to guide decisions about continuous treatment beyond 10 years and management of such patients should be considered on an individual basis. Refer patient for specialist review after 10 years of **continuous** bisphosphonate treatment (without any treatment breaks).

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- Assess **adherence** to bisphosphonate therapy in **all cases** and exclude causes of secondary osteoporosis.

- **Consider specialist referral if:**
  - Patient has recurrent fractures or prevalent vertebral fractures.
  - Bone mineral density has deteriorated despite patient concordance with treatment.
  - Creatinine clearance has decreased to < 35mL/min for alendronate and zoledronic acid or < 30mL/min for ibandronate and risedronate. The creatinine clearance should be calculated using the Cockcroft-Gault formula
  - Patient has been on treatment for ≥ 10 years (without any treatment breaks)
  - Patient reports thigh, hip or groin pain or dental pain, dental mobility or dental swelling which may indicate an atypical femoral fracture or osteonecrosis of the jaw.

Bone mineral density and FRAX

The assessment of BMD provides information on the likelihood of future fractures. The use of BMD alone to assess fracture risk has a high specificity but low sensitivity, which means that fragility fractures can occur in women who do not have osteoporosis (T score ≤ -2.5).

For better assessment of the fracture risk, FRAX score should be calculated using BMD. FRAX calculation tool can be accessed here: https://www.sheffield.ac.uk/FRAX/tool.aspx

References

- National Osteoporosis Guideline Group (NOGG) 2017: Clinical guideline for the prevention and treatment of osteoporosis (March 2017). Available at https://www.shef.ac.uk/NOGG/NOGG%20Guideline%202017.pdf (accessed 28/12/2018).

- Gallacher SJ, Gallagher AP, McQuillian C, Mitchell PJ, Dixon T. The prevalence of vertebral fracture amongst patients presenting with non-vertebral fractures. *Osteoporos Int.* 2006;18(2):185-92.

- Royal Osteoporosis Society. Vitamin D and bone health: a practical clinical guideline for patient management (December 2018). Available at https://nos.org.uk/media/100231/nos_vitamin_d_and_bone_-health_in_adults_web.pdf (accessed 28/12/2018).

- National Osteoporosis Guideline Group (NOGG) 2017: Information for patients and the public on the NOGG clinical guideline for the prevention and treatment of osteoporosis (March 2017). Available at https://www.sheffield.ac.uk/NOGG/NOGG%20PIL%202017.pdf (accessed 28/12/2018).

Produced by
Dr Susan Eisa, Consultant Rheumatologist, Homerton University Hospital Foundation Trust
Dr Piero Reynolds, Consultant Rheumatologist, Homerton University Hospital Foundation Trust
Anh Vu, Interim Joint Formulary Pharmacist, City and Hackney CCG & Homerton University Hospital Foundation Trust

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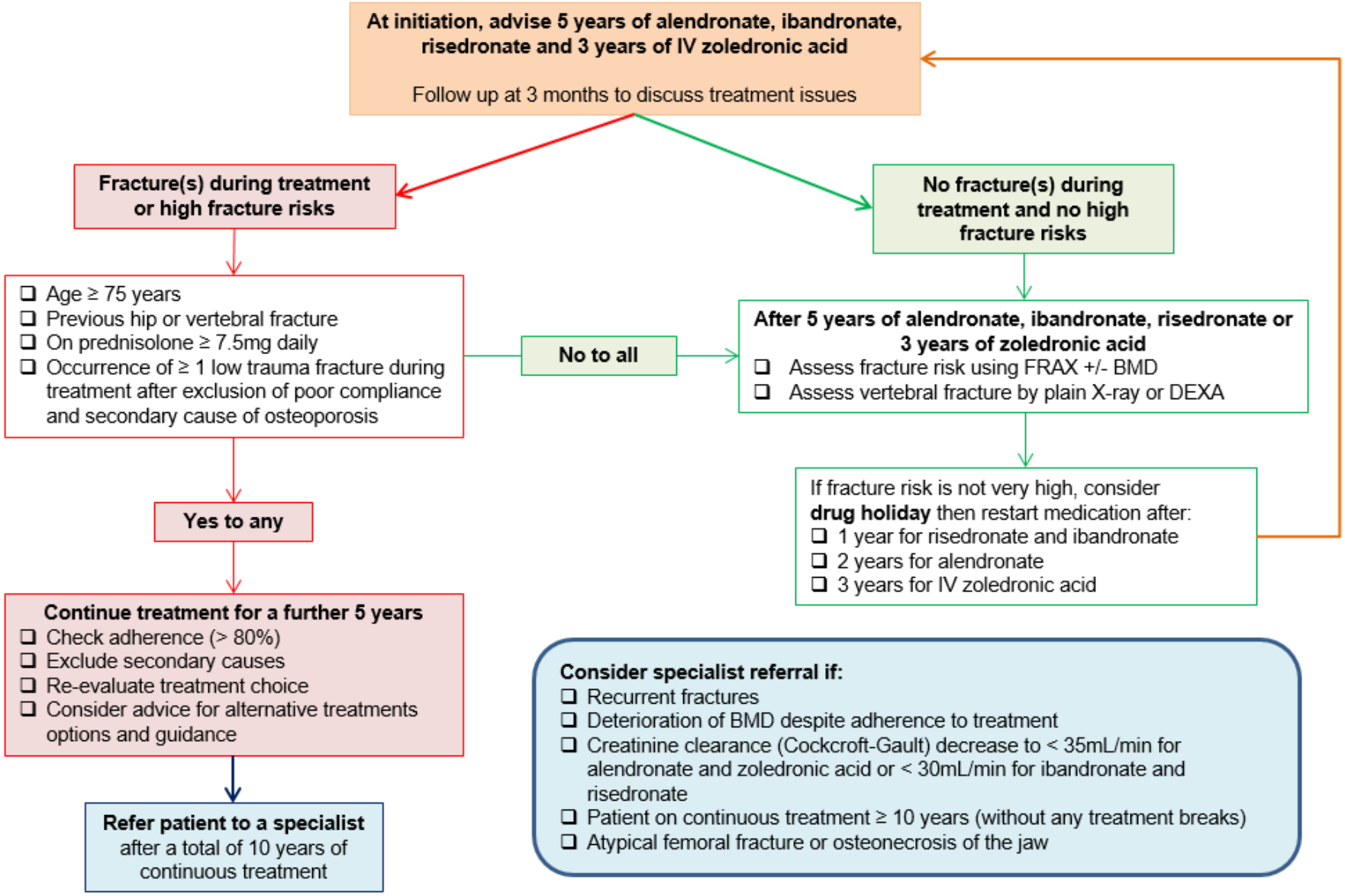
Bisphosphonates: algorithm for drug holidays



Adapted from NOGG : www.sheffield.ac.uk/NOGG/NOGG%20Guideline%202017.pdf

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