

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 or Risedronic acid, and after 3 years for Zoledronic acid.

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

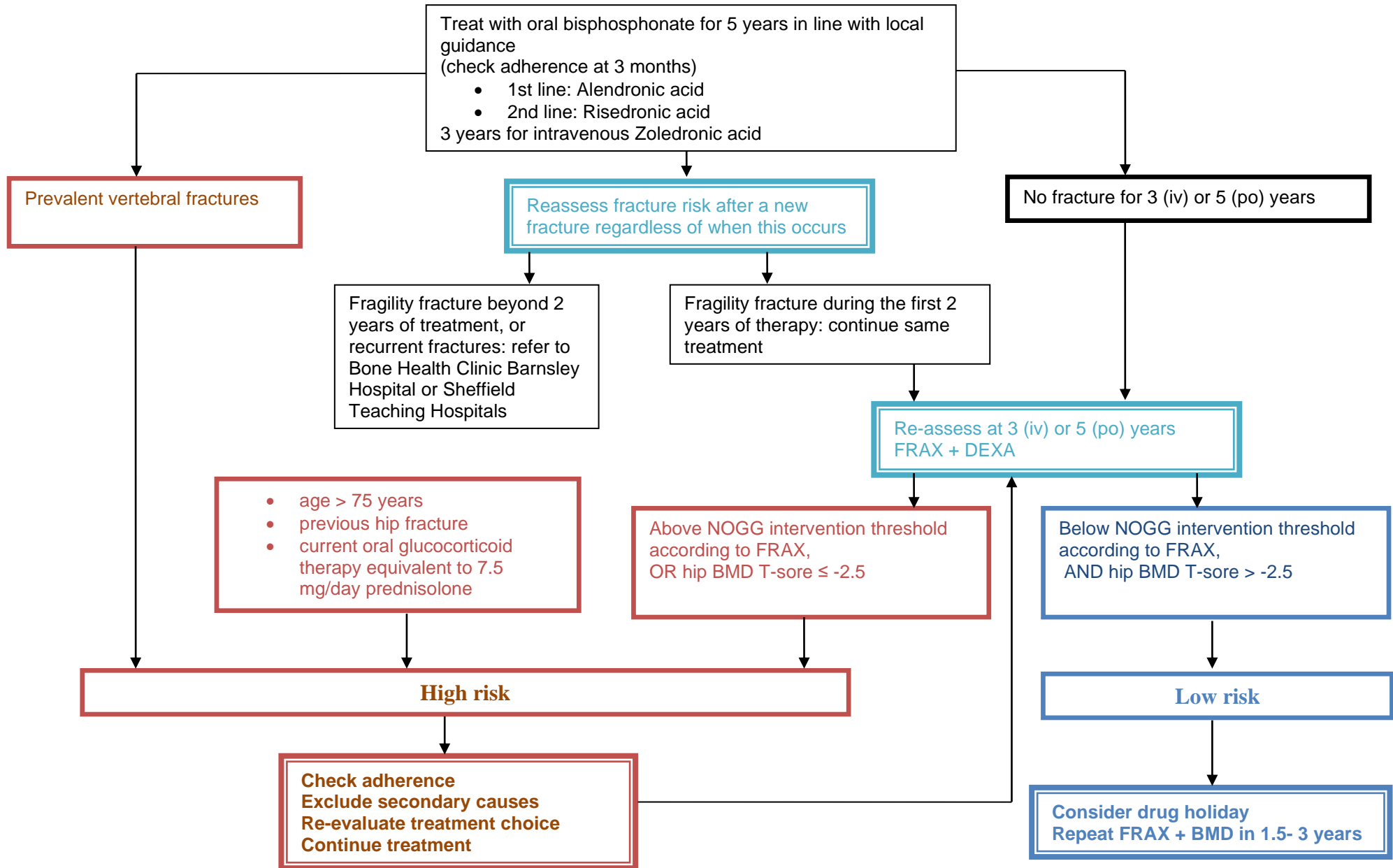
Recommendations

- Review indication for all patients prescribed bisphosphonates.
- Check treatment adherence after 3 months of initiating treatment.
- Exclude secondary causes of osteoporosis.
- Re-assess patients at high risk of osteoporotic fracture every 5 years.
- 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 & vitamin D supplementation) See flowchart below.
- Drug holiday duration –for all bisphosphonates, if treatment is discontinued, fracture risk should be reassessed after a new fracture, regardless of when this occurs and recontinue treatment if indicated. If no new fracture occurs, assessment of fracture risk should be performed again after 18months to 3 years.
- Consider discontinuation of therapy for low risk patients.
- Ensure adequate intake of calcium and vitamin D in all patients including those who discontinue bisphosphonates.

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>). But, ultimately the duration of the holiday should be based on clinical judgment. There is no evidence to guide decisions beyond 10 years of treatment and management options in such patients should be considered on an individual basis.

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.

Treatment Algorithm¹



¹ NOGG 2017: Clinical guideline for the prevention and treatment of osteoporosis. Updated July 2019

References

- Bisphosphonate treatment break. NHS PrescQIPP, Bulletin 110; December 2015
- Biphosphonates - is a holiday necessary? QIPP Detail Aid Support Document. UKMi. June 2013
- Clinical guideline for the prevention and treatment of osteoporosis. NOGG 2017. Updated July 2019. Available online at: <https://www.sheffield.ac.uk/NOGG/NOGG%20Guideline%202017%20July%202019%20Final%20Update%20290719.pdf>
- Biphosphonates – Length of treatment in osteoporosis in primary care – Treatment holiday, Isle of Wight Clinical Commissioning Group. 2017.
- Osteoporosis: assessing the risk of fragility fracture Clinical guideline [CG146] Published: 08 August 2012 Last updated: 07 February 2017. Available online at: <https://www.nice.org.uk/guidance/cg146/chapter/1-Guidance>

This guideline was ratified at the Barnsley Area Prescribing Committee on 9th February 2022.