

**DERBYSHIRE JOINT AREA PRESCRIBING COMMITTEE  
(JAPC)**

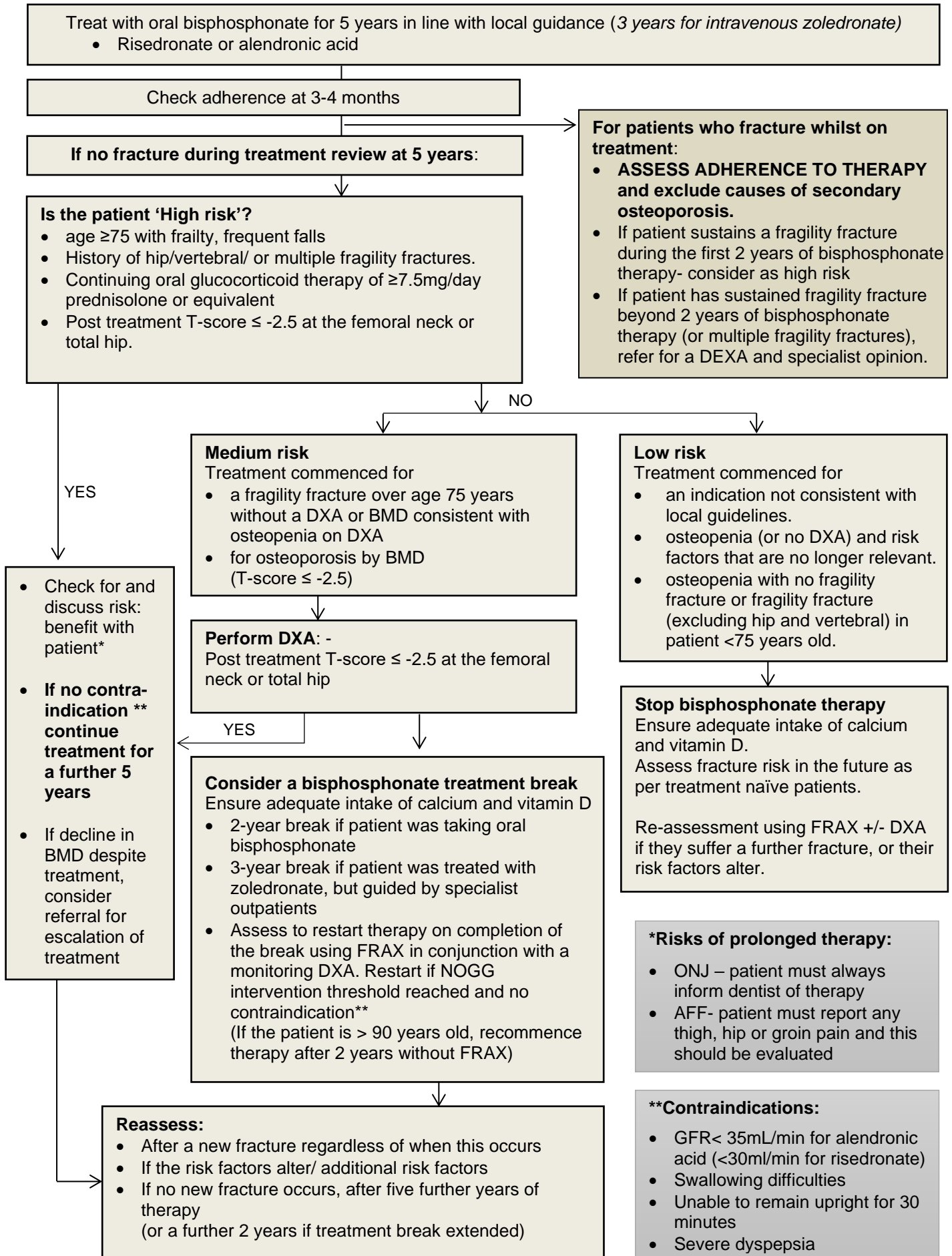
## **Bisphosphonate length of treatment in osteoporosis: Guidance on treatment break**

- The guidance incorporates advice from the National Osteoporosis Guideline Group (NOGG) Clinical Guideline (last updated 2021).
- The guidance recommends **evaluating the continued need for a bisphosphonate at 5 years** (3 years for IV zoledronate), based on an individual's assessment of risk of fracture, but also the balance of risk benefit of continued bisphosphonate treatment.

Patients with risk factors below are deemed at **high risk** of osteoporotic fracture and should **continue** therapy with a bisphosphonate for a further 5 years if no contraindications or intolerance.

- Patient's age  $\geq 75$  in the context of frailty or frequent falls.
  - History of hip/vertebral fracture or multiple other fragility fractures.
  - Continuing oral glucocorticoid therapy of  $\geq 7.5$ mg/day prednisolone or equivalent.
  - Those who sustain low-trauma fracture(s) during treatment: exclude poor adherence to treatment and causes of secondary osteoporosis. Refer for specialist opinion if new fracture sustained after 2 years of bisphosphonate).
  - Post treatment T-score  $\leq -2.5$  at the femoral neck or total hip.
- Patients at medium risk require assessment of BMD with DXA for consideration of a treatment break of 2 years from oral bisphosphonates. If post treatment T-score  $\leq -2.5$  continue for further 5 years if no contraindications or intolerance. These include patients: -
    - Treatment commenced for a fragility fracture (other than hip or vertebral) over age 75 years without a DXA; or BMD consistent with osteopenia on DXA.
    - Treatment commenced for osteoporosis by BMD (T-score  $\leq -2.5$ ).
  - Patients at low risk can stop treatment on completion of 5 years (3 years for IV zoledronate). They would only require re-assessment using [FRAX](#) and DXA if they suffer a further fracture, or their risk factors alter. These include patients commenced on bisphosphonate treatment
    - For an indication not consistent with local guidelines.
    - For osteopenia (or no DXA) and risk factors that are no longer relevant.
    - For osteopenia with no fragility fracture or fragility fracture (excluding hip and vertebral) in patient  $< 75$  years old.
  - Ensure adequate intake of calcium and vitamin D in all patients including those who discontinue bisphosphonates
  - The situation with patients after a very long duration of treatment (e.g.,  $> 10$  years) is less clear. It may still be appropriate for 'high risk' patients to continue without a treatment break, but the definition of high risk for these purposes should probably be more limited. The situation should be judged on a case by case basis with specialist advice/ support, and the current uncertainties of risk versus benefit discussed with patients where appropriate. Local opinion suggests that the majority of patients deemed 'high risk' after 10 years of treatment would benefit from a treatment break of 2 years. The specialist may also recommend that a shortened treatment break of 1-year may be more appropriate in some patients, depending on their individual circumstances.

# Bisphosphonate Treatment algorithm



## **Rationale**

There is good evidence to show that bisphosphonates, such as alendronate, risedronate and zoledronate, reduce the risk of non-vertebral and vertebral fractures in women with osteoporosis. However, there is uncertainty about the optimal duration of therapy, as well as documented rare but serious adverse effects such as [osteonecrosis of the jaw](#) and [external auditory canal](#) and [atypical femoral fractures](#), that increase in risk the longer normal bone remodelling is suppressed.

Decisions to stop or continue bisphosphonate treatment after 5 years (3 years for zoledronate) should be based on individual assessment of risks and benefits, following an informed discussion between the clinician and the individual patient.

## **Recommendations following assessment at 5 years**

Patients at continued high risk of an osteoporotic fracture should continue therapy with a bisphosphonate for a further 5 years, after checking for contra-indications or intolerance, up to which there is clinical trial data of efficacy. However, if post-treatment DXA shows significant BMD loss despite adherence to treatment, refer to specialist outpatients to consider escalation of treatment.

Patients considered medium risk require assessment of BMD for consideration of a treatment break of 2 years or to reclassify as high risk (post treatment T-score  $\leq -2.5$  at the femoral neck or total hip). Practitioners should be aware that fracture risk calculators such as FRAX or Qfracture are only validated in treatment naïve patients, and the use to reassess treated patients should be undertaken with caution.

Low risk patients can stop bisphosphonate treatment without a repeat DXA. Their fracture risk should then be assessed in the future as per treatment naïve patients.

## **Treatment break**

A treatment break should be viewed as a temporary, not permanent, suspension of active therapy. It should be remembered that discontinuing a bisphosphonate can safely be performed due to the persistence of the antiresorptive and anti-fracture effect expected for an undefined period of time (Approximately 1-2 years with risedronate, 2-3 years with alendronate and 2-3 years or more with zoledronate.)

The specialist may decide on a shortened treatment break of 1 year depending on individual patient risk factors.

For patients on a treatment break from oral bisphosphonates, recommencing therapy should be assessed after 2 years, or sooner if additional risk factors become relevant or a new fragility fracture occurs.

- If fracture risk by DXA and a screening tool (FRAX) reaches the NOGG intervention threshold, then restart therapy after checking for contraindications, and discussing with the patient that the risk of side-effects has been reduced by the treatment break.
- If it does not reach threshold, reassess in a further 2 years.
- If the patient is greater than 90 years old within the “Medium Risk” cohort recommence therapy after 2 years without reassessment of fracture risk (FRAX under-estimates fracture risk in the elderly due to confounding mortality statistics).

The treatment break for patients on zoledronate will be managed by specialist outpatients often with monitoring of bone turnover markers to determine duration (approximately 3 years).

## **Other Recommendations**

It is important to ensure patients have adequate levels of dietary calcium and vitamin D during treatment break or on discontinuation of treatment. See [osteoporosis guidance](#) for recommendation on supplementation.

If treatment is discontinued fracture risk should be reassessed:

- After a new fracture regardless of when this occurs.
- If the patient is found to have additional risk factors for fracture.
- If no new fracture or risk factors occur, after five years (or 2 years in the context of a treatment break).

Patients taking long term bisphosphonates should be advised to report any thigh, hip or groin pain which may be indicative of an atypical femoral fracture. Discontinuation of bisphosphonate therapy in patients suspected to have an atypical femur fracture should be considered while they are evaluated. Patients who develop atypical femur fractures whilst on treatment for osteoporosis will inevitably require a review of treatment from the osteoporosis team.

## References

1. NOGG Clinical Guideline March 2017, updated July 2019
2. QIPP detail aid. Bisphosphonates – is a holiday necessary? July 2013
3. MHRA Drug Safety Update June 2011, Vol 4, issue 11.
4. MHRA Drug Safety Update Nov 2009, Vol 3, issue 4.
5. MHRA Drug Safety Update Dec 2015 Vol 9, issue 5
6. McClang M, Harris S et al. bisphosphonate therapy for osteoporosis: benefits, risks, and drug holiday. *Am J Med* (2013), 126, 13-20
7. Fracture Reduction in South Central policy group, Anti-osteoporosis Medication duration of therapy Review 2016  
<https://www.ndorms.ox.ac.uk/files/clinical-trials/secondary-fracture-prevention-management-guidelines.pdf>
8. Royal Osteoporosis Society Duration of Osteoporosis Treatment June 2018  
<https://theros.org.uk/media/100519/duration-of-osteoporosis-treatment-flowchart.pdf>
9. East Kent Prescribing Group Bisphosphonate Drug Holiday Guidelines for Primary care (2018)
10. Black DM, Geiger EJ, Eastell R, et al. Atypical Femur Fracture Risk versus Fragility Fracture Prevention with Bisphosphonates. *N Engl J Med*. 2020;383(8):743-753
11. Schilcher J, Koeppen V, Aspenberg P, Michaëlsson K. Risk of atypical femoral fracture during and after bisphosphonate use. *Acta Orthop*. 2015;86(1):100-107

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Weekly risedronate and alendronic acid both preferred oral bisphosphonate options	May 2023