N.B. This guideline does not apply to patients age 75 or above with a hip fracture. There is separate guidance for secondary fracture prevention after hip fracture for women 75 years or over available on StaffNet (here).

A guideline is intended to assist healthcare professionals in the choice of disease-specific treatments.

Clinical judgement should be exercised on the applicability of any guideline, influenced by individual patient characteristics. Clinicians should be mindful of the potential for harmful polypharmacy and increased susceptibility to adverse drug reactions in patients with multiple morbidities or frailty.

If, after discussion with the patient or carer, there are good reasons for not following a guideline, it is good practice to record these and communicate them to others involved in the care of the patient.

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<th><strong>Version Number:</strong></th>
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**Important Note:**

The Intranet version of this document is the only version that is maintained. Any printed copies should therefore be viewed as ‘Uncontrolled’ and as such, may not necessarily contain the latest updates and amendments.
BISPHOSPHONATE TREATMENT:
GUIDANCE FOR REVIEW OF PATIENTS TREATED
WITH LONGER-TERM ORAL BISPHOSPHONATES
FOR OSTEOPOROSIS

Background

Oral bisphosphonates are the commonest therapy for patients with osteoporosis. Although these drugs have a short half-life in the blood, they are retained in bone for many years. As bone remodels, bisphosphonate can be released back into the blood and become active again. Thus, even when bisphosphonate therapy is stopped, this drug can remain in bone for many years. Once bisphosphonate therapy is stopped the concentration of the drug at sites of bone remodelling is however low and little further anti-resorptive effect is seen.

Most clinical trials of bisphosphonates have lasted for 3 years as this is the requirement for drug registration purposes. Some of these trials have been extended but, in these extensions, randomisation is often lost and numbers of patients treated falls. Long-term safety/benefit issues are therefore difficult to assess in these trial extensions.

In recent years, adverse effects have been described in association with the use of long-term bisphosphonate therapies. These adverse effects are extremely rare and include osteonecrosis of the jaw and atypical (usually femoral shaft) fractures. As noted above these adverse effects have been associated; a causal link has not been proven. Nevertheless, for each patient, this potential for harm must be considered. As with all therapies, the benefit of treatment must be balanced against the possibility of harm. In this situation the proven benefit of treatment is decrease in fracture risk. This benefit needs to be balanced against the risk of potential harms which are generally rare.

The purpose of this guidance is to give some direction regarding the continuation of oral bisphosphonate therapy in the longer term.

Using the Guidance

This guidance is intended to support practitioners in prescribing long term bisphosphonate therapy (>5 years) in the context of osteoporosis. This guideline does not apply to patients age 75 or above with a hip fracture. There is separate guidance for secondary fracture prevention after hip fracture for women 75 years or over available on StaffNet (here).

To use this guidance the user must make an assessment of fracture risk. The greater the fracture risk, the greater will be the benefit of bisphosphonate treatment. Other than at initial referral by primary care practitioner, fracture risk assessment is the responsibility of the Direct Access DXA Service (DADS).
This assessment will largely be based upon clinical judgement. Factors to take into account should include patient age, gender, fracture history and bone mineral density (BMD). Longitudinal trends in BMD change might also be important. Conventional risk calculators (such as WHO-FRAX or QFracture) should be used with caution to assess fracture risk in patients who have been on longer-term bisphosphonate therapy as these tools have not been designed for this situation. Biological age may be more relevant than the chronological to making these decisions.

Bisphosphonate therapy has been shown in clinical trials to reduce fracture risk over a three year period. When a bisphosphonate is stopped after at least two years of treatment it is probable that some residual effects remains on BMD and also fracture risk.

Where a patient is thought to have limited life expectancy, consideration should be given as to whether continuing bisphosphonate therapy is of significant clinical benefit.

This guidance is written in such a way that it should be applicable to patients who are of differing ages and have had differing durations of bisphosphonate treatment. In order to determine next steps; first look for the “grey box” with the patient characteristics that most appropriately match the patient for whom you are looking for guidance.

Where boxes are coloured “red”; this indicates a primary care responsibility to refer (generally to the Direct Access DXA Service – DADS). Where boxes are coloured “green” this indicates a responsibility of the DADS team to make an appropriate recommendation.

Please be aware that there are very limited data regarding efficacy for bisphosphonate patients in the very elderly. Depending on where patients start on treatment; assuming a maximum of 10 years therapy is taken the patient will be over 85 years of age. Generally bisphosphonate treatment should not be continued further in this group. The exception to this may be patients who start on therapy for the first time over the age of 80 where treatment could be potentially continued out to age 90 – assuming this is appropriate in the context of other potential co-morbidities.
**Bisphosphonate Treatment – Guidance for review of patients treated with longer term oral bisphosphonate for osteoporosis**

- **Decision made to start patient on oral bisphosphonate**
  - **Age 80 or above**
    - Start bisphosphonate and continue for a maximum of 10 years.
    - Review with DXA at 5 years. GP refer to DADS.
  - **All patients will be < 85 and will have had 5 years of bisphosphonate**
    - **DADs - High risk of fracture**
      - Age < 80: Continue treatment for further 5 years and review with DXA at 5 years. GP refer to DADS.
      - All patients will be < 85 and will have had 10 years of bisphosphonate.
    - **DADs - Low risk of fracture**
      - Age < 80: Refer to Mineral Metabolism clinic.
      - Age 80 or above: Stop treatment for 2 years then restart for further 2 years only unless limited life expectancy.
  - **DADS team to restart bisphosphonate for 2 years then discontinue without further review.**
  - **DADS - High risk of fracture**
    - Age < 80: DADS team to refer to Mineral Metabolism clinic.
    - Age 80 or above: DADS team to restart bisphosphonate for 2 years then discontinue without further review.
  - **DADS - Low risk of fracture**
    - Age < 80: Repeat DXA scan in 2 years. GP refer to DADS.
    - Age 80 or above: No further review.
  - **All patients will be < 85 and will have had 10 years of bisphosphonate followed by a 2 year gap**
    - **DADs to recommend further 5 years of bisphosphonate then GP to re-refer to DADS for DXA.**
  - **DADs - High risk of fracture**
    - Age < 80: DADS team to refer to Mineral Metabolism clinic.
    - Age 80 or above: DADS to recommend stopping treatment and GP to re-refer to DADS in 2 years regardless of age of patient.
  - **DADs - Low risk of fracture**
    - Age < 80: Discontinue treatment.
    - Age 80 or above: DADS to recommend further 5 years of bisphosphonate then GP to re-refer to DADS for DXA.

**N.B.** This protocol does not apply to patients age 75 or above with a hip fracture. There is separate guidance for these patients. (here)