

## **Bisphosphonate Drug Holiday Guidelines for Primary care**

### **Introduction**

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, Risedronate or Ibandronic acid.

The effects of other anti-resorptive treatments (Denosumab) wear off more rapidly when treatment is stopped and there is no clear case for drug holidays in patients receiving these drugs. However, management of patients receiving Denosumab is not covered in this guideline.

### **Recommendations**

**1. Check treatment adherence after 3 months of initiating treatment.**

**2. Assessment:**

Re-assess patients on oral bisphosphonates every 5 years.

Review indication for all patients prescribed bisphosphonates. Historically some patients will have been incorrectly initiated on treatment.

Consider a treatment break (drug holiday) for patients who have been on oral bisphosphonates for 5 years (patients should continue calcium & vitamin D supplementation).

DEXA should only be used to re-evaluate risk where it has been previously used prior to, or during treatment.

GP's should consider that FRAX or Qfracture may only be useful for patients who are treatment naïve. **The use of FRAX or Qfracture for treated patients should be undertaken with caution.**

## **Re-assessment:**

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.

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.

## **Notes**

- A 3 year drug holiday has been recommended locally as it is the minimum interval for DEXA scanning in East Kent.
- There is currently no evidence of the ongoing benefit of treatment beyond 10 years; therefore this is currently the maximum recommended treatment duration.

## **Follow up after drug holiday**

If a drug holiday is deemed necessary for the patient please read code patient **8B31D “Bisphosphonate prophylaxis suspended”**. Further notes should be added with the duration of treatment holiday. Periodically (every 6 months to a year) a search should be run on the clinical system for this read code and associated text. If the patient is due review after treatment holiday repeat DEXA if treatment with bisphosphonates is indicated again.

## **Disclaimer**

This guidance **does not** apply to patients on aromatase inhibitors or with Paget's disease. Not all patients will fit the scenarios set out below. **As part of de-prescribing guidance all patient factors should be considered before stopping or changing any therapy and patient view must be considered.**

## **References**

Bisphosphonate treatment break. NHS PrescQIPP, Bulletin 110; December 2015

National Osteoporosis Guideline Group. Clinical Guideline for the prevention and treatment of osteoporosis 2017

## Bisphosphonate holiday guidelines algorithm in primary care

**NOT ALL PATIENTS WILL FIT THESE SCENARIOS, SEEK SPECIALIST ADVICE FOR FURTHER GUIDANCE IF FURTHER GUIDANCE IS REQUIRED**

**Patient has been taking oral bisphosphonates for 5 years or more**  
During this time patient has been compliant with treatment, check that bisphosphonate is being taken correctly

**Fracture whilst on treatment?**

YES

- If patient sustained a fragility fracture during the first 2 years of bisphosphonate therapy, **Continue the same treatment as per high risk below**
- If patient has sustained fragility fracture beyond 2 years of bisphosphonate therapy (or multiple fragility fractures), **Refer to secondary care for a treatment review**

NO

Risk assess using DEXA (if this was previously undertaken)  
If DEXA had not previously been undertaken consider assessing without.  
**Consider bisphosphonate holiday as per risk below**

**Consider continuation- check "risk: benefit box as well"**

- Patient over 75
- Previous hip fracture
- Current oral glucocorticoid therapy > 7.5mg/day prednisolone

**Low risk**

- No record of DEXA consider reason for starting and review if still indicated
- Treatment was not indicated in the first place as per local guidance e.g. DEXA did not indicate Osteoporosis
- No history of previous fragility fractures

**Medium risk**  
Treatment was initially indicated eg fragility fracture after age 75 or previous osteoporotic DEXA

**High risk:**

- History of hip/vertebral/or multiple fragility fractures after 2 years of treatment
- Post treatment T score BMD  $\leq -2.5$
- Continuing oral glucocorticoid therapy prednisolone equivalent  $\geq 7.5$ mg daily

**For all patients consider risk vs benefit and consider stopping and referral to falls and osteoporosis clinic if any of following apply**

GFR < 35mL/min.  
Intolerance (risedronate maybe better in mild dyspepsia)  
Bisphosphonate now contraindicated  
Low risk of falls, e.g. immobile, very good mobility  
Patient can no longer sit upright to take the bisphosphonate  
Swallowing difficulties developed  
Poor adherence despite counselling  
Limited life expectancy

**Stop treatment**  
Discontinue and do not restart unless/until the patient meets treatment guidelines eg fracture whilst **NOT** on treatment

**Patient's started on bisphosphonates aged over 75 following fracture (NO DEXA)**

- No history of hip/vertebral/ multiple fragility fractures

**whilst on treatment**

- No oral corticosteroids (prednisolone equivalent  $\geq 7.5$ mg daily)

- Post treatment T score BMD > -2.5
- Stable or improved BMD
- No history of hip/vertebral/ multiple fragility fractures whilst on treatment

**Offer a 'drug holiday' for 3 years**

**Continue to treat** for 10 years, after which then offer a 'drug holiday' of 3 years. Unless previously advised by secondary care.

**Following drug holiday repeat DEXA**