Bisphosphonate length of treatment guideline in osteoporosis (Treatment holiday)

- The guidance incorporates advice from the National Osteoporosis Guideline Group (NOGG) Executive Summary January 2016.

- The guidance recommends evaluating the continued need for a bisphosphonate at 5 years, based on an individual's assessment of risks and benefits. (3 years for IV zoledronate)
  - Patients at high risk of osteoporotic fracture should continue therapy with a bisphosphonate
  - Low risk patients require assessment using FRAX and BMD scan after 5 years to assess appropriateness of continued therapy with a bisphosphonate. The FRAX tool can be found here

- Examples of high risk patients are:
  - Post treatment T-score ≤ -2.5 with history of fragility fractures.
  - History of hip/vertebral/ or multiple fragility fractures (secondary prevention).
  - Continuing oral glucocorticoid therapy of ≥7.5mg/day prednisolone or equivalent
  - Continuing high risk patients (frailty, frequent falls, age ≥75)
  - Those who sustain low-trauma fracture(s) during treatment (exclude poor adherence to treatment and causes of secondary osteoporosis)

- 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 Drug Holiday, 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 and the current uncertainties of risk versus benefit discussed with patients where appropriate. Local opinion suggest that the majority of patients deemed ‘high risk’ after 10 years of treatment would benefit from a Drug Holiday
Treatment algorithm

- Treat with oral bisphosphonate for 5 years in line with local guidance (3 years for intravenous zoledronate)
- 1st line: alendronate
- Alternative option risedronate if alendronate is not tolerated or contra-indicated

Check adherence

If no fracture on treatment:

Is the patient ‘High risk’?
- Post treatment T-score ≤ -2.5 with history of fragility fractures.
- History of hip/vertebral/ or multiple fragility fractures.
- Continuing oral glucocorticoid therapy of ≥7.5mg/day prednisolone or equivalent
- Continuing high risk patients (frailty, frequent falls, age ≥75)

Consider DEXA & FRAX

- Assessed as high risk using FRAX
- Continue treatment for a further 5 years.

Consider a bisphosphonate holiday (Ensure adequate intake of calcium and vitamin D, see osteoporosis guidance for recommendation on supplementation) 2-3 years ‘holiday’ if patient was taking alendronate
- 1 year ‘holiday’ if patient was taking risedronate
- 3 years ‘holiday’ if patient was taking zoledronate

Low risk
- Post treatment BMD > -2.5
- No history of hip/vertebral/ multiple fragility fractures
- No fracture during treatment
- Age<75
- Stable or improved BMD

Assessed as high risk using FRAX

Reassess:
- After a new fracture regardless of when this occurs
- If no new fracture occurs, after two years

For patients who fracture whilst on treatment:
- If patient sustains a fragility fracture during the first 2 years of bisphosphonate therapy, continue the same treatment.
- If patient has sustained fragility fracture beyond 2 years of bisphosphonate therapy (or multiple fragility fractures), refer for a DEXA.

ASSESS ADHERENCE TO THERAPY IN ALL CASES and exclude causes of secondary osteoporosis.
Recommendations

- There is good evidence to show that bisphosphonates, such as alendronate and risedronate, 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 recent reports of rare but serious adverse effects such as osteonecrosis of the jaw and external auditory canal and atypical femoral fractures.

- 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 with the clinician and the individual patient.

- Patients at continued high risk of an osteoporotic fracture should continue therapy with a bisphosphonate. Examples of high risk patients are:
  - Post treatment T-score ≤ -2.5 with history of fragility fractures.
  - History of hip/vertebral/ or multiple fragility fractures (secondary prevention).
  - Continuing oral glucocorticoid therapy of ≥7.5mg/day prednisolone or equivalent.
  - Continuing high risk patients (frailty, frequent falls, age ≥75).
  - Those who sustain low-trauma fracture(s) during treatment (exclude poor adherence to treatment and causes of secondary osteoporosis).

- Other patients require assessment using FRAX programme and BMD scan after 5 years to decide on appropriateness of on-going treatment:
  - If a total hip or femoral neck BMD T-score is < -2.5 or the patient is above the NOGG intervention threshold after 5 years then treatment should be continued.
  - If the total hip or femoral neck BMD T-score is > -2.5 and the patient is below the NOGG intervention threshold after 5 years then treatment withdrawal should be considered (‘Drug Holiday’).

- A drug holiday should be viewed as a temporary, not permanent, suspension of active therapy. It should be remembered that discontinuing a bisphosphonate may not necessarily be a holiday from treatment, because persistence of the antiresorptive effect is expected for an undefined period of time.

- It is important to ensure patients have adequate levels of dietary calcium and vitamin D during treatment break. 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 no new fracture occurs, after two years.

- FRAX is a useful screening tool to identify appropriate patients that are at risk of primary osteoporosis and patients on drug holidays should be assessed regularly. Consider restarting therapy after 1-3 years. FRAX tool can be found here.

- 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 Drug Holiday, 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 and the current uncertainties of risk versus benefit discussed with patients where appropriate. Local opinion suggest that the majority of patients deemed ‘high risk’ after 10 years of treatment would benefit from a Drug Holiday.

- Patients taking long term bisphosphonates should be advised to report any thigh, hip or groin pain which may be indicative of an atypical femoral femur. 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 Executive Summary Updated January 2016
2. Derbyshire preferred choice formulary
3. QIPP detail aid. Bisphosphonates – is a holiday necessary? July 2013
4. Royal National Hospital Rheumatic Disease Bisphosphonate length of treatment guidelines (2013) 
7. MHRA Drug Safety Update Dec 2015 Vol 9, issue 5

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