OSTEOPOROSIS ASSESSMENT AND TREATMENT GUIDANCE

Introduction

The World Health Organization (WHO) describes osteoporosis as a “progressive systemic skeletal disease characterised by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture”. The hip, wrist and spine are the most common areas for fractures.

Osteoporosis is defined by WHO as a bone mineral density (BMD) of 2.5 standard deviations below the mean peak mass (average of young healthy adults) as measured by dual-energy X-ray absorptiometry (DXA). (Reported as a T- Score value)

Bisphosphonates are the most widely prescribed class of agent for the treatment of osteoporosis. There are some rare adverse events that have been attributed to bisphosphonate use, most notably osteonecrosis of the jaw and atypical femoral fractures. When bisphosphonates are prescribed for patients at high risk of future fragility fractures, the antifracture benefits gained from bisphosphonates far outweigh their potential risk.

Diagnosis

The diagnosis of osteoporosis relies on the assessment of BMD by a DXA scan. BMD at the femoral neck provides the reference site.

DXA scans do not allow differentiating between osteoporosis and osteomalacia. Patients should therefore be vitamin D replete prior to scan except fracture patients which should be referred urgently.

The use of BMD has a high specificity but low sensitivity. This means that most osteoporotic fractures will occur in women who do not have osteoporosis as defined by a T-score of less than -2.5. Therefore clinical risk factors and/or BMD can be considered for treatment. (see below)

Assessment tool

Patients with clinical risk factors should be considered for fracture risk assessment using the FRAX® tool (accepts ages between 40-90 years). In the absence of BMD, patients are categorised into three risks as either low, intermediate or high fracture risk based on a 10 year probability of major osteoporotic fracture (%).

- Low risk (green zone on chart) - offer lifestyle advice and re-assess in 5 years or earlier if indicated
- Intermediate risk (amber zone on chart) - consider DXA to measure BMD and recalculate fracture risk.
- High risk (red zone on chart) - can treat without need for BMD, but BMD is helpful especially in younger postmenopausal women

If age is outside of the FRAX® range then clinical judgment should be used to assess fracture risk or seek specialist advice.

NHS
South West Yorkshire
Area Prescribing Committee

Adult Osteoporosis Treatment Pathway – Advice and Treatment Initiation

Taking or will start oral corticosteroids for ≥ 3 months at a dose of prednisolone 15mg daily or more (or equivalent doses of other glucocorticoids)

Clinical Risk Factors – Consider fracture risk assessment using FRAX® in patients with 1 significant risk factor or 3 other risk factors. Do not routinely test fracture risk in people under the age of 50 or premenopausal women (specialist opinion should be sought)

Significant risk factors:
- History of fragility fracture
- Parental history of osteoporosis
- ≥3 months oral corticosteroid use
- Low BMI (<19kg/m2)

Other risk factors
- Women aged >65 or Men >75
- Smoking
- Alcohol intake >3 units/day
- Rheumatoid arthritis
- Diabetes
- Asthma
- Chronic liver disease
- Moderate to severe CKD
- Neurological diseases
- Primary hyperparathyroidism and endocrine diseases
- IBD, caeliac or malabsorption
- Institutionalised patients with epilepsy
- Medications: antiepileptics, PPIs, thiazolidinediones, long-term SSRI, long term depot progesterone acetate.**For those on GnRH agonists (ADT)** or aromatose inhibitors*** refer to guidance below-page 3**

1st line - alendronic acid 70mg standard tablets.
If gastrointestinal tolerance is a problem then consider risedronate 35mg tablets

Once weekly generic preparations are recommended.

For the role of hormone replacement therapy (HRT)* in osteoporosis-see page 3 below

Avoid risedronate if GFR less than 30 ml/min. Avoid alendronic acid if GFR less than 35 ml/min.

Oral bisphosphonates must only be taken on an empty stomach as their absorption is affected by food, drink, and other drugs
Take tablet at least 60min before the first food or drink, with full glass of water. After taking stay upright for at least 30min

See **BNF bisphosphonate MHRA safety information** (atypical femoral fractures, osteonecrosis of jaw, and osteonecrosis of external auditory canal)

Elderly patients that are housebound or living in residential/ nursing homes are likely to gain benefit from lifelong calcium + vitamin D supplementation

Consider secondary care e-consultation if above treatments are not suitable or tolerated

Calculate 10 year probability of major osteoporotic fracture (%) using FRAX®

High risk | **Intermediate** | **Low risk**

DXA & recalculate FRAX®

High risk | **Low risk**

Offer lifestyle advice and re-assess in 5 yrs. Advise-adequate nutrition with calcium and Vitamin D, regular weight bearing exercise, avoid smoking and excess alcohol

*Hormone Replacement Therapy (HRT) for osteoporosis

There are a large number of formulations of oestrogen or oestrogen plus progestogen combinations, some of which are licensed for HRT. Conjugated equine oestrogens 0.625 mg daily ±2.5 mg/ day of medroxyprogesterone acetate has been shown to reduce vertebral, non-vertebral and hip fractures in postmenopausal women.

The unfavourable risk/benefit balance in older postmenopausal women, suggest that the use of HRT for osteoporosis is generally restricted to younger postmenopausal women who are at high risk of fracture and also have menopausal symptoms.

For early menopause,treatment with HRT is appropriate in this patient group up to the approximate age of natural menopause.

Medications associated with osteoporosis:

**GnRH agonists (Androgen Deprivation Therapy ADT)

The use of GnRH analogues in men is associated with bone loss and fractures.NICE (NG131) Prostate Cancer Diagnosis and Management suggests all men starting on ADT;

- should have their fracture risk assessed
- offer bisphosphonates to men who are having ADT and have osteoporosis diagnosed
- consider denosumab for men who are having ADT and have osteoporosis if bisphosphonates are contraindicated or not tolerated

***Aromatase inhibitors (AI)

Breast cancer treatments such as AI lower oestrogen levels therefore the rate of bone turnover increases causing a significant and very rapid bone density loss.

- In all patients initiated on AI treatment the fracture risk should be assessed.
- Bone-directed therapy should be recommended for the duration of AI treatment to all patients with a T-score <-2.0 SD, or with a T-score of <-1.5 SD with one additional risk factor, or with two or more risk factors (without BMD).

Bisphosphonate treatment length guidelines in osteoporosis

The optimal duration of bisphosphonate treatment for osteoporosis has not been established. Recent data has suggested that the long-term use of bisphosphonate treatment may be associated with increased risk of drug related side effects.

Bisphosphonates bind strongly to bone mineral and inhibit bone turnover, alendronate can potentially remain within the bone with a half-life of upto ten years. Therefore the duration of treatment needs discussion as these drugs can accumulate in bone, reducing bone turnover and ultimately decreasing healing. There is some debate over the ideal duration of therapy, particularly with the emergence of links with the rare but serious complications of osteonecrosis and atypical femoral fractures.

Table 1 – Side effects and risk reduction

Potential side effects	How to reduce risk/advice
Gastrointestinal - oesophageal irritation, dysphagia, abdominal pain and changes in bowel movement	Tablets should be taken with plenty of water and patient should remain upright for 30-60 minutes after dose. Drink extra water if possible.
Nephrotoxicity - can affect kidney function	To avoid renal injury, do not use risedronate if GFR less than 30ml/min, or alendronate if GFR is less than 35ml/min or ibandronate if GFR less than 30ml/min.
Atypical femoral fractures (AFF) - rarely reported with bisphosphonates, mainly in patients on long-term treatment and can occur after minimal or no trauma.	Patients should be advised to report any thigh, hip or groin pain during treatment. Consider urgent X-ray of the femur and X-ray constralateral femur if periosteal changes confirmed. Discontinuation of treatment should be considered after an assessment of the benefits and risks of continued treatment.
Osteonecrosis of the jaw (ONJ) - this is a rare complication and the incidence is much greater with the Intravenous route, long term usage, smokers and long term use of prednisolone. Symptoms include delayed healing following a dental extraction or other oral surgery, pain, soft tissue infection and swelling.	Recommend a dental check before commencing treatment, or as soon as possible after starting. Advise all patients to maintain good oral hygiene and report any oral symptoms such as pain, swelling, non-healing sores to doctor or dentist. Also encourage smoking cessation.
Osteonecrosis of external auditory canal - very rarely reported with bisphosphonate treatment and mainly in patients on long-term treatment (2 years or longer)	Advise patients to report any ear pain, ear discharge and ear infections during treatment.

Advice for prescribers

- Review indication and adherence for all bisphosphonate medication
- Re-assess patients at high risk of osteoporotic fracture at regular intervals and at least every five years
- Consider secondary care E-consultation if taking for 5 years or more
- Consider treatment break for those on an oral bisphosphonate for 5 years if at moderate risk of osteoporotic fracture
- Review the continued need for bisphosphonates after:
  - 3 years for patients with multimorbidity* on oral or IV bisphosphonates
  - 3 years for zoledronic acid
  - 5 years for alendronic acid, risedronate and ibandronic acid for patients without multimorbidity* (*2 or more long-term conditions)
- Consider deprescribing for patients that are at low risk
- When stopping a bisphosphonate note they can be stopped immediately
- Ensure adequate intake of calcium and vitamin D in all patients including those who discontinue bisphosphonates

- During a treatment break the anti- fracture effect of the bisphosphonate will persist due to the long half-life of bisphosphonates

Continuation of treatment beyond 3-5 years without a treatment break up to 10 years is recommended in high risk pts:

- Age > 75ys
- Previous vertebral or hip fracture
- Low trauma fracture whilst on treatment (if poor adherence and causes of secondary osteoporosis have been excluded)
- Taking >7.5mg/day oral prednisolone or equivalent corticosteroid

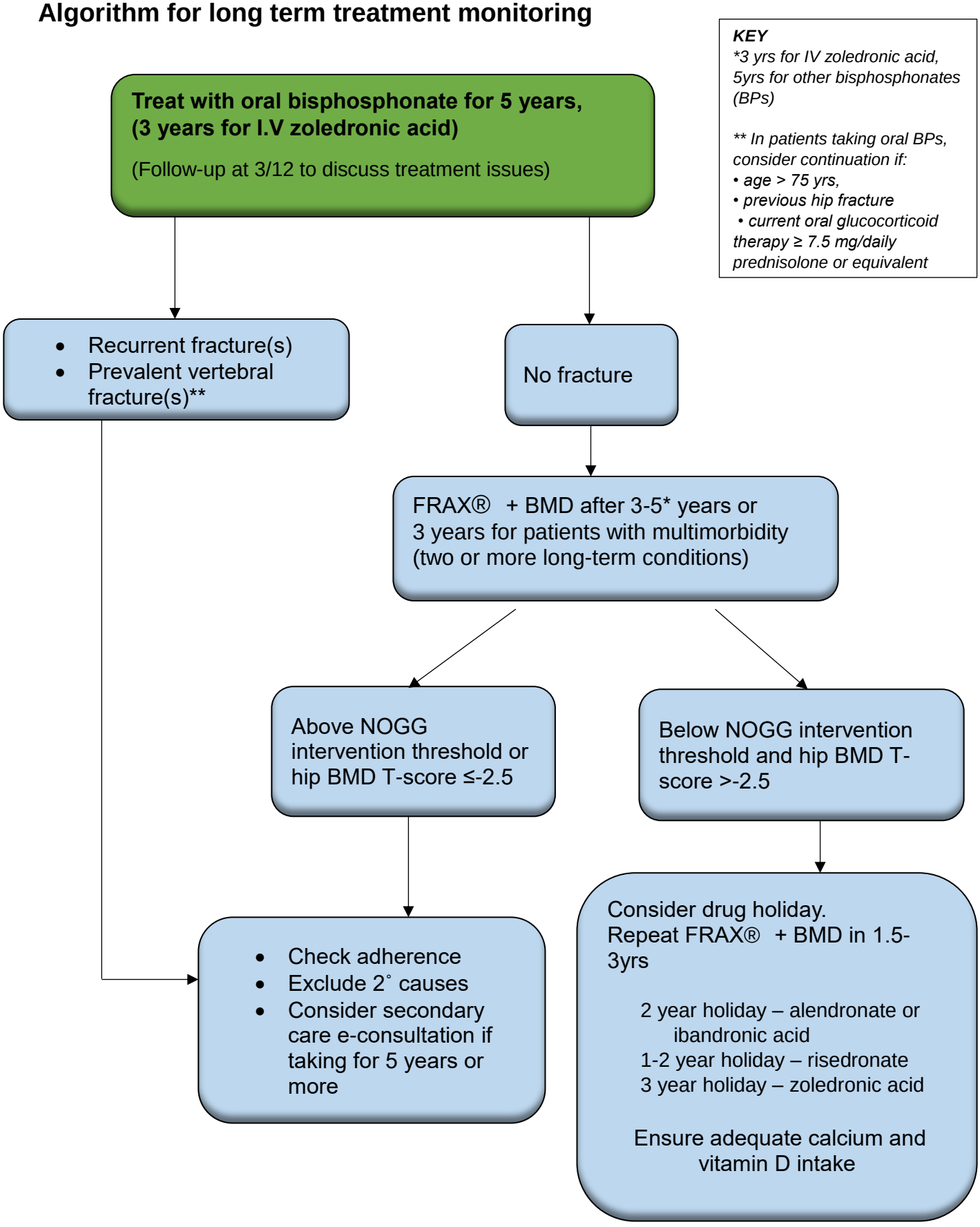
For other patients, re-assess fracture risk using FRAX® and DXA scan for bone mineral density (BMD)

- If FRAX® score above national osteoporosis guideline group (NOGG) intervention threshold or hip BMD T-score is ≤-2.5, treatment should be continued.
- Otherwise, consider treatment break and repeat FRAX® + BMD in 1.5 – 3yrs time.

NOTE: There is no evidence base to guide the decision about treatment beyond 10 years and these patients should be reviewed by rheumatology.

A drug holiday should be seen as a temporary, not permanent, suspension of drug therapy.The effects of other anti-resorptive treatments (denosumab, raloxifene, teriparatide) wear off much quicker when treatment is ceased and there is no strong evidence to date for drug holidays in patients receiving these drugs. A drug holiday should not be considered in patients with denosumab without consultation with a secondary care specialist as a follow-on treatment such as zoledronic acid may be required.

Algorithm for long term treatment monitoring



Flow chart adaped from NOGG guidelines 2017-bisphosphonates:algorithm for long term treatment monitoring

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