Appendix 6A - Guidance on Diagnosis and Management of Osteoporosis

Pathway from Fracture or Risk Factor to Treatment

Fragility Fracture = fracture sustained from a low energy fall from standing height or less

Risk Factors:
- Non-modifiable: age over 65 years, female, Caucasian, previous fracture, family history, early menopause
- Modifiable: alcohol > 2 drinks daily, smoking, BMI <20,
- Comorbidities: Rheumatoid Arthritis, Chronic liver disease, malabsorption, Diabetes, Coeliac Disease, Cystic Fibrosis, hyperparathyroidism, Alzheimer’s Disease, Parkinson’s Disease, Multiple Sclerosis, chronic renal disease
- Medications: long-term anti-depressants, anticonvulsants, aromatase inhibitors, long-term depot medroxyprogesterone acetate, proton pump inhibitors, high dose inhaled corticosteroids, oral corticosteroids, pioglitazone.

![Diagram of the pathway from fracture or risk factor to treatment](image-url)
Standard Investigations

Should be performed prior to treatment to exclude underlying conditions e.g. renal impairment, hyperparathyroidism

Thyroid stimulating hormone (TSH), Bone profile, Liver Function Tests (LFTs), Full Blood Count (FBC), Plasma viscosity (PV), serum vitamin D3

Additional investigations where indicated: Testosterone (in men), Luteinising hormone (LH)/ Follicle stimulating hormone (FSH) in women (if menopausal status uncertain)

Options for Treatment of Osteoporosis

In osteoporosis, fractures occur due to a combination of factors, only one of which is low bone density. In treating osteoporosis and fracture risk, pharmacological therapy should form part of a programme of care designed to reduce falls and improve general health in those at risk of fracture.

Choice of therapy is determined by age and sex of patient and other medical conditions.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Therapy options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary prevention of postmenopausal osteoporotic fracture where fracture risk &gt;20% (FRAX score)</td>
<td>1&lt;sup&gt;st&lt;/sup&gt; line Weekly Bisphosphonate* + Calcium with Vitamin D&lt;sub&gt;3&lt;/sub&gt;/Vitamin D&lt;sub&gt;3&lt;/sub&gt;</td>
</tr>
<tr>
<td>2&lt;sup&gt;nd&lt;/sup&gt; line Denosumab** + Calcium with Vitamin D&lt;sub&gt;3&lt;/sub&gt;/Vitamin D&lt;sub&gt;3&lt;/sub&gt; or IV Zoledronate (choice based on likely compliance)</td>
<td></td>
</tr>
<tr>
<td>Treatment of postmenopausal osteoporotic fracture</td>
<td>Bisphosphonate* + Calcium with Vitamin D&lt;sub&gt;3&lt;/sub&gt;/Vitamin D&lt;sub&gt;3&lt;/sub&gt;</td>
</tr>
<tr>
<td>Treatment of postmenopausal osteoporotic fracture in women over 80 years</td>
<td>Bisphosphonate + Calcium with Vitamin D&lt;sub&gt;3&lt;/sub&gt;/Vitamin D&lt;sub&gt;3&lt;/sub&gt; Or consider referral for parathyroid hormone (PTH)</td>
</tr>
<tr>
<td>Corticosteroid induced osteoporosis</td>
<td>Consider referral for treatment with PTH</td>
</tr>
<tr>
<td>Severe osteoporosis (T score &lt; -4 or -3.5 and other risk factors)</td>
<td></td>
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<tr>
<td>Further fracture despite appropriate drug therapy</td>
<td></td>
</tr>
</tbody>
</table>

*Weekly bisphosphonate alendronate or risedronate  
** Denosumab 60mg/ml (Prolia®) should only be considered when treatment with both alendronate and risedronate is ineffective or inappropriate.
## Prescribing Information on Drugs for Osteoporosis

### Bisphosphonates (BNF 6.6.2)

Calcium & Vitamin D **must be co-prescribed** with all bisphosphonates.

<table>
<thead>
<tr>
<th>Formulary options</th>
<th>Dose</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alendronate 70mg</strong></td>
<td>70mg once weekly in the morning</td>
<td>Swallow whole with a full glass of water on an empty stomach at least 30 minutes before breakfast. Stay upright (can sit) for 30 minutes. If dyspeptic symptoms occur, check patient compliance with dosage instructions and if required, change to risedronate. Avoid if eGFR less than 35ml/min/1.73m$^2$.</td>
</tr>
<tr>
<td><strong>Risedronate 35mg</strong></td>
<td>35mg once weekly in the morning</td>
<td>May be used 1st line in patients with oesophageal disease such as GORD or hiatus hernia. Swallow whole with a full glass of water on an empty stomach at least 30 minutes before breakfast. Stay upright for 30 minutes. Avoid if eGFR less than 30ml/min/1.73m$^2$.</td>
</tr>
<tr>
<td><strong>Intravenous Zoledronic acid</strong></td>
<td>5 mg annually for 3 years then 3 year break from treatment</td>
<td>IV zoledronic acid is used in patients who are unable to tolerate oral medication or comply with complex dosing instructions. It is useful in the very frail elderly who may just require one or two doses. It is given in the Day Intervention Unit in Queen Margaret Hospital or any Acute Ward. Avoid if eGFR less than 35ml/min/1.73m$^2$.</td>
</tr>
</tbody>
</table>

### Non-compliance with bisphosphonates
- If due to initial dyspeptic symptoms check patient compliance with dosage instructions before replacing alendronate with risedronate.
- If non-compliance continues, consider use of denosumab (Prolia®).

### Denosumab (BNF 6.6.1)

<table>
<thead>
<tr>
<th>Formulary options</th>
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</tr>
</thead>
<tbody>
<tr>
<td><strong>Denosumab 60mg/ml (Prolia®)</strong></td>
<td>60mg, 6 monthly by subcutaneous injection</td>
<td>Specialist initiation/recommendation. Hypocacaemia is a contraindication to denosumab administration. Shared Care Protocol available. Must be stored in fridge.</td>
</tr>
</tbody>
</table>

### Indications
- Primary prevention and treatment of postmenopausal osteoporosis in women at increased risk of fractures
- 2nd line option in patients when oral bisphosphonates are ineffective/unsuitable.
Fife Area Drug and Therapeutics Committee

<table>
<thead>
<tr>
<th>Formulary options</th>
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<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strontium ranelate (Protelos®)</td>
<td>2g sachet once daily in water</td>
<td>Restricted to use in severe osteoporosis in patients with a high risk of fracture who cannot be treated with other medicines approved for use in osteoporosis. Specialist initiation only. Contraindicated in patients with established, current or past history of ischaemic heart disease, peripheral arterial disease and/or cerebrovascular disease or those with uncontrolled hypertension. The patients risk of developing cardiovascular disease should be evaluated before starting treatment and then on a regular basis (generally every 6-12 months). Strontium should taken at bedtime, avoiding food for 2 hours before and after taking granules. Calcium + Vitamin D₃ should not be taken at the same time.</td>
</tr>
</tbody>
</table>

Oestrogen based Hormone Replacement Therapy (HRT) (BNF 6.4.1.1)

There is Grade A evidence that HRT reduces hip fractures but this benefit is lost within 5 years of stopping HRT. The adverse effects of HRT outweigh the benefits in most patients. Individual circumstances should be taken into consideration.

HRT and raloxifene should NOT be considered first-line therapy for long-term prevention of osteoporosis in women over 50. They remain an option where other therapies are contra-indicated, cannot be tolerated, or there is lack of response.

Parathyroid hormone preparations (BNF 6.6.1)

<table>
<thead>
<tr>
<th>Formulary options</th>
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<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Teriparatide (Forsteo®)</td>
<td>20 micrograms daily by subcutaneous injection</td>
<td>Recombinant fragment (1-34) of PTH. Maximum duration of treatment 24 months. Must be stored in fridge.</td>
</tr>
</tbody>
</table>

Indications

Treatment of severe postmenopausal osteoporosis and severe osteoporosis in men. For initiation only by specialists experienced in the treatment of osteoporosis. Prevention and treatment of glucocorticoid-induced Osteoporosis.

Comments

Treatment option for the secondary prevention of osteoporotic fragility fractures in women aged ≥65 years who have had an unsatisfactory response to bisphosphonates, intolerance to bisphosphonates and who have an extremely low BMD (T-score -4 SD or below), or very low BMD (T-score -3 or below) plus, at least 2 fractures plus, one or more age-independent risk factors:

- Low body mass index (<19Kg/m²)
- Family history of maternal hip fracture before the age of 75 years
- Untreated premature menopause
- Conditions associated with prolonged immobility.

Evidence suggests that bone density is maintained for at least one year after PTH therapy is stopped. This effect is maximised if patients commence bisphosphonate on stopping.
Calcium with Vitamin D3 (BNF 9.6.4)

<table>
<thead>
<tr>
<th>Formulary options</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adcal-D3® Caplets</td>
<td>2-4 caplets daily</td>
</tr>
<tr>
<td>Adcal D3 Dissolve</td>
<td>1-2 tabs daily</td>
</tr>
<tr>
<td>Adcal Chewable Tablets</td>
<td>1-2 tabs daily</td>
</tr>
</tbody>
</table>

Vitamin D Preparations

Fultium D3® capsules, Desunin® tablets

Comments

Vitamin D₃ deficiency or insufficiency is very common.
If a larger dose of vitamin D₃ is required, replace with Fultium® or Desunin® instead.
Ensure adequate dietary calcium intake or add half dose calcium with vitamin D₃ supplement.
If patient has high dietary intake of calcium (>1000mg daily), vitamin D₃ may only be required (Fultium® or Desunin®).
The most appropriate formulation of Adcal D₃ to aid compliance should be chosen.
Calcium preparations are better taken at night to improve absorption and to avoid interaction with other compounds such as levothyroxine and bisphosphonates.
Patients should be advised to attain adequate calcium with vitamin D₃ status regardless of other treatment recommendations.

Non-compliance with Calcium with Vitamin D₃ Preparations

To reduce non-compliance, calcium with vitamin D₃ supplements should preferably be prescribed as caplets (e.g. Adcal D₃ - 2 caplets twice daily).
Check vitamin D level:
If > 50 nmol/l, replacement may not be required but ensure high calcium diet.
If level 30-50nmol/l, prescribe alternative calcium with vitamin D₃ supplement.
If level <30nmol/l, consider full replacement therapy with either Fultium D₃® or Desunin® (See Appendix 9C).
NHS Fife Guidance on duration of bisphosphonates therapy for Osteoporosis

(adapted from NHS Lothian advice, courtesy of Prof S. Ralston)

**Background**

The optimal duration of oral bisphosphonate therapy is a subject of debate because bisphosphonates bind strongly to bone mineral and exert inhibitory effects on bone turnover for many months after treatment has stopped. This has led to the concern that long term treatment may increase bone fragility by suppressing normal bone remodelling which is essential for repair of skeletal micro-damage. In clinical practice, adverse effects of long term bisphosphonate therapy are rare, but atypical subtrochanteric fractures have been reported to occur in patients on long term Alendronic acid therapy at a rate of about 0.0005% of patients treated per year. Since the typical patient with osteoporosis has a fracture risk of >1% per year, the benefit risk of bisphosphonate treatment is overwhelmingly favourable in most cases.

Long term safety data exists for most bisphosphonates for periods of up to 10 years, but the only comparative data on optimal duration of bisphosphonate therapy comes from the FLEX study in which patients who had received 5 years therapy with oral Alendronic acid and whose BMD values were still in the osteoporotic range (T <-2.5) were randomised to stop treatment and receive placebo for 5 years or to receive a further 5 years Alendronic acid. Total number of fractures and adverse effects in the two treatment groups were similar, but clinical vertebral fractures were significantly fewer in the patient receiving 10 years Alendronic acid therapy. Accordingly this evidence suggests that 10 years treatment may be superior than 5 years treatment in patients with postmenopausal osteoporosis.

No data exists on the optimal duration of treatment with oral bisphosphonates in patients with corticosteroid induced osteoporosis, but it is currently believed that bisphosphonate therapy should be continued on a long-term basis in these patients because of their high fracture risk.

Based on the above evidence we offer the following guidance for duration of oral bisphosphonate therapy in patients with osteoporosis.
Fife Area Drug and Therapeutics Committee

ALGORITHM FOR DURATION OF BISPHOSPHONATE THERAPY FOR OSTEOPOROSIS

**Postmenopausal woman or man on oral bisphosphonate for 5 years**

Clinical review*
Arrange repeat DXA

- **BMD T-score > -2.5 and no further fractures:**
  - Stop treatment.
  - Repeat DXA scan at 5 years

- **BMD T-score < -2.5 and FRAX >20% for any fracture or Further fractures on treatment:**
  - Continue treatment
  - Repeat DXA scan at 5 years

**Postmenopausal woman or man on oral bisphosphonate for 10 years**

Clinical review*
Repeat DXA unless >80 years and frail

- **BMD T-score > -2.5 and no further fractures or FRAX < 20%**
  - Stop treatment.
  - Repeat DXA scan at 5

- **BMD T-score < -2.5 or FRAX 20-30% but no further fractures:**
  - Drug holiday:
  - Risedronate for 1 year
  - Alendronate for 2 years then restart treatment

- **BMD T-score < -3.5 or FRAX >30% or Further fractures or >80 years old and frail:**
  - Continue treatment
  - Consider referral to OP clinic for alternative therapy

Review patients on oral bisphosphonates regularly for concordance with therapy.

*Clinical review comprises assessment of falls, frailty, concordance, fractures, renal function, adverse effects of therapy.
Refer to Osteoporosis Service when required for further advice or alternative therapy.
Patients commenced on treatment without DXA eg >75 years with hip fracture should have DXA at 10 years if mobile and active.
Management of glucocorticoid-induced osteoporosis

Glucocorticoids contribute to the increase in fracture risk over and above the effect of low bone mineral density. Therefore for a given bone mineral density the risk is greater in corticosteroid-induced osteoporosis than in postmenopausal osteoporosis.

General Measures
- Reduce dose of steroid when possible
- Consider steroid-sparing therapy
- Consider alternative route of administration
- Recommend good nutrition especially with adequate calcium and vitamin D
- Recommend regular weight-bearing exercise
- Maintain body weight
- Avoid tobacco use and alcohol abuse
- Assess falls risk and give advice if appropriate

Commitment or exposure to oral glucocorticoids for >3 months

Age <65 years

No previous fragility fracture

Measure BMD (DXA scan hip and spine)

T-score above 0

Reassure
General measures

T-score between 0 and -1.5

Repeat BMD not indicated unless very high dose of glucocorticoids required

T-score -1.5 or lower

Repeat BMD in 1-3 years if glucocorticoids continued

Age >65 years

Previous fragility fracture or incident fracture during glucocorticoid therapy

Investigations

General measures
Advise treatment

Alendronate (L) Risedronate (L) HRT

L = licensed

All patients must have calcium with vitamin D3/vitamin D3 equivalent to 1.2g calcium plus 800iu of vitamin D daily

Hospital use only
IV Zolendronic Acid Parathyroid hormone

Fragility fracture
Defined as a fracture occurring on minimal trauma after the age of 50 years (female) or 60 years (male) and includes forearm, spine, hip, ribs or pelvis.

In patients with previous fragility fracture:
- FBC and PV
- Bone profile and LFTs
- Serum creatinine
- Serum TSH
- Serum 25-OH-D3 (25-hydroxyvitamin D3)

If indicated:
- Lateral thoracic and lumbar spine x-rays
- Serum paraproteins and urinary Bence Jones Protein
- Isotope bone scan
- Serum FSH (if hormonal status unclear)
- Parathyroid hormone (PTH)
- BMD if monitoring required

Consider treatment depending on age and fracture probability.

Adapted from Guidelines for prevention and treatment of glucocorticoid-induced osteoporosis

Author Dr. J. Gibson, Rheumatology Version No.: 2 Date: February 2014
Approved on behalf of NHS Fife by Fife Area Drug & Therapeutics Committee:
Date: February 2014
Review Date: February 2017