Nottinghamshire Osteoporosis Guidelines

Primary Prevention / no previous fragility fracture
For women receiving adjuvant aromatase inhibitors for breast cancer see here
For people with anorexia nervosa see NICE guidance

Age ≥ 50 with 2 or more risk factors

Calculate 10 year probability of fracture using FRAX® tool http://www.shef.ac.uk/FRAX/ (Consider investigation if concerns about Malabsorption or Family history of early onset osteoporosis)

High risk
(or patient unable or unwilling to go for scan)

Intermediate risk
(or have concerns re: Malabsorption / Family History / concordance / need for future monitoring by a DXA scan)

Low risk

Age < 50 with major risk factors (e.g. current or frequent recent use of oral or systemic glucocorticoids, or untreated premature menopause)

Use FRAX® and measure BMD and consider referral if necessary

Above NOGG treatment threshold*
Consider primary prevention (consider referral if T-score below -4.5 or concerns regarding severity of disease)

- Exclude secondary causes - see routine investigations
- Check baseline fasting bone marker, U&Es, Ca²⁺, Vit D
- Replace Ca²⁺ and/or Vit D if required

Calculate Creatinine Clearance (see calculator here)

Creatinine Clearance ≥ 30ml/min

1st line unless contraindicated
Alendronic acid PO 70mg weekly +/− Ca²⁺ and/or Vit D
2nd line if alendronic acid not tolerated or Creatinine Clearance 30-35ml/min
Risedronate PO 35mg weekly +/− Ca²⁺ and/or Vit D

Review at 3 months:
Repeat fasting bone marker + U&Es and review concordance / side-effects, (counsel patient and repeat in 3/12 if poor concordance or inappropriate administration detected)

- Adequate response (> 50% reduction in bone marker and no new fractures) and
- tolerated (renal function stable / no intolerable side-effects)

Continue therapy and review:
- When patient has a fracture OR
- 5 years or earlier as indicated by DXA report, if no fractures.
See bisphosphate treatment review

Creatinine Clearance < 30ml/min

Below NOGG treatment threshold*
Consider Lifestyle advice
Review routinely in 2 - 3 years or if patient presents with new risk factors / fragility fracture

Consider referral to Osteoporosis service (secondary care) or Primary Care Nurse Specialist (where available) :
E.g. if oral bisphosphonates contraindicated, patient unable to take, or inadequate response.

- Inadequate response < 50% reduction in bone marker despite appropriate administration and good concordance
- or new fragility fracture
- or CrCL <30ml/min
- or intolerance

Review at 3 months:
Repeat fasting bone marker + U&Es and review concordance / side-effects, (counsel patient and repeat in 3/12 if poor concordance or inappropriate administration detected)

- Adequate response (> 50% reduction in bone marker and no new fractures) and
- tolerated (renal function stable / no intolerable side-effects)

Continue therapy and review:
- When patient has a fracture OR
- 5 years or earlier as indicated by DXA report, if no fractures.
See bisphosphate treatment review

* National Osteoporosis Guideline Group (NOGG) treatment threshold - See NOGG website
Secondary Prevention / Previous fragility fracture

- **Age ≥ 75 years**
  - Hip fracture
  - FRAX® tool and DXA scan (optional)
  - T-score below -2.5 confirmed by DXA scanning
  - Exclude secondary causes
    - see routine investigations
  - Check baseline bone marker, U&Es, Ca\(^{2+}\), Vit D
  - Replace Ca\(^{2+}\) and/or Vit D if required
  - Calculate Creatinine Clearance (see calculator here)
  - Creatinine Clearance ≥30ml/min

- **Age 50-74 years**
  - Limb or vertebral fracture
  - Severe osteoporosis (T-score below -4.0) or multiple vertebral fractures
  - Or T-score below -3.5 and fracture
  - Hip fracture
  - T-score below -2.5 confirmed by DXA scanning
  - Refer for specialist assessment
  - Severe osteoporosis (T-score below -4.0) or multiple vertebral fractures
  - Or T-score below -3.5 and fracture

- **Age <50 years**
  - Refer for specialist assessment

**Creatinine Clearance < 30ml/min**
- Consider referral to Osteoporosis service (secondary care) or Primary Care Nurse Specialist (where available)
  - E.g. if oral bisphosphonates contraindicated, patient unable to take, or severe osteoporosis

**Creatinine Clearance ≥30ml/min**
- **1st line unless contraindicated**—Alendronic acid 70mg weekly +/− Ca\(^{2+}\) and/or Vit D
- **2nd line if alendronate not tolerated or Creatinine Clearance 30-35ml/min**
  - Risedronate 35mg weekly +/− Ca\(^{2+}\) and/or Vit D

**Repeat fasting bone marker, renal function and concordance / side-effect review at 3/12 (if poor concordance or inappropriate administration detected, counsel patient and recheck again in 3/12)**

- **Adequate response** ( > 50% reduction in bone marker and no new fractures)
- **and tolerated** (renal function stable / no intolerable side-effects)

- **Inadequate response** ( < 50% reduction in bone marker despite appropriate administration and good concordance or new fragility fracture)
  - or CrCL <30ml/min
  - or intolerant of oral bisphosphonates

**Continue therapy**
- Review at 5 years or earlier as indicated by DXA report (see bisphosphate treatment review)

**Consider referral** to Osteoporosis service in secondary care or Primary Care Nurse Specialist (where available)
Bisphosphonate treatment review

**Timing of review:**
- after 5 years treatment with alendronate, risedronate or ibandronate
- Or after 3 years treatment with zoledronic acid
- Or post fracture

**Investigations:**
- DXA scan and FRAX® recalculation
- Repeat U+E's, Ca2+ and Vit D, and bone marker

**Consider specialist referral if:**
- a. Patient has recurrent fracture(s) or prevalent vertebral fracture(s)
- b. BMD has deteriorated despite patient concordance with treatment
- c. Creatinine Clearance has decreased to < 35ml/min
- d. Patient has been on treatment for ≥10yrs
- e. Patient reports thigh, hip or groin pain or dental pain, dental mobility or dental swelling which may indicate an atypical femoral fracture or osteonecrosis of the jaw

**Patient has sustained one or more low trauma fractures despite adequate concordance (≥80% concordance for ≥1 year):**
- Exclude secondary causes (see routine investigations)

**Patient is above NOGG treatment threshold OR Hip BMD T-score below -2.5:**
- Reasons for ineffectiveness identified? E.g.:
  - Poor concordance to treatment (i.e. if <80%)
  - Check Ca2+ and Vit D and replace if required

**Patient is below NOGG treatment threshold OR Hip BMD T-score above -2.5:**
- Is patient still high risk? due to:
  - Taking continuous oral steroids (≥7.5mg/ day prednisolone)
  - Age > 75
  - Previous hip or vertebral fracture

**Consider Drug holiday**
- Discontinue bisphosphonate for:
  - 1 year - risedronate, ibandronic acid - limited information
  - 2-3 years alendronic acid
  - 3 years zoledronic acid
- Continue Ca2+ and Vit D supplements

**Consider referring to specialist**
- E.g. change bisphosphonate or refer to secondary care for assessment of non-bisphosphonate therapy

**Consider continuing existing therapy (with measures to correct ineffectiveness as required):**
- Consider specialist opinion at 10 years continuous therapy if no fracture **

**Drug Holiday Reassessment (at indicated interval OR if new fracture):**
- Repeat DXA scan, bone marker and redo FRAX®
- Consider restarting treatment if any of:
  - Indication of deterioration on DXA scan
  - Doubling of bone marker
  - New fracture
  - Above NOGG treatment threshold

**Advise patient to report any side effects including thigh, hip, groin or dental pain, dental mobility or dental swelling**

**Consider second line therapy**
- E.g. change bisphosphonate or refer to secondary care for assessment of non-bisphosphonate therapy

**Consider restarting treatment if any of:**
- **Advise patient to report any side effects including thigh, hip, groin or dental pain, dental mobility or dental swelling**
Lifestyle Advice

All patients should be encouraged:

• Not to smoke
• To avoid excessive alcohol consumption (Women <14 units; Men <21 units per week)
• To undertake weight bearing exercise (within limits imposed by underlying disease)
• To ensure adequate calcium and vitamin D intake [RNID for calcium 700mg/day with 400 units daily of vitamin D for over 65s] See NOS leaflet** for calcium content of a wide variety of foods or Calcium calculator or SIGN guideline. For housebound / nursing home elderly patients consider 800 units daily of vitamin D (See Vitamin D guideline)
• To maintain good nutrition and normal body weight (where possible)

Falls risk assessment and advice should be performed in those at increased risk of falling (see Nottingham Integrated Falls Services for Older People. Guidelines and Joint Strategic Framework 2005-2010 or NICE guidelines 2013)

Patient information leaflets:
NOGG leaflet on osteoporosis available here
NOS leaflet for all about osteoporosis available here and facts about food available here

Calcium and Vitamin D replacement

• See Nottinghamshire Vitamin D guidelines (search Vitamin D)
• When co-prescribing vitamin D supplements with an oral antiresorptive agent (alendronate, risedronate etc), maintenance therapy may be started without the use of loading doses
• For patients about to start a potent antiresorptive agent (zoledronic acid or denosumab), rapid correction of vitamin D deficiency may be required. Consider prescribing a treatment regimen of loading doses followed by regular maintenance doses (e.g. regimen for treatment of osteomalacia patients in Vitamin D guidelines).
• For patient with severe hypocalcaemia consider specialist advice regarding replacement and/or investigation

Bone Markers (see separate guidance)

• Fasting CTx (i.e. only water pre test) is currently the preferred test in Nottinghamshire and is a marker of bone resorption. It can be used to monitor concordance and effectiveness of treatment
• A 30% reduction from baseline of CTx is considered to indicate a significant reduction in bone turnover.
• Samples should be collected in EDTA (Purple top tubes). Stability of sample has been demonstrated for up to 24 hours in EDTA. Collection in other sample tubes not advisable for stability reasons.

References

• Alendronate, etidronate, risedronate, raloxifene and strontium ranelate for the primary prevention of osteoporotic fragility fractures in postmenopausal women, NICE technology appraisal guidance 160 (2011)
• Alendronate, etidronate, risedronate, raloxifene, strontium ranelate and teriparatide for the prevention of osteoporotic fragility fractures in postmenopausal women NICE technology appraisal guidance 161 (2011)
• Denosumab for the prevention of osteoporotic fractures in postmenopausal women. NICE technology appraisal guidance 204 (2010)
• NICE Clinical Knowledge Summaries: Osteoporosis - prevention of fragility fractures last revised Sept 2013
• National Osteoporosis Guidelines Group (NOGG): Osteoporosis - Clinical Guideline for prevention and treatment (Executive Summary) updated May 2013
• WHO FRAX Tool available at: http://www.shef.ac.uk/FRAX/
• Nottinghamshire Area Prescribing Committee Guidelines on Vitamin D deficiency available at: http://www.nottsapc.nhs.uk
• UKMI Q&A: Do gastric adverse events influence the choice of bisphosphonate for the treatment of osteoporosis?
• Adjuvant Use of Aromatase Inhibitors for Early Breast Cancer, NUH Breast Services Guideline
• NICE CG 69: Eating disorders : recognition and treatment. May 2017
### Appendix 1: Specialist Initiation Treatment Options

<table>
<thead>
<tr>
<th>Table 1: Drug</th>
<th>Restrictions / Contraindications</th>
<th>Dose</th>
<th>Monitoring and Side-Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ibandronic Acid (oral)</td>
<td>3rd line oral option where alendronate and risedronate have not been tolerated. No data available for hip fracture reduction. Not recommended if Creatinine Clearance ≤30ml/min</td>
<td>150mg PO monthly</td>
<td>As per other oral bisphosphonates</td>
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<tr>
<td><strong>Amber 2 - specialist recommendation</strong></td>
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<td></td>
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</tr>
<tr>
<td>Raloxifene (oral)</td>
<td>NICE recommended for secondary prevention only in postmenopausal women when alendronate/risedronate can’t be used. Contraindicated in women with child-bearing potential, a history of venous thromboembolism, unexplained uterine bleeding, Hepatic impairment and severe renal impairment (although &lt;6% of dose excreted in urine) Caution in women with a history of stroke or with risk factors for stroke</td>
<td>60mg PO daily</td>
<td>Side-effects include leg cramps, oedema, flu syndrome and hot flushes. Increased risk of VTE</td>
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<tr>
<td><strong>Amber 2 - specialist recommendation</strong></td>
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<tr>
<td>Ibandronic Acid (IV; Bonviva®)</td>
<td>For initiation by osteoporosis specialists only in patients with an unsatisfactory response, intolerant, contraindicated or physically unable to comply with oral bisphosphonates or yearly IV zoledronic acid</td>
<td>3mg IV injection every 3 months</td>
<td>See algorithm notes regarding drug holidays. Please note date received by patient on GP systems to prevent inappropriate use of oral bisphosphonates</td>
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<tr>
<td><strong>Red - specialist prescribing only</strong></td>
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<tr>
<td>Zoledronic acid IV</td>
<td>Available for initiation only by osteoporosis specialists if unsatisfactory response, intolerant, contraindicated or physically unable to comply with oral bisphosphonates</td>
<td>5mg IV yearly</td>
<td>See algorithm notes regarding drug holidays. Please note date received by patient on GP systems to prevent inappropriate use of oral bisphosphonates</td>
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<tr>
<td><strong>Red - specialist prescribing only</strong></td>
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<tr>
<td>Denosumab (SC; Prolia®)</td>
<td>For initiation by osteoporosis specialists only in postmenopausal women as per NICE TA for patients in whom IV bisphosphonates aren't suitable. Correct hypocalcaemia and vitamin D deficiency before starting. Consider dental check-up and carry out invasive procedures before initiating treatment (risk of osteonecrosis of the jaw)</td>
<td>60mg subcutaneous injection every 6 months +/- oral Ca^{2+} and/or Vit D.</td>
<td>Side-effects include skin infection, predominantly cellulitis, and hypocalcaemia. See MHRA safety updates on Osteonecrosis of the Jaw and Hypocalcaemia (Aug 2014), Hypocalcaemia (Oct 12) Atypical femoral fractures Feb 13</td>
</tr>
<tr>
<td><strong>Red - specialist prescribing only</strong></td>
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<tr>
<td>Teriparatide (SC; Forsteo®)</td>
<td>For initiation by osteoporosis specialists only in postmenopausal women as per NICE TA in patients unable to take or have had an unsatisfactory response to oral bisphosphonates AND meet NICE criteria regarding age and T-scores Caution in moderate renal impairment; avoid if severe. Maximum duration of treatment limited to 18 months as per NICE.</td>
<td>20 micrograms subcutaneous injection daily. +/- oral Ca^{2+} and/or Vit D.</td>
<td>Side effects include headache, nausea, dizziness and postural hypotension.</td>
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<td><strong>Red - specialist prescribing only</strong></td>
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<tr>
<td>Parathyroid Hormone (SC; Preotact®)</td>
<td>Secondary prevention only Postmenopausal women only Second line to Teriparatide if unable to take or have had an unsatisfactory response to oral bisphosphonates AND meet NICE criteria regarding age and T-scores. Duration of treatment limited to 18 months.</td>
<td>100 micrograms subcutaneous injection daily.</td>
<td>Hypercalcaemia and/or hypercalciuria develop in approximately 25% of treated patients and serum and urine calcium should be monitored at 1, 3 and 6 months after starting treatment, with adjustment of calcium and vitamin D supplementation ± frequency of PTH administration if required.</td>
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</tbody>
</table>
Appendix 2: Fracture prevention efficacy table

Table 2: Anti-fracture efficacy of approved treatments for postmenopausal women with osteoporosis when given with calcium and vitamin D (traffic lighted according to Nottinghamshire Joint Formulary classification). Adapted from NOGG guidelines 2013. Colours reflect the traffic light classifications for the medicines in Nottinghamshire Drug Vertebral Fracture Non-vertebral fracture Hip fracture

<table>
<thead>
<tr>
<th>Drug</th>
<th>Vertebral Fracture</th>
<th>Non-vertebral fracture</th>
<th>Hip fracture</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alendronate (Green)</td>
<td>A</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>Risedronate (Green)</td>
<td>A</td>
<td>A</td>
<td>A</td>
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<tr>
<td>Raloxifene (Amber 2)</td>
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<tr>
<td>Zoledronic acid (Red)</td>
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<tr>
<td>Ibandronate (Red)</td>
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<tr>
<td>Denosumab (Red)</td>
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<tr>
<td>Teriparatide (Red)</td>
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<tr>
<td>PTH i.e. Preotact (Red)</td>
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</tbody>
</table>

Nae not adequately evaluated  
# in subsets of patients only (post-hoc analysis)  

Evidence grading:  
A : based on meta-analysis or at least one randomised controlled

PTH: Parathyroid hormone

Appendix 3: Recommended routine investigations

Recommended routine investigations to exclude non-osteoporotic causes of fragility fractures and undiagnosed secondary causes of osteoporosis include:

- X-ray of the fracture. Arrange lateral X-rays of the lumbar and thoracic spine when there is spinal pain, loss of height, or kyphosis.

- Blood tests: -
  - Full blood count
  - renal function tests
  - ESR or C-reactive protein
  - bone profile
  - liver function tests
  - thyroid function tests

- For people with a fragility fracture, exclude non-osteoporotic causes and arrange investigations as appropriate if there are features of:
  - Metastatic bone cancer
  - Multiple myeloma
  - Osteomalacia
  - Paget’s disease

- Consider undiagnosed secondary causes for osteoporosis and arrange investigations as appropriate, especially in people with a fragility fracture who are at low risk for the condition (including men of any age, pre-menopausal women, and women in early menopause). Consider:
  - Endocrine conditions such as untreated premature menopause in women, hypogonadism in men, diabetes, and hyperthyroidism.
  - Rheumatological conditions such as rheumatoid arthritis, and other inflammatory arthropathies.
  - Chronic gastrointestinal diseases that cause malabsorption such as Crohn’s disease, ulcerative colitis, and coeliac disease.
  - Chronic liver disease.
  - Chronic obstructive pulmonary disease.
Appendix 4: Risk Factors

Clinical risk factors used for the assessment of fracture probability
(from NOGG guideline)

- Age
- Sex
- Low body mass index (≤19kg/m²)
- Previous fragility fracture, particularly of the hip, wrist and spine including morphometric vertebral fracture
- Parental history of hip fracture
- Current glucocorticoid treatment (any dose, by mouth for 3 months or more)
- Current smoking
- Alcohol intake of 3 or more units daily
- Secondary causes of osteoporosis including:
  - Rheumatoid arthritis
  - Untreated hypogonadism in men and women
  - Prolonged immobility
  - Organ transplantation
  - Chronic obstructive pulmonary disease
  - Type I diabetes
  - Hyperthyroidism
  - Gastrointestinal disease that causes malabsorption e.g. Crohn’s, UC or coeliac
  - Chronic liver disease
  - Falls *

Major risk factors (relating to primary prevention in the <50 year olds)
- Current or recent use of high-dose oral corticosteroids of more than or equivalent to 7.5mg prednisolone daily for more than 3 months
- Untreated premature menopause

Appendix 5: Preventing glucocorticoid induced osteoporosis

Prevention of glucocorticoid induced osteoporosis is available in the Royal College of Physicians guidelines 2002. Please see them for advice on management beyond the scope of these guidelines available at:

Appendix 6: Counselling for patients on oral bisphosphonates

All patients should be informed;
- To keep taking their bisphosphonate as it is a long term therapy to prevent fragility fracture. That they will also be prescribed calcium and vitamin D supplementation if their dietary calcium intake and vitamin status have been assessed and are inadequate.
- Advise the person to stop taking the bisphosphonate and seek medical advice if they experience any signs or symptoms of possible oesophageal reaction, e.g. dysphagia, pain on swallowing, retrosternal pain, or new/worsened heartburn.
- Advise the person to have regular dental check-ups, before starting oral bisphosphonate treatment if they have poor dental status, and to tell their dentist that they are taking a bisphosphonate, particularly if they are going to undertake invasive dental procedures (due to a very rare risk of osteonecrosis of the jaw). Advise patient to inform of any dental mobility, pain or swelling.

Patient concordance;
- Patient concordance with this treatment is poor due to side effects. To ensure the benefits are realised it is suggested patients are assessed a month after starting treatment to the GP, practice nurse or pharmacist to check how things are going and assess concordance.

Administration advice;
- The tablet must be swallowed whole and taken with a glass of plain water (at least 200 ml); it must not be sucked or chewed because of a potential for oropharyngeal ulceration.
- It should be taken while in an upright position and they should not lie down for at least 30 minutes after taking the tablet.
- The tablet must not be taken at bedtime or before getting up in the morning.
- Once weekly preparations should be taken on the same day each week.
- **Alendronate** must be taken at least 30 minutes before the first food, other medicinal product, or drink (other than plain water) of the day.
- **Risedronate** should be taken at least 30 minutes before the first food, other medicinal product, or drink (other than plain water) of the day. Alternatively it may be taken between meals — should be taken at least 2 hours before or at least 2 hours after any food, other medicinal product, or drink (other than plain water).
- Do not take with **food, milk and dairy products, and medicinal products containing polyvalent cations** (such as calcium, magnesium, iron, and aluminium — for example antacids as they interfere with absorption of the bisphosphonate).

Missed doses: For once-weekly preparations of alendronate or risedronate, advise the person:
- To take the missed tablet on the day that it is remembered.
- To continue taking one tablet once a week, on the day the tablet is normally taken.
- That two tablets should not be taken on the same day.

Helpful information:
- **The National Osteoporosis Society** ([www.nos.org.uk](http://www.nos.org.uk)) provides support and information to people affected by osteoporosis, influences health and social care provision, and works to improve public understanding of osteoporosis.
- **NHS Choices** has a health encyclopaedia which has a printable article on Osteoporosis at: [http://www.nhs.uk/conditions/Osteoporosis/Pages/Introduction.aspx](http://www.nhs.uk/conditions/Osteoporosis/Pages/Introduction.aspx)