BLMK Primary Care guideline

Primary and Secondary prevention of osteoporosis in post-menopausal women and men ≥ 50 years old*

Points to note:

- **Pre-menopausal women, and men less than 50 years old** lie outside these guidelines as they will require an individual assessment– primary care clinicians should use 'advice and guidance' to seek advice / arrange a referral to a specialist**.**

- **Transgender (Transpeople)*: -**
  Assess fracture risk on an individual basis and consider seeking specialist advice
  (For further information see:- :Royal Osteoporosis Society factsheet Transgender people & osteoporosis)

- These guidelines should be used to aid management decisions, but do not replace the need for clinical judgement in the care of individual patients in clinical practice.

- To assist in decision making, NICE have published a Patient Decision Aid for the use of bisphosphonates in the treatment of osteoporosis - Available here

For background information relating to osteoporosis – click here

The following organisations contribute to and participate in the BLMK APC – Bedfordshire, Luton and Milton Keynes Integrated Care Board; Bedfordshire Hospitals NHS Foundation Trust; Cambridgeshire Community Services NHS Trust; Central and North West London NHS Foundation Trust; East London NHS Foundation Trust; Milton Keynes University Hospital NHS Foundation Trust

Approved by BLMK Area Prescribing Committee: May 2025; Review date: May 2028

Contents

Treatment Management Algorithm

Stage 1: Patients at risk of osteoporosis or with Suspected Osteoporosis: – Investigations and Diagnostic Tests

Back to contents page

Primary prevention

Use a case finding strategy to identify individuals who:

- have suspected osteoporosis
- are at high risk of fragility fractures

Secondary Prevention

- For patients presenting with a new or previous history of a fragility fracture

Patients who have:

- Frailty
- increased fall risk ± housebound
- care home residents

Things to consider :

- Age of patient
- Current use or frequent recent use of oral or systemic glucocorticoids (see separate guidance)
- Presence of any relevant clinical risk factors
- Any secondary causes of osteoporosis
- Other potential causes for any fracture

Who to assess for fragility fracture risk

- All postmenopausal women and men over 50 years old with a clinical risk factor(s) for fragility fracture
- All postmenopausal women and all men over 50 years old who have a fragility fracture / history of fragility fracture
- All women over 65 years and all men over 75 years (regardless of presence of any risk factors)

How to assess fragility fracture risk ?

- NICE recommend using either FRAX® or QFracture® risk assessment tools to predict the absolute risk of hip fracture, and major osteoporotic fractures (spine, wrist, or shoulder) over 10 years.
- Consider using FRAX® (unless not suitable) as it provides an absolute 10 year risk % score **and** a link to the National Osteoporosis Guideline Group (NOGG) individualised recommendations graph – this can help decide a management plan - Click here to see example of the NOGG template graph

DEXA (DXA) Scan:-
Take individual risk factors, DXA scan waiting times, time to get DXA result report into account.

- **Offer a DXA scan and start bone protective treatment** (see drug choices) **plus** vitamin D **or** calcium plus Vit D supplementation (if low dietary calcium intake) **before** DXA results are known **in the following scenarios:**
  - In patients who are close to the NOGG intervention threshold line (refer to NOGG graph)
  - In patients with a fragility fracture**,** especially in older patients due to risk of refracture
  - In patients who present with a spontaneous vertebral fracture (here DXA is only requested to help determine extent of BMD to help decide if anabolic treatment required
  - In patients currently taking / recently taken oral glucocorticosteroids (see separate guidance)
- **Offer a DXA scan in the following scenarios:-**
  - Post menopausal women and men over 50 with a fragility fracture **(NB:** older patients are at risk of refracture – see above bullet point)
  - Patients whose FRAX® fragility risk score falls within the amber zone on the NOGG fragility risk graph

DXA results / reports

- Results and suggested management plan will be sent to GP - for examples of actions required – click here
- **Consider recalculating** the FRAX® risk score using the BMD results (from DXA report) and generate an updated NOGG intervention graph(s) if this is **the first DXA scan** requested: - this can help to identify patients who maybe at a very high risk of a major fracture and require specialist advice / referral to a specialist
- For information regarding how often a DXA scan should be performed - click here

Notes regarding DXA scans

- Women ≥ 75 yrs - osteoporosis diagnosis may be assumed if a DXA scan is clinically inappropriate/ unfeasible (a scan is preferrable however to determine if the patient is at a very high risk).
- Men – require a DXA scan or use clinical judgment
- Patients with a **low fragility fracture risk score** and no other significant clinical risk factors generally do not require referral for a DXA scan - Offer lifestyle advice and consider a follow up review in approx. 5 years (exact timing will vary depending on age of patient).

DEXA (DXA report information

Back to contents page

- A DXA scan report will be sent to GP detailing bone mineral density (BMD), T- scores results
- DXA report will advise a management plan particularly in those with clinical risk factors such as hyperparathyroidism, aromatase inhibitors/steroids use etc.

T – score Result	Interpretation	Action to be taken
Greater than -1	**Normal**	• Reassure patient and follow general measures
Between -1 and -2.4	**Osteopenia**	• **Re-calculate FRAX®** fragility fracture risk score by adding in BMD results (from DXA scan report) and generate a new NOGG intervention graph(s) as the patient may warrant treatment even though T score indicates osteopenia. • Modify any risk factors where possible • Treat any underlying conditions • Repeat the DXA scan at an interval appropriate for the person based on their risk profile, using clinical judgement (but usually within 2 years). Ref CKS
Less than or equal to -2.5 (NB This is a general "cut-off" and is not strictly in accordance with NICE guidance which is more complex).	**Osteoporosis**	**Treatment plan for osteoporosis:** - Carry out full set of investigations - **Re-calculate FRAX®** fragility fracture risk score by adding in BMD results (from DXA scan report) and generate a new NOGG intervention graph(s) to determine whether patients are at high risk or a very high risk (if very high risk seek specialist advice / specialist referral. - Prescribe bone protective drug treatment (click to see drug choices) **And** - Prescribe vitamin D supplementation **or** calcium plus vitamin D supplementation (if low dietary calcium intake) (To assess daily calcium intake using the online calcium intake calculator) - If Vitamin D monotherapy required:- prescribe colecalciferol 800 IU - If calcium plus vitamin D combination required:- prescribed calcium 1-1.2g / colecalciferol 800 IU - **If frailty / care home residents:-** prescribe calcium 1-1.2g / colecalciferol 800 IU

Management of Osteoporosis (T Score ≤ -2.5)

General points

Back to contents page

Consider the age of the person, level of fracture risk, any additional clinical risk factors, secondary causes of osteoporosis when deciding whether to start treatment before DXA scan results are known and when deciding on a particular drug treatment.

- For patients who have **symptomatic osteoporotic vertebral fracture**: -
  - **Start treatment promptly to reduce the risk of further fracture**
  - Investigate for underlying causes of fragility fracture.
  - Consider referral to an exercise programme which provides progressive muscle strengthening activity, including back extensor muscle strengthening and/or endurance exercise. (Ref NOGG)
- If BMD results are known, consider **recalculating** fragility fracture risk (using FRAX®) and refer to the new NOGG intervention graph(s) to determine if patient is at high risk or very high risk of fracture.
- Discuss the advantages and disadvantages of the various treatment choices available.
- Consult electronic BNF or Summary of Product Characteristics (SmPC) for full prescribing details.
  (NB: licensed indications for bisphosphonates may vary, in particular relating to their use in men. Alendronic acid use in men is off label however it is recommended by specialists.
- Clinicians should be aware of the various MHRA drug safety advice (DSU) documents relating to bisphosphonates and denosumab regarding osteonecrosis of the jaw, osteonecrosis of external auditory canal, atypical fractures, hypercalcaemia; increased risk of multiple vertebral fractures after stopping or delaying ongoing treatment (with denosumab) - Click here to view individual MHRA DSU advice
- If considering a bisphosphonate or denosumab treatment options , ensure dental examinations / any required dental treatment is carried out as appropriate **before** starting treatment and give advice regarding dental hygiene etc. due to low risk of Osteonecrosis of the Jaw (ONJ) associated with bisphosphonates and denosumab therapy.
- Check compliance with bisphosphonate therapy after first month, after 3 months and then annual review
- Prescribe generic products when available.

Important note:-

- Clinicians should seek specialist opinion if patient sustains a fracture while on therapy.
- Refer patients at very high risk to specialist team for consideration of anabolic treatment.
- Discontinue oral bisphosphonates if patient is started on an IV bisphosphonate / denosumab / teriparatide / romosozumab / abaloparatide by secondary care clinician.
- Denosumab treatment should not be stopped or delayed without specialist review (due to increased risk of vertebral fractures)
- Secondary care clinician will advise GP on **which follow on bone therapy** treatment is required post use of an IV bisphosphonate / denosumab / teriparatide / romosozumab / abaloparatide.

Click here for drug treatment options

Click here for criteria for secondary care referral

Drug Treatment Choices

Back to contents page

NB: Refer to **general prescribing points** before starting treatment – click here

First line options:-

Bisphosphonates

- **Oral bisphosphonate**
  - Alendronic acid 70mg once weekly or Risedronate 35mg once weekly

Note:-

- Alendronic acid 70mg once weekly in men is an **off-label** use, however it is recommended by local specialists.
- Weekly dosing is the preferred option, however daily preparations of alendronic acid and risedronate are available if preferred – see eBNF for dosing information.
- Ibandronic acid 150mg **monthly** tablets can be used as an alternative if compliance is an issue.

NB:-
IV bisphosphonate should be considered in patients who have a 10-year FRAX % probability of osteoporotic fragility fracture of at least 10%, **and** in patients who have had a hip fracture or at high fracture risk – **IV treatment requires a specialist referral**

- Zolendronic acid IV 5mg once a year or IV Ibandronic acid 3mg every 3 months

Note:

- **Bisphosphonates (PO and IV) are contraindicated in severe renal impairment -** refer to specialist for consideration of s/c denosumab
- **Patients who cannot take or who are intolerant of oral bisphosphonates** – refer to Specialist team for consideration of IV bisphosphonate or denosumab s/c.

Prescribing Notes:-

- Emphasise administration advice specific to oral bisphosphonates (see eBNF). If patient not willing / able to follow the timing schedule, consider alternative treatment.
- If oesophageal irritation occurs, consider prescribing a proton pump inhibitor unless contra-indicated.
- Consider a switch to the alternative oral bisphosphonate if intolerance* occurs
- Alendronic acid is also available as an effervescent tablet or as a liquid for patients who have difficulties swallowing tablets.

*Intolerance is defined as persistent upper GI disturbance that is sufficiently severe to warrant discontinuation of treatment, and that occurs even though the instructions for administration have been followed correctly.

Hormone replacement Therapy (HRT)*:–

- HRT can be considered as a treatment option in younger postmenopausal women (age ≤ 60 years) **who have menopausal symptoms***, and a high fracture risk and low baseline risk for adverse malignant and thromboembolic events.
- Discussion should take place with the individual to determine if HRT is the best treatment option for them
- Discuss continued use of HRT after the age of 60 years with the patient, with treatment based on an individual risk-benefit analysis
- When HRT is discontinued, reassess fracture risk and consider an alternative treatment if indicated

* National Menopause guidance recommends using HRT only for women with menopausal symptoms and for the shortest possible period.

Second line options (require specialist referral)

- Denosumab (Prolia®) 60mg s/c every 6 months (specialist initiation , then GP prescribing via shared care)
  or
- Zoledronic acid IV 5mg once a year or IV Ibandronic acid 3mg every 3 months (secondary care only)

Note:-

- **Oral bisphosphonates** should be **discontinued** if patient is started on an IV bisphosphonate or s/c denosumab, or teriparatide, romosozumab, or abaloparatide.
- **Denosumab** treatment should **not** be stopped or delayed without specialist review (due to risk of vertebral fractures).

Criteria for secondary care referral

Back to contents page

Specialist referral should be considered if treatment is required in the following scenarios:-

- If patient sustains a fracture while on current osteoporosis treatment
- If patient has been identified as being at very high risk of fracture and may benefit from anabolic treatment (as per NOGG recommendations)
- Patients with severe renal impairment
- Pre-menopausal women at risk of fracture / risk of developing osteoporosis
- Male osteoporosis if less than 50 years old
- Male osteoporosis if considering prescribing a drug unlicensed for treating osteoporosis in men
- For consideration of IV bisphosphonates / denosumab due to intolerance or poor response to treatment with oral bisphosphonates
- For patients already prescribed denosumab – GP should seek further specialist advice if there is a need to stop or delay treatment as per MHRA DSU advice

Treatment options that may be prescribed by secondary care are:- (no GP prescribing)

- **Anti-resorptive drugs**
  - IV zolendronic acid or IV Ibandronic acid
  - Denosumab s/c (initiation by specialist, continuation by GP via shared care)

- **Anabolic drugs:-**
  - Teriparatide (NICE TA 161)
  - Romosozumab (NICE TA 791) (for post-menopausal people at high risk of fracture)
  - Abaloparatide (NICE TA 991) (for post-menopausal people at very high risk of fracture)

Note:-

- **Oral bisphosphonates** should be discontinued if patient is started on IV bisphosphonate, denosumab, teriparatide, romosozumab, or abaloparatide.
- Anabolic treatment is for a defined time period - the specialists will advise if anti-resorptive therapy should be restarted once the anabolic treatment course has finished

- **Strontium**
  The Specialist may consider Strontium if all other options have failed or are contraindicated – Specialist only prescribing (no primary care prescribing)

Treatment Duration review: Guidance for GPs

Back to contents page

Bisphosphonate therapy

- **Review** treatment +/- DXA after 3- 5 years (duration of treatment is dependent on presence of risk factors)

  For further information on treatment duration; when to consider a drug holiday; how to stop therapy; when to request a repeat DXA scan request a repeat DXA scan **-** click here

Denosumab therapy

- **Review** treatment +/- DXA after 3-5 years **and seek specialist advice** on whether to continue or stop therapy / the need to repeat DXA scans.
  NB Denosumab should **not** be stopped or ongoing treatment delayed **without** a specialist review.
  For further information on treatment duration; how to stop therapy; when to request a repeat DXA scan request a repeat DXA scan **-** click here

For further information regarding DXA scan frequency – click here

Background Information

Back to contents page

- In adults, approximately one in two women and one in five men will sustain one or more fragility fractures in their lifetime, and this number is set to increase with an ageing population.
- Osteoporosis is characterised by low bone mass density and structural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture.
- Osteoporosis is asymptomatic, and often not diagnosed until a bone fracture occurs.
- The risk of getting an osteoporotic fracture depends on the person's risk of falls, their bone strength (determined by bone mineral density [BMD]), and other risk factors.
- There are over 50 clinical risk factors for osteoporosis and fragility fractures, many of which are not accommodated in the Fracture Risk Assessment Tool (FRAX), but should trigger a fracture risk assessment
- An osteoporotic fracture is a fragility fracture occurring as a consequence of osteoporosis. Typically, fragility fractures occur in the wrist, spine, and hip, but they can also occur in the arm, pelvis, ribs, and other bones.
    - A fragility bone fracture is classed as a fracture that occurs from a fall from standing height or less and
    - Vertebral fractures may occur spontaneously, or as a result of routine activities such as bending or lifting.
- Osteoporosis is defined by the World Health Organization 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) applied to the femoral neck and reported as a T-score.
  NB: However, BMD measurement does not assess the structural deterioration in bone and consequently, most osteoporotic fractures occur in women who do not have osteoporosis as defined by a T-score equal to or less than -2.5.
  (Ref : CKS Osteoporosis – Prevention of fragility fracture guideline (accessed Jan 2025), GP Notebook

Clinical risk factors

Back to contents page

The risk of having an osteoporotic fracture depends on the person's risk of falls, their bone strength (determined by bone mineral density [BMD]), and other risk factors.
Presence of risk factors that should be taken into account when assessing the patient:-

- Increasing age (both male and female)
- Parent history of a hip fracture
- Previous fragility fracture
- BMI < 18.5 kg/m2.
- Smoking
- Alcohol intake of more than 14 units per week for men and women.
- Current or frequent recent use of oral or systemic glucocorticoids
- Other causes of secondary osteoporosis e.g. premature menopause, post menopausal, inflammatory arthropathies e.g. rheumatoid arthritis. (see secondary causes)

(Ref NICE Clinical Guideline)

NB: The above risk factors are accommodated within the FRAX® fragility fracture risk assessment tool.

Additional risk factors to consider (Ref NOGG guidelines 2024, CKS)

Back to contents page

In addition to the risk factors listed above, there are numerous other clinical risk factors for osteoporosis and fragility fractures, many of which are not accommodated in the Fracture Risk Assessment Tool (FRAX), **but** should trigger a fracture risk assessment. (see below)
These additional clinical risk factors are listed below:

- Thoracic kyphosis
- Height loss (> 4cm)
- Falls and frailty
- Inflammatory disease: e.g., ankylosing spondylitis, other inflammatory arthritides, connective tissue diseases, systemic lupus erythematosus

- Endocrine disease: e.g., Type I and II diabetes mellitus, hyperparathyroidism, hyperthyroidism, hypogonadism, Cushing's disease/syndrome
- Inflammatory Bowel disease: Crohn's, Ulcerative colitis
- Bariatric surgery, and other conditions associated with intestinal malabsorption e.g. coeliac disease, bowel surgery
- Haematological disorders/malignancy e.g., multiple myeloma, thalassaemia
- Muscle disease: e.g., myositis, myopathies and dystrophies, sarcopenia
- Lung disease: e.g., asthma, cystic fibrosis, chronic obstructive pulmonary disease
- HIV
- Neurological/ psychiatric disease e.g., Parkinson's disease and associated syndromes, multiple sclerosis, epilepsy, stroke, depression, dementia
- Nutritional deficiencies: calcium, vitamin D [note that vitamin D deficiency may contribute to fracture risk through under mineralisation of bone (osteomalacia) rather than osteoporosis]
- Bariatric surgery and other conditions associated with intestinal malabsorption
- (Excess) thyroid hormone treatment (levothyroxine and/or liothyronine). Patients with thyroid cancer with suppressed TSH are at particular risk

- Certain Medications, e.g.:
    - Selective serotonin reuptake inhibitors
    - Proton pump inhibitors
    - Some immunosuppressants (calmodulin/calcineurine phosphatase inhibitors)
    - Drugs affecting gonadal hormone production (aromatase inhibitors, androgen deprivation therapy, medroxyprogesterone acetate, gonadotrophin hormone releasing agonists, gonadotrophin hormone receptor antagonists)
    - Some diabetes drugs (e.g., thiazolidinediones)
    - Some antiepileptics (e.g., phenytoin and carbamazepine)

Secondary causes of osteoporosis

Back to contents page

- Hypogonadism in either sex, including untreated premature menopause (menopause before 40 years of age), treatment with aromatase inhibitors (such as exemastane) or gonadotrophin-releasing hormone agonists (such as goserelin).
- Endocrine conditions, including diabetes mellitus, Cushing's disease, hyperthyroidism, hyperparathyroidism, and hyperprolactinaemia.
- Conditions associated with malabsorption, including inflammatory bowel disease, coeliac disease, and chronic pancreatitis.
- Rheumatoid arthritis and other inflammatory arthropathies.
- Haematological conditions such as multiple myeloma and haemoglobinopathies.
- Chronic obstructive pulmonary disease.
- Chronic liver failure.
- Chronic kidney disease.
- Immobility.

Investigations / Blood tests

Back to contents page

- FBC, ESR
- Bone and liver function tests (calcium, phosphate, Alkphos, albumin, ALT/γGT)
- Serum creatinine
- Serum TSH
- Serum PTH
- Serum paraproteins and urine Bence Jones protein
- Anti TTG (coeliac antibody)

Additional test if indicated:

- Serum testosterone and PSA in men, LH and SHBG
- Serum Vitamin D
- Lateral thoracic and lumbar spine X rays, or VFA* (if available)

* **VFA -** Vertebral fracture assessment (Sheffield criteria) should be considered in:-

- women >65 or men >70
- history of: 4cm height loss or kyphosis
- recent or current corticosteroid therapy (prednisolone ≥5mg for >3 months)
- BMD T-score lower than or equal to -2.5
- vertebral fracture in patients over 45
- non-vertebral fracture in patients over 50

10 Year Fragility Fracture Risk Assessment

Back to contents page

The NOGG guidelines (2024) recommend using the FRAX® tool to calculate an individual's 10 year fragility fracture risk.

The 10 year fragility fracture risk should be assessed in :-

- all women aged 65 years and over
- all men aged 75 years and over
- women aged under 65 years and men aged under 75 years in the **presence of risk factors.**

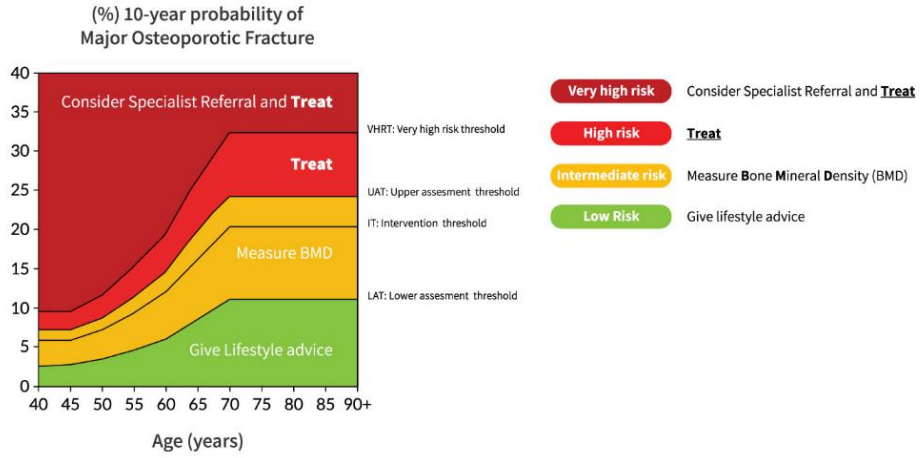
NB: Do not routinely assess fracture risk in people aged under 50 years unless they have major risk factors (e.g. current or frequent recent use of oral or systemic glucocorticoids, untreated premature menopause or previous fragility fracture), because they are unlikely to be at high risk.

The FRAX tool generates a 10 year fragility fracture % score. By clicking the 'view NOGG guidance' button below the % score, an individual's fracture risk is displayed on a graph, which defines the individual's risk for an osteoporotic fracture:-

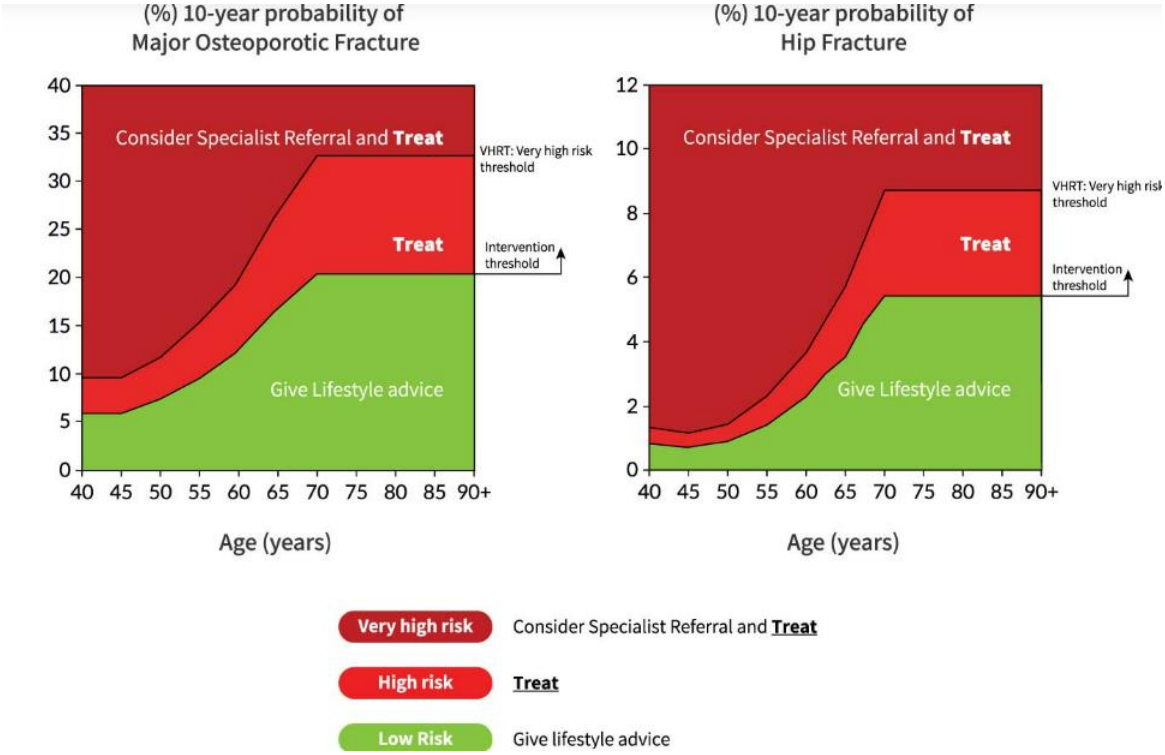
- low risk (green zone)
- intermediate risk (orange zone)
- high risk (red zone)
- very high risk (dark red zone)

The NOGG intervention threshold graph for the 10 year probability of a major osteoporotic fracture (MOF) is shown below:

Back to contents page



If an individual's Bone Mass Density (BMD) is known and is entered into the FRAX tool, the NOGG recommendation also provides intervention thresholds based on the 10-year probability of hip fracture, in addition to the 10-year probability of a MOF - example of the two separate intervention graphs are shown below.



To access more details relating to the NOGG accompanying information, click here.

When using FRAX, clinicians should be aware it underestimates some risk factors, including:

- Regular use of corticosteroids equivalent to or less than 5 mg prednisolone daily.
- Use of corticosteroids more than or equivalent to 7.5 mg prednisolone daily for more than 3 months.
- A history of multiple fragility fractures.
- High alcohol intake.
- Heavy smoking.
- Short term fracture risk in people aged over 80 years may be underestimated.

Ref NOGG and CKS

DEXA (DXA) scan

Back to contents page

- Bone mineral density (BMD) measurement by dual-energy x-ray absorptiometry (DXA) is an internationally accepted standard-of-care screening tool used to assess fragility-fracture risk.
- BMD of the lumbar spine and hip should be measured by dual energy x-ray absorptiometry (DXA scan).
- DXA scanning and the use of FRAX® (fracture risk assessment tool) can help guide decisions regarding the best treatment options for the treatment of osteoporosis.

DXA Scan Results

- A DXA report will contain BMD results and T- scores. (A T-score is the number of standard deviations above or below normal peak bone mass.)

  T-Scores:-

  - If T-score is -1 or higher:– healthy bone
  - If T-score is -1 to -2.5:- osteopenia

- If T-Score is -2.5 or lower:- osteoporosis

- The risk of broken bones increases by 1.5 to 2 times with each 1 point drop in T-score
- Osteoporosis is diagnosed if the T score is less than or equal to −2.5 at either site. However, please note fragility fractures often occur in individuals with osteopenia (T score −1 to −2.5).
- DXA scan results will be assessed by a specialist and a recommended course of action, including drug treatment recommendations, will be sent to the GP.

Ref National Institute of arthritis and musculoskeletal and skin disease Bone Mineral Density Tests: What the Numbers Mean)

Frequency of repeat DXA scans:-

A guide to when repeat DXA scans should be requested is below. Please note the exact frequency will vary depending on clinical risk factors and individual circumstances.

Osteopenia

Patients with osteopenia (T score -1 to -2.4)	Repeat the DXA scan at an interval appropriate for the person based on their risk profile using clinical judgement (but usually within 2 years).

Osteoporosis

Following initiation of bisphosphonate (oral or IV) or denosumab therapy	Consider repeating DXA after 3-5 years
Ongoing bisphosphonate / denosumab therapy	Consider repeating DXA every 2-3 year
Presence of a recent fracture	Consider a repeat DXA after 1-3 years
Patients receiving glucocorticosteroids (long term)	Consider repeating DXA every 1-3 years
Patients over 65 years who have had a recent fracture **and** who are prescribed short intermittent courses of steroids (i.e. not on a course for > 3 months	Consider repeating DXA after 1-3 years

Bisphosphonates (Oral & IV)

Back to contents page

- **Review treatment +/- DXA after 3- 5 years, (duration of treatment is dependent on presence of risk factors**)

Treatment Duration / stopping criteria:-

Key points

- 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 up to ten years.[12] 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.
- There is some debate over the ideal duration of therapy, particularly with the emergence of links with the rare but serious complications of osteonecrosis of the jaw and atypical subtrochanteric fracture.

- 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). Where possible, patients should have a 'drug holiday' or treatment stopped based on a DXA scan.
- The FLEX and HORIZON extension trials which have demonstrated that bone loss after discontinuation of bisphosphonate therapy was modest compared with continued therapy.[13,14]
- NICE Guidance[5,6] recommends the **re-evaluation of the individual patient** after at least 3 years of treatment of bisphosphonate treatment.
- The recommendation is that after three years of treatment, for patients not considered high risk of fracture, consider a "drug holiday" period and stop bisphosphonate treatment where appropriate.
- Discuss stopping bisphosphonates after 3 years of treatment and include patient choice, fracture risk and life expectancy in the decision.
- Inform the patient who has been taking bisphosphonate for osteoporosis that there is no consistent evidence of:
    - further benefit from continuing bisphosphonate for another 3 years.
    - harm from stopping bisphosphonate after 3 years of treatment.
- In patients considered high risk, data suggests it is safe to continue for up to 10 years of treatment. The need to continue treatment should be re-evaluated periodically and a repeat DXA scan may be considered appropriate. Continuing therapy will be based on the benefits v potential risks of therapy for individual patients after 3 or more years of use.
- Patients considered high risk include: patients taking oral glucocorticoids, patients that have had a fragility fracture (and compliant) while on therapy and those that have had a previous hip or vertebral fracture[6].
- **Please note that oral bisphosphonates should be discontinued if patient is started on an IV bisphosphonate / denosumab / teriparatide / romosozumab / abaloparatide by secondary care clinician.**
- NB: Secondary care clinician will advise GP on which **follow on bone therapy** treatment is required post use of an IV bisphosphonate / denosumab / teriparatide / romosozumab / abaloparatide

Denosumab

Back to contents page

- **Review treatment +/- DXA after 3-5 years <u>and</u> seek specialist advice on whether to continue or stop therapy / the need to repeat DXA scans.**

  (**NB:** Denosumab treatment – **do not stop** or delay ongoing treatment without a specialist review)
  (Ref : MHRA advice)

Treatment Duration / Stopping criteria:

Key points

- The advice on "drug holiday" does not apply to denosumab whose bone turnover suppressive effect appears to start wearing off 6 or more months after discontinuation.
- Prescribers must ensure that patients are **recalled to receive denosumab every 6 months**. Compliance to this regimen is very important. Studies of denosumab suggest a rapid loss of gain in bone density and anti-fracture efficacy upon withdrawal.
- The Specialist will advise the GP on the likely appropriate length of treatment at the onset of treatment (may vary on an individual patient basis).
- **Prescribers must ensure that bisphosphonate treatment is discontinued when denosumab is started.**
- A repeat DXA scan should be considered after 3-5 years as part of the ongoing review process. GPs should contact the specialist for advice using 'Advice and Guidance'.
- The optimal total duration of denosumab has not been established. Specialists may recommend for 10 years or even longer, based on the benefits and potential risks of denosumab.

- In line with MHRA advice (Aug 2020), denosumab **should not be stopped or ongoing treatment delayed without a specialist review** (due to increased risk of vertebral fracture).

- **If the specialist advises to stop denosumab treatment, they will advise the GP which alternative treatment the patient may require** as discontinuation of denosumab leads to a sudden drop in bone density and increases the risk of vertebral fractures. Following denosumab with another osteoporosis treatment has been found to stop this from happening.

NB : For patients on glucocorticoid steroids :- see separate guidance for info on treatment duration and stopping criteria for bisphosphonates and denosumab

Vitamin D / Calcium plus Vitamin D supplementation

Back to contents page

- Assess for evidence of vitamin D deficiency and low dietary calcium intake, especially if**:-**
  - >65 years
  - low exposure to sunlight
  - dietary calcium intake <700mg / day
  - risk of falls

- Prescribe vitamin D supplementation **or** calcium plus vitamin D supplementation (if low dietary calcium intake)

  (To assess daily calcium intake using the online calcium intake calculator)

– If Vitamin D monotherapy required:-
prescribe colecalciferol 800 IU.

– If calcium plus vitamin D required:-
prescribe calcium 1-1.2g / colecalciferol 800 IU

If frailty / care home residents:-
– prescribe calcium 1-1.2g / colecalciferol 800 IU

Do not prescribe calcium and vitamin D preparations to people with:
- Any disease or condition that results in hypercalcaemia and/or hypercalciuria (for example some malignancies, such as myeloma).
- Hyperparathyroidism.
- Renal stone disease.
- Hypervitaminosis D.
- Severe chronic kidney disease (chronic kidney disease [CKD] stage 4 or 5).
- An allergy to peanuts or soya — soya oil-free products are available.

Prescribe calcium and vitamin D preparations with caution to people with:
- Mild to moderate CKD (stages 2–3B) or mild hypercalciuria. Manufacturers recommend periodic checks of plasma calcium levels.
- In patients with severe renal failure (creatinine clearance of less than 30 mL/minute) dosage adjustments may be necessary.
- A history of renal stone disease.

- **See eBNF for side effects and drug interaction information regarding calcium and vitamin D preparations.**

Ref CKS

Back to contents page

Calcium & Vitamin D

- Re-analysis of data from a large randomised controlled trial has found a modest increase in the risk of some cardiovascular events in post-menopausal women using calcium and vitamin D supplements to prevent osteoporotic fractures. The MHRA has considered the data, and **no change to prescribing practice is currently recommended. (Oct 2011)** Prescribers should consider the recent data in discussions with patients and weigh the potential benefits and risks of using calcium and vitamin D on an individual basis in line with current NICE guidance.

Bisphosphonates

- **MHRA/CHM advice: atypical femoral fractures (June 2011)**
  Atypical femoral fractures have been reported rarely with bisphosphonate treatment, mainly in patients receiving long-term treatment for osteoporosis.

  The need to continue bisphosphonate treatment for osteoporosis should be re-evaluated periodically based on an assessment of the benefits and risks of treatment for individual patients, particularly after 5 or more years of use.

  Patients should be advised to report any thigh, hip, or groin pain during treatment with a bisphosphonate.

  Discontinuation of bisphosphonate treatment in patients suspected to have an atypical femoral fracture should be considered after an assessment of the benefits and risks of continued treatment.

- **MHRA/CHM advice: Osteonecrosis of the jaw**
  The risk of osteonecrosis of the jaw is substantially greater for patients receiving intravenous bisphosphonates in the treatment of cancer than for patients receiving oral bisphosphonates for osteoporosis or Paget's disease.

  Risk factors for developing osteonecrosis of the jaw that should be considered are: potency of bisphosphonate (highest for zoledronate), route of administration, cumulative dose, duration and type of malignant disease, concomitant treatment, smoking, comorbid conditions, and history of dental disease.

  All patients should have a dental check-up (and any necessary remedial work should be performed) before bisphosphonate treatment, or as soon as possible after starting treatment.

  During bisphosphonate treatment patients should maintain good oral hygiene, receive routine dental check-ups, and report any oral symptoms.

  Guidance for dentists in primary care is included in Oral Health Management of Patients Prescribed Bisphosphonates: Dental Clinical Guidance, Scottish Dental Clinical Effectiveness Programme, April 2011 (available at www.sdcep.org.uk).

Denosumab (Prolia®)

There has been several MHRA Safety Updates issued:-

- **MHRA/CHM advice: atypical femoral fractures (February 2013)**
  Atypical femoral fractures have been reported rarely in patients receiving denosumab for the long-term treatment (2.5 or more years) of postmenopausal osteoporosis

Patients should be advised to report any new or unusual thigh, hip, or groin pain during treatment with denosumab. Discontinuation of denosumab in patients suspected to have an atypical femoral fracture should be considered after an assessment of the benefits and risks of continued treatment.

- **MHRA advice: Minimising the risk of osteonecrosis of the jaw; monitoring for hypocalcaemia – updated recommendations (September 2014): Advice for healthcare professionals**
  (NB: The MHRA have issued advice regarding the use of denosumab 60mg (treatment of osteoporosis) and 120mg (cancer indication).

  The extract below relates to the denosumab 60mg for Osteoporosis indication only. (See MHRA website for full details):-

  Denosumab 60 mg (osteoporosis indication):-

  Osteonecrosis of the jaw

  Check for ONJ risk factors before starting denosumab 60 mg. A dental examination and appropriate preventive dentistry are now recommended for patients with risk factors.

  Tell all patients to maintain good oral hygiene, receive routine dental check-ups, and immediately report any oral symptoms such as dental mobility, pain, or swelling to a doctor and dentist.

  Hypocalcaemia

  Calcium levels should now be monitored as follows:

  Check calcium levels:

  - before each dose
  - within two weeks after the initial dose in patients with risk factors for hypocalcaemia (e.g. severe renal impairment, creatinine clearance <30 ml/min)
  - if suspected symptoms of hypocalcaemia occur.

  Tell all patients to report symptoms of hypocalcaemia to their doctor (e.g. muscle spasms, twitches, or cramps; numbness or tingling in the fingers, toes, or around the mouth).

  Click here for full details regarding ONJ and hypocalcaemia.

- **MHRA advice: reports of osteonecrosis of the external auditory canal (June 2017)**
  The MHRA issued an additional warning in relation to denosumab. The possibility of osteonecrosis of the external auditory canal should be considered in patients receiving denosumab who present with ear symptoms including chronic ear infections or in those with suspected cholesteatoma.
  https://www.gov.uk/drug-safety-update/denosumab-prolia-xgeva-reports-of-osteonecrosis-of-the-external-auditory-canal

- **MHRA DSU, Published August 2020: Increased risk of multiple vertebral fractures after stopping or delaying ongoing treatment**
  In august 2020, the MHRA published a DSU article reporting an increased risk of multiple vertebral fractures in patients within 18 months of stopping or delaying ongoing denosumab 60mg treatment for osteoporosis. Patient's individual benefits and risks should be evaluated before initiating therapy. **Treatment for existing patients should not be stopped without specialist review.**
  Click here for full information: Denosumab: Increased risk of multiple vertebral fractures after stopping or delaying ongoing treatment

General Measures

Back to contents page

- 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

For patients on glucocorticoid steroids :- (see separate guidance)

- Reduce dose of glucocorticoid when possible
- Consider glucocorticoid sparing therapy if appropriate or consider alternative route of administration

References

National Osteoporisis Guideline Group (NOGG) :- Clinical guideline for the prevention and treatment of osteoporosis (Updated December 2024)

CKS :- Osteoporosis - prevention of fragility fractures (Last revised in April 2025)

Abaloparatide for treating osteoporosis after menopause (TA991) (August 2024)

Romosozumab for treating severe osteoporosis (TA791 (May 2022)

Bisphosphonates for treating osteoporosis (TA464(July 2019)

Denosumab for the prevention of osteoporotic fractures in postmenopausal women (TA204) Oct 2010