SOUTH EAST LONDON

OSTEOPOROSIS TREATMENT PATHWAY

Guideline Summary

This clinical guideline outlines the treatment pathway for adult patients with Osteoporosis

This guideline incorporates some of the recommendations from SIGN, NICE, National Osteoporosis Guideline Group (NOGG) and local expert opinion. It adopts a pragmatic approach to assess patients' risk of fracture in conjunction with the use of bone mineral density (BMD) measurement

This guideline was developed by the osteoporosis treatment pathway short life task and finish group via the rheumatology sub-group of the SEL Integrated Medicines Optimisation Committee

Approval date: December 2023 **Review date:** December 2025 **(or sooner if evidence or practice changes)**

South East London Integrated Medicines Optimisation Committee (SEL IMOC). A partnership between NHS organisations in South East London Integrated Care System: NHS South East London (covering the boroughs of Bexley/Bromley/Greenwich/ Lambeth/Lewisham and Southwark) and GSTFT/KCH /SLaM/ Oxleas NHS Foundation Trusts and Lewisham & Greenwich NHS Trust

Contents

1. Scope

This treatment pathway applies to adult patients with a diagnosis of osteoporosis, including post-menopausal women, men and pre-menopausal women diagnosed with osteoporosis (e.g., steroid-induced osteoporosis).

The pathway is set out to guide the treatment options available for primary and secondary prevention of osteoporosis across non-specialist and specialist providers.

2. Rationale

This treatment pathway provides an evidence-based approach for the management of osteoporosis across primary and secondary care, whilst maximising cost-effectiveness and clinical outcomes. The aim is to standardise care across South East London and ensure equitable access to treatments.

3. Background

Osteoporosis is the most common chronic bone disease and is characterised by the loss of bone tissue, accompanied by structural changes, leading to a loss of bone strength and an increased risk of fracture. Osteoporosis results from an imbalance between formation of new bone and resorption (breakdown) of existing bone. In a person with osteoporosis, the bones become porous and brittle, losing their density and strength. Osteoporosis typically develops over a long period of time and is often referred to as a "silent disease" because it progresses without obvious symptoms or signs - until a fracture occurs. Fractures caused by osteoporosis are termed low-trauma or 'fragility' fractures and occur following even minor stresses such as a trip, bending over, coughing, or lifting. The formal definition of a low-trauma or fragility fracture is one that occurs after a fall from standing height or less, and the commonest osteoporotic fractures are spine, hips, and wrist.

One in two women and one in five men will break a bone after age 50 years[1]; and an estimated 549,000 new fragility fractures occur each year in the UK (a third in men) – with population ageing, a 19.6% increase is expected by 2030[2]. Costs of fragility fractures to the NHS exceed £4.7 billion per annum, of which £2.6 billion is directly incurred after an incident fracture (£1.1 billion for hip fractures alone)[3]. As well as the burden of health and social care resources from hip and non-hip fragility fractures, the impact of fractures on individuals can be devastating, leading to loss of independence, mobility and capacity to carry out everyday tasks.

After a first fracture, affected individuals have a high (two-to three-fold) risk of another fracture, particularly within the next 12 months. 23% of second fractures in women over the age of 50 occur within one year of the first event and many of these women are not on any fracture prevention, despite their sentinel event.

Risk factors for osteoporosis are known – both modifiable and non-modifiable. Osteoporosis affects females more than males, older people more than younger people, has social determinants (low income, poor diet, reduced access to physical activity, correlation with smoking and excess alcohol); and risk of osteoporosis is increased by many other conditions and/or their treatment (see table 3.1 below).

Osteoporosis is a clinical diagnosis based on a number of factors (most obviously, a history of low trauma fracture). Tools such as Dual Energy X-ray Absorpiometry (DEXA) scanning and Fracture Risk

Assessment (FRAX) may be used to support the diagnosis, or to identify individuals at risk of osteoporotic fracture, enabling timely intervention. DEXA scans give results in absolute terms (g/cm^2), noting that this is an areal measurement of a volume and in relative terms: a T-score (a measure of bone density compared with the mean and standard deviations (SD) for young healthy adults of the same sex) and Z-scores (compared with age- and gender-matched population).

- A T-score of -1 and +2 is considered 'normal' bone
- T-score of lower than '-2.5' is termed osteoporosis.
- T scores between -1 and -2.4 is termed osteopenia. This is not a disease state, but a description of Bone Mineral Density (BMD) relative to young healthy individuals. To illustrate, by definition 1 in 6 people will have BMD more than one SD below average at the age of 20-30 years, so will have an 'osteopenic' T score. The clinical utility of identifying osteopenia depends on the individual patient (e.g., it may provide the rationale for considering bone protection in someone on high-dose steroids); but it does not necessarily require management or monitoring.

The use of BMD alone to assess fracture risk has a high specificity but low sensitivity. Thus, although individuals with lower BMD are at highest individual risk for osteoporotic fractures, most osteoporotic fractures will occur in people who do not have T-score lower than -2.5. BMD results should not be reviewed in isolation when making the diagnosis of osteoporosis in an individual with a low-trauma fracture; it is important to also consider the individual patient factors and characteristics which are presented.

3.1 Diagnosis

Ø Who is at risk of osteoporosis?

Risk Category	Causative Factor
Non-modifiable risk factors	**Previous fracture** **Parental history of osteoporosis** **History of early menopause (below age of 45)**
Modifiable risk factors	**Low BMI (<20kg/m²)** **Smoking (risks associated with vaping unknown)** **Low bone mineral density** **Excess alcohol intake**
Co-existing disease	**Coeliac disease** **Diabetes mellitus** **Inflammatory musculoskeletal diseases** **Inflammatory bowel disease** **Malabsorption** **Institutionalised patients with or without epilepsy** **Human immunodeficiency virus** **Primary hyperparathyroidism and endocrine diseases** **Chronic liver disease** **Neurological diseases (including Alzheimer's disease, Parkinson's disease, multiple sclerosis, stroke)** **Moderate to severe chronic kidney disease (including end stage renal failure)**
Drug Therapy *This is not an exhaustive list.*	**Oral glucocorticoids** **Anti-epileptics** **Aromatase inhibitors** **Androgen deprivation therapy** **Long-term antipsychotics (associated with hyperprolactinaemia)** **Chronic proton pump Inhibitors** **Thiazolidinediones (oral hypoglycaemic agent)**

Adapted from: *Scottish Intercollegiate Guidelines Network (SIGN)[4].*

Ø Diagnosing osteoporosis

Assessments should include:

- Past medical history with a focus on risk factors for osteoporosis *(modifiable and non-modifiable – see above list)*
- Lifestyle history with focus on smoking cessation, safe alcohol consumption, and weight-bearing activity
- Falls risk *(falls history, screen of vision, balance, MSK disease, L&S BP, peripheral neuropathy)*
- Frailty assessment *(Timed Up and Go test [TUAG] or grip strength, Clinical Frailty Scale [CFS])* and cognitive screen *(concordance, higher level balance problem)*
- FRAX score *(especially for primary prevention)*

Diagnosis is clinical, largely based on assessment of risk factors and previous fracture history. DEXA scanning may help in establishing the diagnosis or when considering specialist treatments, but it is not a requirement for diagnosis or starting treatment. For example, osteoporosis can be confidently diagnosed and treated without DEXA in the following situations:

- Postmenopausal women >64 years old with vertebral compression fractures, in the absence of a pertinent history of trauma
- A neck of femur (NOF) fracture in a >74 year old
- A fragility fracture in nonagenarian (person above 90 years old) or in a person living with moderate to severe frailty (CFS ≥6)

Ø Investigations

There is no diagnostic blood test for osteoporosis. However, bloodwork analysis is important in identifying potential causes and mimics and is critical in personalised planning of pharmacological treatments; this is usually carried out by initiating clinician.

Baseline bloodwork may include:

- Renal profile
- Bone profile, vitamin D level and PTH
- Liver function tests
- TFT and coeliac screen
- ESR and FBC

If ESR is raised without straightforward explanation, especially in those >75 years of age, a myeloma screen may be indicated.

A DEXA scan is frequently undertaken in the diagnostic work-up of osteoporosis, but it is not always required for diagnosis. The World Health Organisation[5] describe osteoporosis as the presence of bone mineral density (BMD) measurement equal to or more than 2.5 SD below the average BMD of a 30-year-old female (T-score ≤-2.5 SD). However, there are many situations where a DEXA scan is not required for diagnosis of osteoporosis (for example after a low trauma hip fracture in an elderly person). Research studies which provide the evidence-base for drug treatment of osteoporosis, largely use fracture reduction as the primary outcome, not change in T-score. Please see section 4.4 for more information.

3.2 Glucocorticoid-Induced Osteoporosis

The highest rate of bone loss occurs within the first 3-6 months of starting steroid treatment and decreases rapidly after steroid cessation[6]. When considering bone protection in individuals on oral steroids, some nuances in treatment choice might be appropriate. For example, in someone starting a 3 - 6 month course of steroids, risedronate (a powerful but short-acting bisphosphonate) might be the best option. In contrast, in someone in whom the course of steroid is likely to be 1 - 2 years, a dose of zoledronic acid early after treatment commences might be a good option.

Initiation of bone-protective treatment is recommended (at the same time as glucocorticoid initiation, without waiting for a DEXA scan to be performed) in the following people:

- Women and men aged 70 years or older prescribed oral steroids at any dose
- Postmenopausal women of any age, and men aged 50 – 70 years or older, if starting the equivalent of 7.5mg/day or greater of prednisolone
- Postmenopausal women of any age, and men aged 50 – 70 years or older, with a FRAX probability of a major osteoporotic fracture/ hip fracture exceeding the intervention threshold.
- Anyone with a prior fragility fracture prescribed steroids at any dose *(to note this patient cohort should already be on appropriate anti-fracture treatment)*

Patients initiated on less than prednisolone 7.5mg/ day (or equivalent) who have a FRAX probability near to, but below, the intervention threshold should have their FRAX repeated after 12-18 months with a BMD if they remain on steroids.

Treatment of younger male and female patients may be appropriate in some scenarios, particularly those with previous history of fracture. This should be initiated by a secondary care specialist using FRAX as a tool to support decision making.

Treatment options for glucocorticoid-induced osteoporosis include:

- Alendronic acid)/ risedronate *(weekly dosing - off-label)*
  - For those expected to be on long-term steroids (more than 3 months), plan for a treatment duration of 5 years then review
  - For those expected to be on short-term steroids (less than 3 months), consideration should be given for use of a shorter-acting bisphosphonate (e.g., risedronate), particularly in younger individuals. This should be for the duration of the steroid treatment.
  - These treatments are non-specialist and therefore should be initiated alongside or at the point of steroids being initiated and do not routinely require referral to bone specialist or equivalent
- Zoledronic acid
  - For those on long term steroids, plan for a treatment duration of 6 years or longer
- Denosumab
  - Should typically be reserved for those expected to be on longer–term steroid treatment. Treat for 5 years and then reassess. Do not stop without initiating alternative bone protection.

4. Treatment Pathway

4.1 Suggested referral into specialist care for:

- Osteoporosis in premenopausal women
- Osteoporosis in men aged <60 years old
- Treatment difficulties (e.g., intolerance to both alendronic acid and risedronate, despite review of drug administration)
- Individuals who fracture after 12 months of treatment, with good compliance
- Glucocorticoid-induced osteoporosis, if unable to be managed according to existing guidelines such as NICE CKS and National Osteoporosis Guideline Group (NOGG)

Please see flowchart 4.6 and 4.7 below for further information

4.2 Calcium and Vitamin D Supplementation[7,8,9,10]

- Despite extremely large studies there is little evidence that supplemental calcium and/or vitamin D, reduce fracture risk substantially in most individuals living in the community. **Therefore, calcium and/or vitamin D should not be regarded as adequate treatment or prevention of osteoporosis.**
- There is some evidence that calcium and vitamin D may reduce fracture in individuals in residential care; however, there is also good evidence that increasing dairy intake in these individuals can prevent both fractures and falls
- In individuals receiving antiresorptive drugs, usual clinical practice is to ensure sufficient calcium intake and vitamin D levels (e.g., to avoid hypocalcaemia). Here 'sufficient' means a calcium intake >1g/daily and vitamin D level of >50nmol/L (and >70nmol/L before going into winter).
- There is little additional benefit for giving calcium in individuals with excellent dairy intake (3-4 serves a day, equivalent to >1g daily), whether or not someone is on an antiresorptive agent. To see whether a patient is getting enough calcium from what they eat and drink, an online calcium calculator is available here. The calcium content of non-dairy products can be accessed here.
- There is little additional benefit in giving supplementary vitamin D in individuals who already have sufficient vitamin D levels, whether or not someone is on an antiresorptive agent
- When co-prescribing vitamin D supplements with an oral anti-resorptive agent (e.g. alendronic acid or risedronate), dose will depend on prior vitamin D status. Some individuals may require a loading dose before moving to a maintenance dose (typically, 1000-2000 IU daily).
- For patients about to start a parenteral anti-resorptive agent (e.g. zoledronic acid or denosumab), rapid correction of vitamin D deficiency may be required (to reduce the risk of hypocalcaemia). Consider prescribing a treatment loading regimen if the vitamin D level is below 50nmol/L, followed by regular maintenance doses. See SEL vitamin D guidelines for further information.

4.3. Bone Turnover Markers

- Bone turnover markers (BTM) are not routinely used in simple osteoporosis care but can be a useful tool in measuring efficacy of antiresorptive medication, particularly where compliance is unclear
- Potential areas of further utility are in prediction of atypical femoral fractures, and determining duration of bisphosphonate treatment suspension

- Serum C-terminal telopeptide of type I collagen (CTX-I, a resorption marker) and serum propeptide of type I collagen (PINP, a formation marker) are the most commonly used BTM. P1NP has lower circadian rhythm and is less affected by food intake, compared with CTX. P1NP is therefore often the preferred BTM in clinical practice as translation to the primary care setting is uncomplicated.
- All BTMs are elevated after recent fracture and therefore levels are difficult to interpret in the immediate post fracture period (pragmatically, up to a year).

4.4 Repeat DEXA Scan

DEXA scans are sometimes repeated after a course of osteoporosis treatment (for detailed rationale please see NOGG guidance for more information). However, treatments are designed to reduce risk of further fracture, and the reduction in fracture risk with appropriate treatments for osteoporosis (typically, 50-60% for vertebral fracture and 30% for non-vertebral fractures) is much greater than BMD change (typically 1-2% per annum with bisphosphonates, mainly due to excess mineralisation in bone with reduced turnover). Therefore, DEXA scans should only be undertaken if the result will change management. For most individuals, there is little reason to repeat DEXA until at least five years after starting treatment.

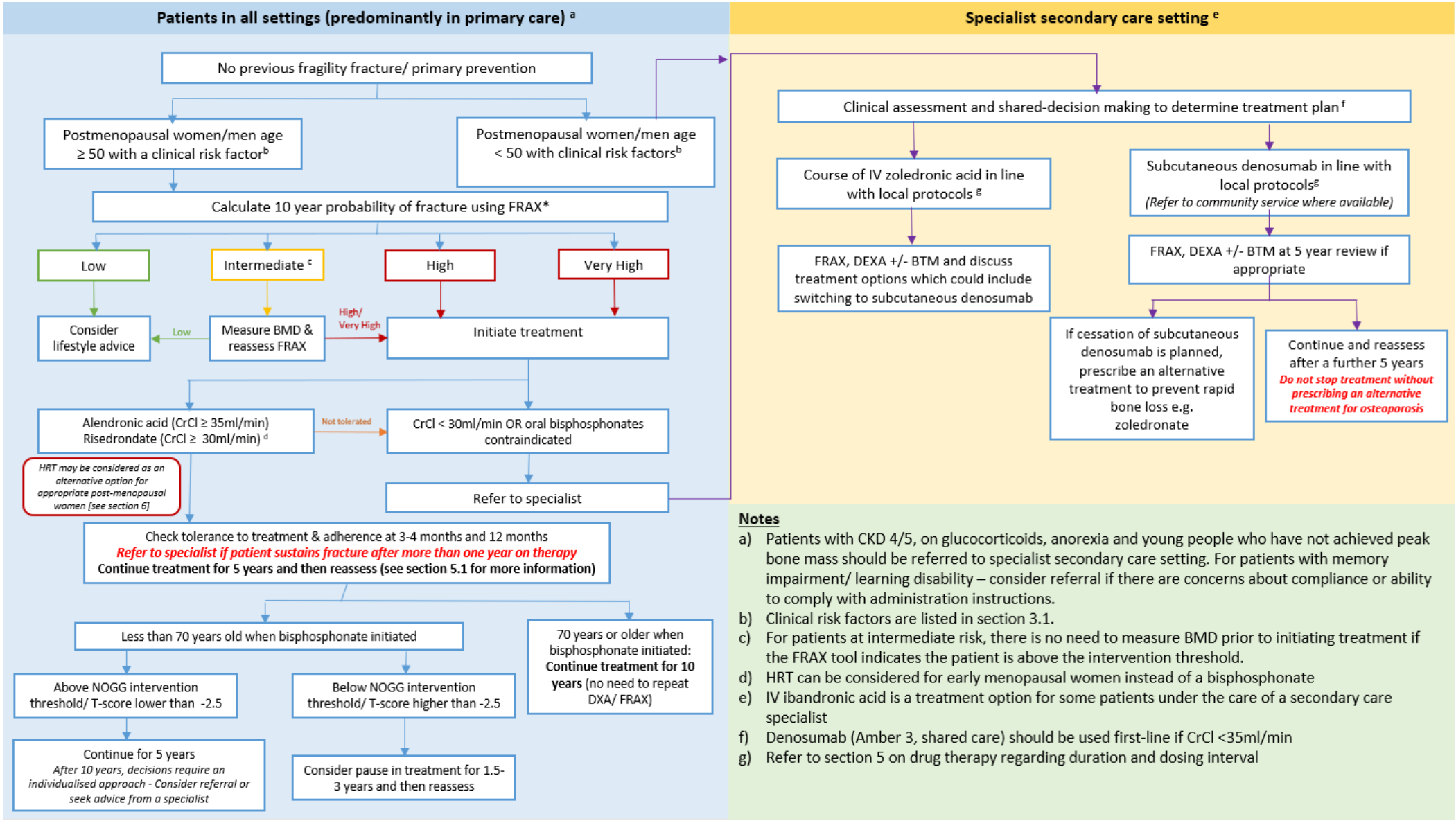
4.5 Overprescribing Considerations

All patient encounters provide opportunity for deprescribing. Some medications such as proton pump inhibitors can often persist on routine prescriptions long after a steroid or antiplatelet has been stopped. Antihypertensive medications may increase falls risk in older adults as other changes in an individual's physiology or multimorbidity alter their homeostasis.

Pauses in treatment can be considered with bisphosphonate therapy, reducing burden of treatment at intervals (see section 4.6, 4.7 and section 5 for more information), further information available via the Royal Osteoporosis Society. Calcium +/- vitamin D replacement may be appropriate in individuals receiving specific osteoporosis therapy (such as antiresorptive therapies in individuals in residential care and at high risk of deficiency). However, there is no evidence for prescribing calcium/vitamin D in isolation.

All patient encounters present an opportunity for potential deprescribing of medications as part of personalised care, reflecting changes in treatment burden, symptoms, risk and benefits and patient choice.

4.6 Primary Prevention of Fragility Fractures



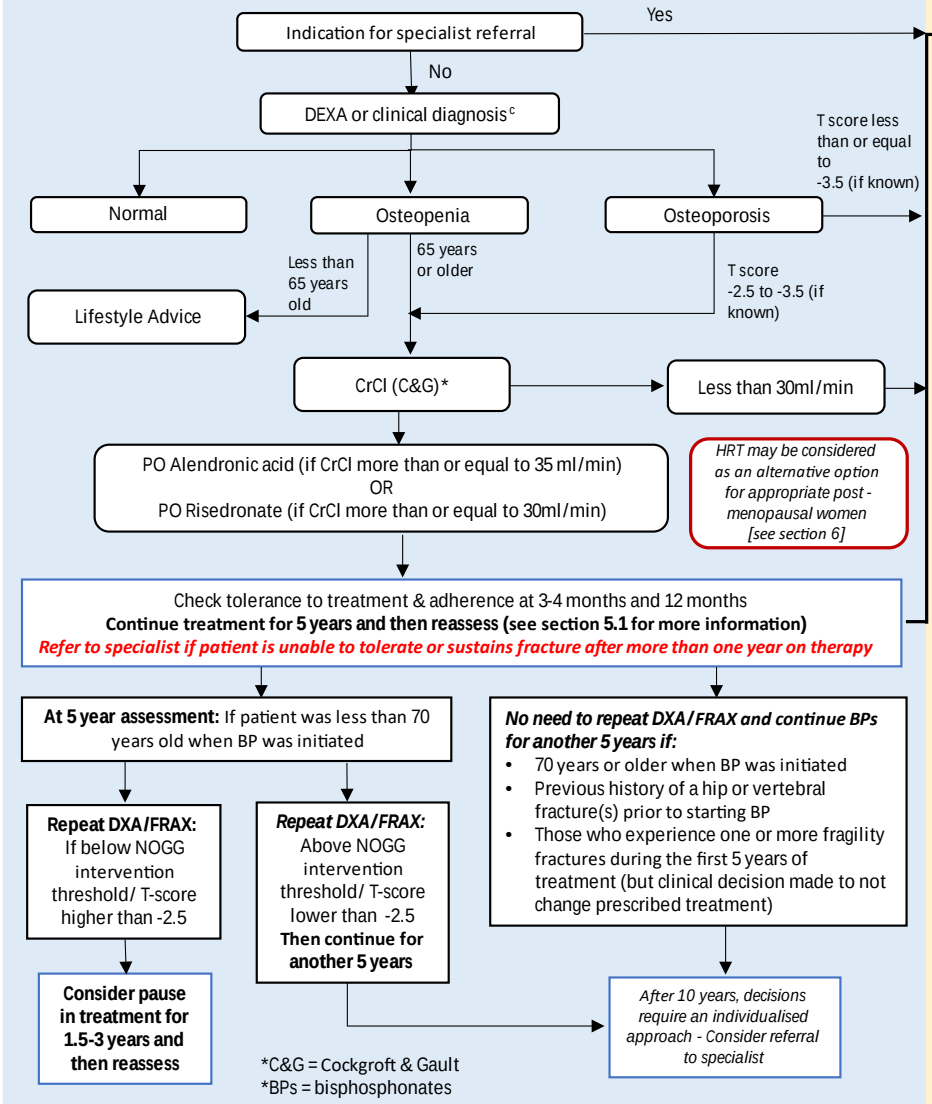
Notes

a) Patients with CKD 4/5, on glucocorticoids, anorexia and young people who have not achieved peak bone mass should be referred to specialist secondary care setting. For patients with memory impairment/ learning disability – consider referral if there are concerns about compliance or ability to comply with administration instructions.
b) Clinical risk factors are listed in section 3.1.
c) For patients at intermediate risk, there is no need to measure BMD prior to initiating treatment if the FRAX tool indicates the patient is above the intervention threshold.
d) HRT can be considered for early menopausal women instead of a bisphosphonate
e) IV ibandronic acid is a treatment option for some patients under the care of a secondary care specialist
f) Denosumab (Amber 3, shared care) should be used first-line if CrCl <35ml/min
g) Refer to section 5 on drug therapy regarding duration and dosing interval

*Fracture Risk Assessment Tool (FRAX)

4.7 Secondary Prevention of Fragility Fractures

Patients in all settings (predominantly in primary care)[a]



Specialist secondary care setting

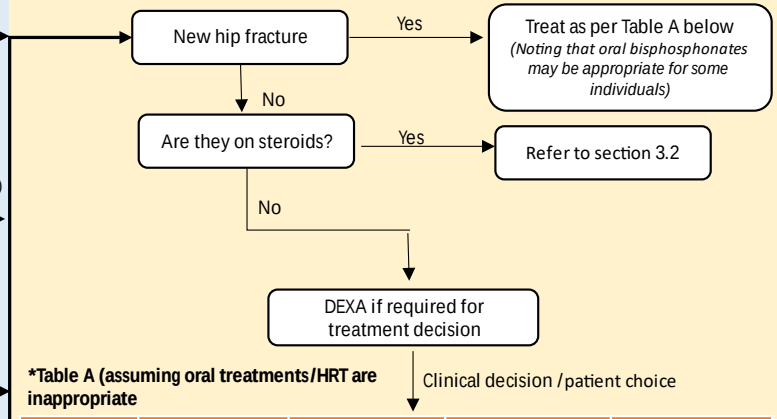


***Table A (assuming oral treatments/HRT are inappropriate**

Drug:	IV Zoledronic acid	Subcutaneous Denosumab	Subcutaneous Teriparatide	Subcutaneous Romosozumab *postmenopausal women only
Clinical Eligibility	All patients (assuming CrCl above 35 ml/min)	All patients	Consider in all patients who meet NICE/NHSE criteria. *See full criteria in additional notes section*	1) Severe osteoporosis 2) Major osteoporotic fracture in last 24 months *see further information in Section 5.5*

Denosumab can be prescribed in non specialist settings in line with the Amber 3 (shared care) formulary categorisation

For switching treatment e.g. new fragility fractures on treatment, adverse drug reactions, new contraindication à specialist to consider alternative treatment options available as per Table A

Additional Notes

a) Referral to specialist secondary care setting:
Patients with CKD 4/5, difficult to manage patients on glucocorticoids, anorexia and young people who have not achieved peak bone mass. Consider referral for patients if there are concerns about compliance or ability to comply with administration instructions, for example patients with a learning disability or dementia.

If an individual fractures after at least 12 months of treatment, they may be eligible for anabolic treatments, so should be considered for specialist referral.

b) Clinical risk factors are listed in Section 3.1.
c) If there is clear evidence of Osteoporosis without a DXA scan i.e. presence of fragility fractures in presence of clinical risk factors, do not delay treatment.
d) Ibandronic acid is a treatment option for some patients under the care of a secondary care specialist
e) Refer to section 5 on drug therapy regarding duration and dosing interval

Teriparatide Eligibility

- Unable to take/contraindication to alendronate and risedronate or who have had an unsatisfactory response to treatment with alendronate or risedronate **AND**
- 65 years or older with a Tscore of –4.0 SD or below, or a Tscore of –3.5 SD or below plus more than two fractures **OR**
- 55–64 years and have a Tscore of –4 SD or below plus more than two fractures.

5. Drug Information

NB. For full list of side effects, cautions and contraindications, please see the BNF and Summary of Product Characteristics. Some of these drugs are subject to MHRA alerts; please follow links below to MHRA website for further details.

5.1 Oral Bisphosphonates	
Dose	Alendronic acid – 70mg once weekly (off-label in men) (CrCl ≥ 35ml/min) Risedronate sodium – 35mg once weekly (CrCl ≥ 30ml/min) *Weekly dosing off-label for the management of glucocorticoid-induced osteoporosis*
Recommended Duration of therapy	Check treatment tolerance after 12 to 16 weeks and check adherence at 1 year. Continue treatment for 5 years. At 5 years, or sooner if fracture sustained or risk factors change, reassess adherence, risk factors and treatment choice. This may include a FRAX assessment and BMD measurement. Longer durations of treatment, for at least 10 years, are recommended in the following men and women: · Age ≥70 years at the time that the bisphosphonate is started, or · Who have a previous history of a hip or vertebral fracture(s), or · Treated with oral glucocorticoids ≥7.5 mg prednisolone/day or equivalent, or · Who experience one or more fragility fractures during the first 5 years of treatment (if treatment is not changed). After 10 years, treatment decisions should be made on an individual basis. Specialist advice may need to be sought.
Supporting information	· NICE TA 464 bisphosphonates for treating osteoporosis patient decision aid · MHRA/CHM advice - Bisphosphonates: atypical femoral fractures (June 2011) - Atypical femoral fractures have been reported rarely with bisphosphonate therapy, mainly in patients receiving long-term treatment for osteoporosis; atypical femoral fractures are considered a class effect of bisphosphonates - During bisphosphonate treatment, patients should be advised to report any thigh, hip, or groin pain. Any patient who presents with such symptoms should be evaluated for an incomplete femur fracture

	· MHRA/CHM advice - Bisphosphonates: osteonecrosis of the jaw (November 2009) - The risk of developing osteonecrosis of the jaw (ONJ) in association with oral bisphosphonates seems to be low. The risk of ONJ is substantially greater for patients receiving intravenous bisphosphonates for cancer indications than for patients receiving oral bisphosphonates for osteoporosis or Paget's disease. - There is clear evidence to suggest there is bisphosphonate-specific and indication-specific risk factors for ONJ such as potency (highest for zoledronic acid); route of administration (e.g., intravenous ibandronate, pamidronate, and zoledronic acid); and cumulative dose. - A history of dental disease, including invasive dental procedures, dental trauma, periodontal disease, and poorly fitting dentures is associated with an increased risk. - All patients with cancer should have a dental check-up before bisphosphonate treatment. All other patients who start bisphosphonates should have a dental examination only if they have poor dental status. - During bisphosphonate treatment, patients should maintain good oral hygiene, receive routine dental check-ups, and report any oral symptoms such as dental mobility, pain, or swelling of ONJ. · MHRA/CHM advice - Bisphosphonates: very rare reports of osteonecrosis of the external auditory canal (December 2015) - The possibility of osteonecrosis of the external auditory canal should be considered in patients receiving bisphosphonates who present with ear symptoms, including chronic ear infections, or in patients with suspected cholesteatoma - Possible risk factors include steroid use and chemotherapy, with or without local risk factors such as infection or trauma - Patients should be advised to report any ear pain, discharge from the ear, or an ear infection during bisphosphonate treatment

5.2 Zoledronic acid (Red – hospital only)

Dose	**Licensed dosing:** 5mg given intravenously every 12 months. **Extended dosing interval (off-label)**[11,12,13]: Alternatively, on specialist advice, the dosing interval may be extended up to 18 months in the **non-hip fragility fracture population** i.e., 3-4 doses administered over up to 4.5-6 years. As per SIGN guidance, the following patients may be suitable for extended interval dosing: · Primary prevention: 1. Age ≥ 65 years 2. 10-year risk ≥10% 3. DXA scan: T score -1.0 to -2.5 (if clinically appropriate or available)

	· Secondary prevention: 1. Age ≥ 65 years 2. DXA scan: T score -1.0 to -2.5 (if clinically appropriate or available) **It is increasingly clear that a lower dose and longer spacing between zoledronic acid treatments can still provide excellent fracture protection for women with osteopenia[12] and men and women with osteoporosis[13]. There is extremely similar reduction in fracture and improvement in BMD whilst acknowledging not head-to-head comparisons[12].** It is not the intention of this document to be overly prescriptive regarding exact dosing and dosing intervals, as all treatment decisions are individualised, patient centered and based on previous treatment success e.g., BMD, frailty, dementia, residential care considerations, contemporaneous glucocorticoid use, etc. Using bone turnover markers to guide dosing frequency may be a reasonable means of tailoring personalised approaches in individual patients, at clinician's discretion. Excellent fracture prevention has been shown with longer dosing intervals (e.g., 5mg every eighteen months, over six years[11]) and even after a single 5mg dose - extremely similar fracture reduction and BMD improvement over three years was seen after a single dose of zoledronate, compared with annual dosing for three years[12,13], acknowledging this was not a head-to-head comparison. As an example of individual tailoring of these off-label options, a single dose may be appropriate to provide appropriate fracture protection for a frail elderly individual with life expectancy less than 3 years; if the individual survives longer than expected another dose could then be considered.
Recommended Duration of therapy	3 years (or 3 doses for patients on extended dosing intervals) and then re-assess fracture risk. For patients on 12 monthly dosing schedules, longer durations of treatment, for at least 6 years, are recommended in the following men and women: · Age ≥70 years at the time that the bisphosphonate is started · Who have a previous history of a hip or vertebral fracture(s) · Treated with oral glucocorticoids ≥7.5 mg prednisolone/day or equivalent · Who experience one or more fragility fractures during the first 3 doses of treatment (if treatment has not changed). Clinical review to re-assess fracture risk after 3 doses; review sooner if fracture sustained during treatment or risk factors change (e.g., start glucocorticosteroids). This may include repeat DXA scan (see NOGG guidelines for further information).
Supporting information	**Post hip fracture** Zoledronic acid is recommended first line post hip fracture for suitable patients. In line with licensing, it is recommended to wait at least two weeks after hip fracture repair, although it is acknowledged that due to reasons of practicalities, it may be given earlier as patients must be provided infusion prior to discharge.

	MHRA/CHM advice: Denosumab (Xgeva™ and Prolia™); intravenous bisphosphonates: osteonecrosis of the jaw—further measures to minimise risk (July 2015) The risk of osteonecrosis of the jaw should be explained to patients and the precautions to take, patients should be advised to: · tell their doctor if they have any problems with their mouth or teeth before starting treatment; if they wear dentures, they should make sure their dentures fit properly before starting treatment · maintain good oral hygiene and get routine dental check-ups during treatment · tell their doctor and dentist that they are receiving denosumab or an intravenous bisphosphonate if they need dental treatment or dental surgery · tell their doctor and dentist immediately if they have any problems with their mouth or teeth during treatment (e.g. loose teeth, pain, swelling, non-healing sores or discharge)

5.3 Denosumab (Prolia™) (Amber 3 – shared care)	
Dose	60mg subcutaneous injection every 6 months
Recommended Duration of therapy	Current evidence shows safety and efficacy are maintained for at least 10 years of treatment
Supporting information	**Recognised risk of hypocalcaemia** · Denosumab is contraindicated in patients with hypocalcaemia; this should be corrected before starting treatment · Risk of post dose hypocalcaemia increases in patients with a CrCl of less than or equal to 30ml/min; check serum corrected calcium level two weeks after each dose · Patients established on haemodialysis or peritoneal dialysis - consider increasing monitoring frequency e.g., weekly levels for 4 weeks. · Adequate intake of calcium and vitamin D is important in all patients. **MHRA Drug Safety Update: Risk of vertebral fractures on interruption or cessation of treatment (2022):** · Denosumab cessation leads to rapid reductions in BMD and elevations in bone turnover to levels above those seen before treatment initiation · Therefore, patients who discontinue denosumab have an increased risk of sustaining multiple vertebral fractures. · If denosumab therapy is stopped, prescribe an alternative treatment to prevent rapid bone loss e.g. zoledronic acid after the last injection of denosumab if suitable · If zoledronic acid is given post denosumab, bone turnover markers may be measured 3 and 6 months after administration of zoledronic acid. This can help to guide subsequent zoledronic acid infusions

	See section 5.2 for more information regarding MHRA/CHM advice: Denosumab (Xgeva™ and Prolia™); intravenous bisphosphonates: osteonecrosis of the jaw—further measures to minimise risk (July 2015) *Please see SEL denosumab (Prolia ®) for the treatment of osteoporosis and prevention of osteoporotic fractures in adults shared care guideline for further information*

5.4 Teriparatide (Red – Hospital only) (*local choice of most cost-effective brand)	
Dose	20 microgram subcutaneous injection every day for 24 months
Recommended Duration of therapy	24 months as per NICE TA 161
Supporting information	To be prescribed in accordance with NICE TA 161 - Raloxifene and teriparatide for the secondary prevention of osteoporotic fragility fractures in postmenopausal women and NHS England Interim Clinical Commissioning Policy Statement: Teriparatide for Osteoporosis in Men (Adults). **Transient elevations in calcium:** · In normocalcaemic patients, slight and transient elevations of serum calcium concentrations have been observed following teriparatide injection. Serum calcium concentrations reach a maximum between 4 and 6 hours and return to baseline by 16 to 24 hours after each dose of teriparatide. Therefore, if blood samples for serum calcium measurements are taken, this should be done at least 16 hours after the most recent teriparatide injection. **Stopping treatment:** · Initiate treatment with anti-resorptive without delay after completion of the course. This should be planned at the time teriparatide is instigated to avoid a gap in treatment. **Homecare:** · Teriparatide is provided by a homecare service, which includes delivery of the injections and injection training if required. Patients should be deemed competent to self-administer or a suitable carer that can support a daily injection to facilitate treatment.

5.5 Romosozumab (Evenity™) (Red – hospital only)	
Dose	210mg subcutaneous injection once a month for 12 months
Recommended Duration of therapy	12 months as per NICE TA
Supporting information	To be prescribed in accordance with NICE TA 791 - Romosozumab for treating severe osteoporosis: · Post-menopausal women · A major osteoporotic fracture (spine, hip, forearm or humerus fracture) within the last 24 months · Severe osteoporosis, usually defined by a T score of lower than -2.5 and an osteoporotic/fragility fracture **Cardiovascular risk:** · Romosozumab is contraindicated in patients with a history of myocardial infarction or stroke · Carefully consider cardiovascular risk vs fracture risk over the following 12 months and ensure shared decision making with patient to come to a personalised decision **Hypocalcaemia:** · Romosozumab is contraindicated in patients with hypocalcaemia; correct before starting treatment **Homecare:** · Romosozumab may be provided by a homecare service, which includes delivery of the injections and injection training if required

5.6 Additional Treatment Options	
Intravenous ibandronic acid (Red)	This treatment option is available for treating post-menopausal women at increased risk of fracture, who do not tolerate oral bisphosphonates in line with NICE TA 464. However, IV ibandronate is not the usual first choice for parenteral bisphosphonates as although a reduction in the risk of vertebral fractures has been demonstrated, efficacy on femoral neck fractures has not been established. **Please note oral ibandronate is non-formulary in SEL.**
Raloxifene	Can be prescribed to post-menopausal women in accordance with NICE TA 160 (primary prevention) and NICE TA 161 (secondary prevention)
Hormone Replacement Therapy (HRT)	HRT is an alternative treatment option available for post-menopausal women at increased risk of fracture. Please see NICE guideline NG23 – Menopause diagnosis and management for further information

6. Appendix

Appendix 1: Anti-fracture efficacy of approved drug treatments for postmenopausal women, and men, with osteoporosis when given with calcium and vitamin D

Intervention	Vertebral fracture	Non-Vertebral fracture	Hip fracture	Evidence of superiority or inferiority for vertebral fracture prevention in postmenopausal women with very high fracture risk	Licenced for use in Men
Romosozumab	Ib	IIb	IIb	Superior to Alendronate (Ib)	No
Teriparatide	Ia	Ia	Ia	Superior to Risedronate (Ib)	Yes
Alendronate	Ia	Ia	Ia	Inferior to Romosozumab (Ib)	Yes
Ibandronate	Ib	Ib	NAE	NAE	No
Risedronate	Ia	Ia	Ia	Inferior to Teriparatide (Ib)	Yes
Zoledronate	Ia	Ia	Ia	NAE	Yes
Calcitriol	IIa	NAE	NAE	NAE	Yes
Denosumab	Ia	Ia	Ia	NAE	Yes
HRT	Ia	Ia	Ia	NAE	No
Raloxifene	Ia	NAE	NAE	NAE	No
Strontium Ranelate	Ia	Ia	IIb	NAE	Yes

Taken from National Osteoporosis Guideline Group UK (NOGG)[3]

HRT: hormone replacement therapy
NAE: No available evidence
Ia: Systematic reviews or meta-analysis of level I studies with a high degree of homogeneity
Ib: Systematic reviews or meta-analysis with moderate or poor homogeneity
IIa: Systematic reviews or meta-analysis of level II studies
IIb: Level II studies (inappropriate population or lacking an internal control)

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