BEDFORDSHIRE, LUTON AND MILTON KEYNES AREA PRESCRIBING COMMITTEE (APC)

OSTEOPOROSIS

GUIDELINES FOR PRIMARY CARE

(updated June 2022)

The following organisations contribute to and participate in the BLMK APC – Bedfordshire, Luton and Milton Keynes Clinical Commissioning Group; 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

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Introduction

These guidelines cover :-

- Management of osteoporosis in post-menopausal women and men (age ≥ 50 years) in primary care (both primary and secondary prevention of osteoporotic fragility fractures)

- Prevention and Treatment of glucocorticoid-induced osteoporosis in post-menopausal women and men (age ≥ 50 years) (in primary care)

NB: 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 Decision Aid for the use of bisphosphonates in the treatment of osteoporosis - **Click here**

Specialist Advice :-

The relevant hospital specialists can be contacted via the Advice and Guidance' facility.
If a GP has a patient who they regard as 'at risk of osteoporosis' and requires DXA but does not fit the criteria within these guidelines, please contact the relevant specialist for advice using the 'Advice and Guidance' facility.

Luton and Dunstable Hospital

- Dr Muhammad Nisar, Consultant Physician,
- Dept email :- ldh-tr.rheumatologyluton@nhs.net

- **Bedford Hospital**
- Dr Sarah Rae, Consultant Rheumatologist, Tel 01234 792280 or email Sarah.Rae@bedfordhospital.nhs.uk

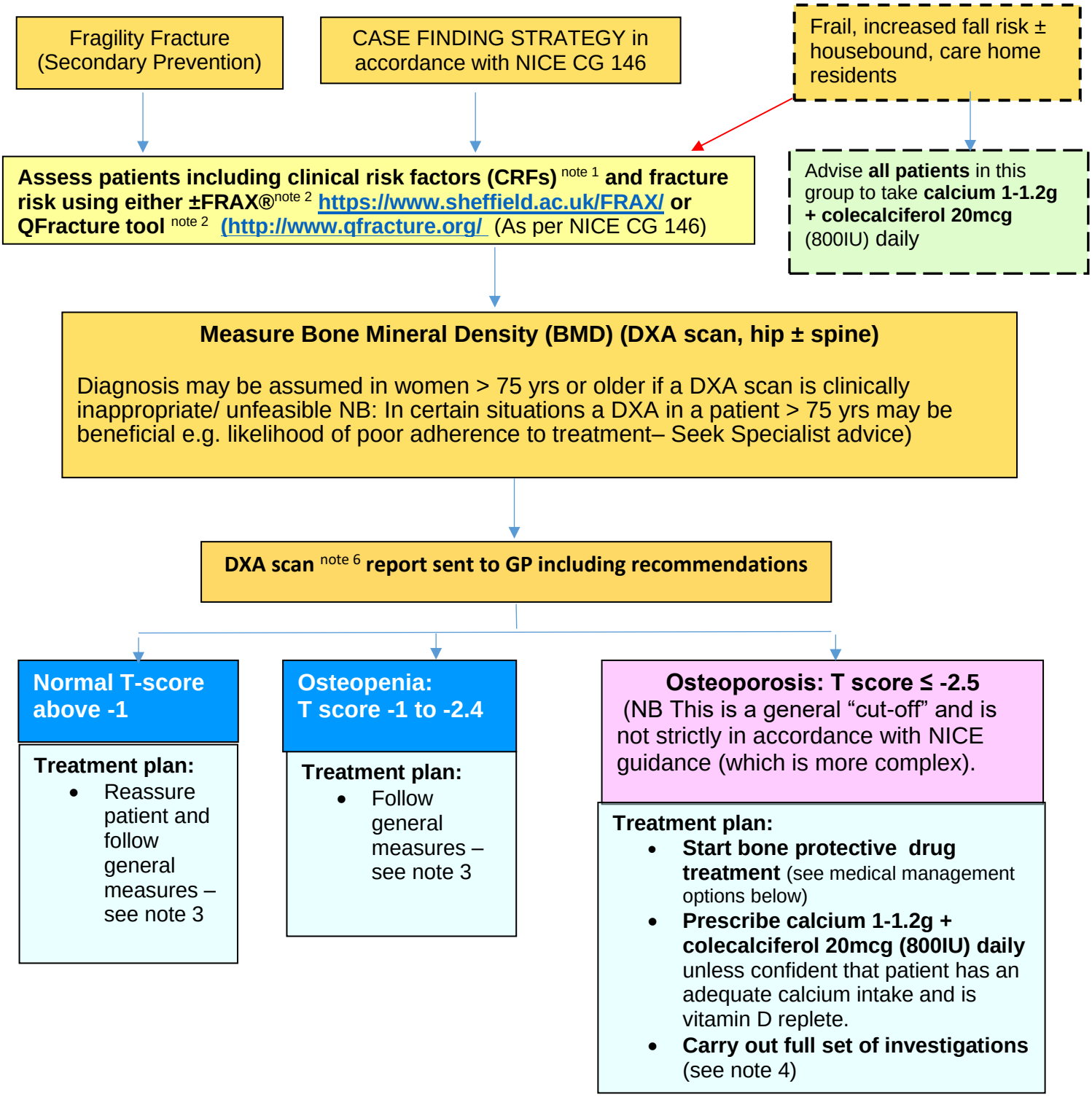
Milton Keynes Hospital

- Dr Ioanna Papadaki , Consultant Rheumatologist

Management of Osteoporosis in Post-Menopausal Women & in Men (age ≥ 50 years) in the Primary Care Setting

(Pre-menopausal women and men less than 50 years should be referred to a metabolic bone disease specialist) **– Algorithm A**

Stage 1: Patients with Suspected Osteoporosis: – Investigations and Diagnostic Tests



STAGE 2 MEDICAL MANAGEMENT

1. Choice of therapy should be tailored to the individual and patient choice must be factored in.
2. Licensed indication for individual bisphosphonates vary, in particular relating to their use in men – see note 7
3. Consult electronic BNF or Summary of Product Characteristics (SmPC) for full prescribing details (e.g. licensed indications, contra-indications, use in elderly, renal, hepatic impairment, counselling, adverse effects etc.).
4. Ensure dental examinations are carried out as appropriate before starting bisphosphonate/ denosumab therapy and give advice regarding dental hygiene etc. due to risk of Osteonecrosis of the Jaw (ONJ) associated with these medications. (See supporting notes for more information)
5. Clinicians should seek specialist opinion if patient sustains a fracture on therapy

First Line Choices: Treatment options depend on 10 year probability of osteoporotic fracture risk:-

If 10-year probability of osteoporotic fragility fracture is at least 1%:

- **Consider treatment with an oral bisphosphonate:-**
  - Use either **alendronic acid 70mg WEEKLY tablets or risedronate sodium 35mg WEEKLY tablets** (Ibandronic acid 150mg MONTHLY tablets can be used as an alternative if compliance is an issue)
  - NB local specialists advise that although not licensed for use in men, once weekly alendronate is routinely used (off label use) - See note 7, for summary of licensed indications)

If 10-year probability of osteoporotic fragility fracture is at least 10%:

- **Consider treatment with an IV bisphosphonate:-**
  - use either **IV zoledronic acid or IV ibandronic acid** (NB: Local specialists favour IV zoledronic acid as it is given once a year.) (See note 7 for summary of licensed indication)

NB: In patients with **SEVERE RENAL IMPAIRMENT** (GFR < 35ml/min) **–** use **denosumab (Prolia®)** s/c **first line** as po/IV bisphosphonates should be avoided in severe renal impairment

Additional Prescribing notes:

- All bisphosphonates should be prescribed generically
- **IV zoledronic acid or IV ibandronic acid can** be used for patients with a 10yr probability of osteoporotic fragility fracture of at least 1% who have difficulty taking an oral bisphosphonate or if there are any contraindications or intolerances to any of the oral options listed above

Second Line Choice (when using oral therapy)

- An alternative oral bisphosphonate can be used as a 2nd line option if contraindications, intolerance, poor compliance or poor response to the initial choice of oral bisphosphonate occurs. (See note 5).
- Alendronic acid is also available as an effervescent tablet or as a liquid however please note these preparations are considerably more expensive and use should be limited to specific patients only)

Third Line Choices (choice to be determined by Specialist)

Consider treatment with either:-

- **denosumab (Prolia®) 60mg s/c every 6 months or IV zoledronic acid 5mg once a year or IV Ibandronic acid 3mg every 3 months**

Additional Prescribing notes:

- **Denosumab-** Initial dose to be given by specialist team then GP to take over prescribing, monitoring responsibility and arrangement of administration (See separate JPC guidance on denosumab for prescribing and monitoring requirements). **NB: Denosumab prescribing, administration and monitoring responsibility should stay with secondary care if patient has severe renal impairment – no GP prescribing for this patient group**
- **IV zoledronic acid and IV ibandronic acid – secondary care prescribing only**
- Please note **oral bisphosphonates** should be discontinued if patient is started on an IV bisphophonate / denosumab / teriparatide / romosozumab by secondary care clinician.

Treatment Duration review: Guidance for GPs

- **bisphosphonate therapy**- review treatment +/- DXA after 3- 5 years (duration of treatment is dependent on presence of risk factors – see supporting notes (pg 14) for further details on whether to continue treatment / consider a drug holiday / stop therapy / the need to repeat DXA scans.
- **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. (see supporting notes for further details pg 13)

STAGE 3 : Consider SPECIALIST REFERERAL

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

- **Severe renal impairment**
- **Pre-menopausal women**
- **Male osteoporosis if less than 50 years old**
- **Male osteoporosis if considering prescribing a drug unlicensed for treating osteoporosis in men**
- **Intolerance or poor response to treatment with oral bisphosphonates**
- **If patient fractures while on current treatment**
- **If on Denosumab treatment** - seek further specialist review 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)

Treatment options that may be prescribed in secondary care (no GP prescribing) are :-(also see notes page 15)

- **Teriparatide**
- **Romosozumab* – approved for use for severe osteoporosis in post-menopausal patients**

*Romosozumab has been NICE approved in May 2022,TA 791, as an option for treatment of severe osteoporosis in people after menopause who are at high risk of fracture, only if:

- they have had a major osteoporotic fracture (spine, hip, forearm or humerus fracture) within 24 months (so are at imminent risk of another fracture)

Prevention and Treatment of Glucocorticoid-induced Osteoporosis in Post-menopausal Women & Men (age ≥ 50 years) in the Primary Care Setting

(Pre-menopausal women and men less than 50 years – seek advice from a metabolic bone disease specialist) - **Algorithm B**

Stage 1 Suspected or at risk of Glucocorticoid-induced Osteoporosis

Applicable Criteria: Post-menopausal Women & Men (age ≥ 50 years)

- **Patients starting on long term corticosteroids** (i.e. (typically a steroid dose of prednisolone ≥ 5mg per day (or equivalent), and expected to be for ≥ 3 months)
- **Patients already on long term glucocorticosteroid therapy (**irrespective of dose prescribed as it depends on cumulative dose exposure)
- **Patients who have received repeated shortterm courses of steroids (eg for asthma) with a cumulative dose equivalent to 1.5g per year.**

(High dose inhaled corticosteroids for COPD -Clinicians should be aware of the potential risk of developing osteoporosis and other side effects from the use of high-dose inhaled corticosteroids and should discuss the risk with patients. There are no set guidelines available and the need for bone protective therapy should be decided on a case by case basis (i.e. may be required if patient has multiple risk factors).

Initial Treatment plan : applicable to all patients who fit the criteria above

- Initiate bone protective therapy (see medical management options below)
- Prescribe calcium 1-1.2g + colecalciferol 20mcg (800IU) daily unless confident that patient has an adequate calcium intake and is vitamin D replete.
- Request a DXA scan (if appropriate)

(NB: treatment should always be started straight away regardless of whether a DXA scan has been requested or not, as it is known that rapid bone loss occurs within the first 3 – 6 months of steroid therapy)

The decision of how long bone protective therapy should continue for is dependent on several factors such as age , steroid dosage , length of steroid exposure and other clinical risk factors.

For patients Age ≤ 65

No previous fragility fracture

Previous fragility or incident fracture

Carry out relevant investigations (see note 4) and measure Bone Mineral Density (BMD) (DXA scan, hip ± spine)

DXA scan report sent to GP including recommendations

T-score > 0

Treatment plan:

- **Reassure patient**
- **STOP bone protective therapy**

T-score 0 to -1.4

Treatment plan:

- **General measures (see note 3)**
- **STOP bone protection therapy**

T score below ≤ -1.5

(NB:-treat as if osteoporosis due to the addition risk conferred by steroid therapy)

Treatment plan

- **Continue bone protective therapy**
- **For duration – see below ***

For patients Age ≥ 65

Carry out relevant Investigations – see note 4

Treatment plan

- **Continue bone protective therapy**
- **For information regarding treatment duration – see below ***

ALGORITHM B cont.

STAGE 2 MEDICAL MANAGEMENT:

1. Choice of therapy should be tailored to the individual and patient choice must be factored in.
2. Licensed indication for individual bisphosphonates vary, in particular relating to their use in men – see note 7 for details)
3. Consult electronic BNF or Summary of Product Characteristics (SPC) for full prescribing details (e.g. licensed indications, contra-indications, use in elderly, renal, hepatic impairment, counselling, adverse effects etc.).
4. Ensure dental examinations are carried out as appropriate before starting bisphosphonate/ denosumab therapy and give advice regarding dental hygiene etc. due to risk of Osteonecrosis of the Jaw (ONJ) associated with these medications. (see Supporting notes for more info)
5. Clinicians should seek specialist opinion if patient sustains a fracture on therapy

First Line Choices:

- **Consider treatment with oral bisphosphonate:-**
  - **either alendronic acid 70MG WEEKLY tablets or risedronate sodium 35MG WEEKLY tablets**
    (ibandronic acid 150mg MONTHLY tablets can be used as an alternative if compliance is an issue)
  - local specialists advise that although not licensed for this indication, once weekly bisphosphonates are routinely used (off label use) - See note 7 for summary of licensed indications)

NB:

- **Patients with severe renal impairment**- refer to Specialist team for consideration of denosumab s/c, as bisphosphonates are contraindicated in these patients.
- **Patients who cannot take or who are intolerant of oral bisphosphonates** – refer to Specialist team for consideration for IV bisphosphonate therapy or denosumab s/c.

Additional Prescribing notes:

- All bisphosphonates should be prescribed generically
- Alendronic acid is also available as an effervescent tablet or as a liquid however please note these preparations are considerably more expensive and use should be limited to specific patients only.
- Please note **oral bisphosphonates** should be discontinued if patient is started on an IV bisphophonate / denosumab / teriparatide

2nd Line Choice:

- **An alternate oral bisphosphonate can be used as a 2nd line option if contraindications, intolerance, poor compliance or poor response[5] to the initial choice of drug occurs.**

***Treatment Duration Review: Guidance for GPs**

For patients on long term steroids :

Continue to prescribe bone protective therapy

- **bisphosphonate therapy**- review treatment +/- DXA after 3- 5 years **(**duration of treatment is dependent on presence of risk factors –see supporting notes (pg 12) for further details on whether to continue treatment / consider a drug holiday / stop therapy / the need to rep eat DXA scans.
- **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 treatment should not be stopped or ongoing treatment delayed without a specialist review) (see supporting notes pg 13)

For patients where steroid therapy has been discontinued:-

- Bisphoshonates - review patient and consider stopping treatment when steroid therapy is stopped (as long as no other risk factors.)
- Denosumab – **seek specialist advice** as denosumab should not be stop or ongoing treatment delayed

STAGE 3 Consider SPECIALIST REFERRAL:-

- **Severe renal impairment**
- **Pre-menopausal women**
- **Male osteoporosis if considering a drug unlicensed for indication**
- **Male osteoporosis if less than 50 years old**
- **Intolerance or poor response to treatment with oral bisphosphonates[5]**
- **If patient fractures on treatment**
- **Denosumab treatment** - seek further 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)
- **Teriparatide – secondary care prescribing only**

Supporting notes to accompany algorithm A and B within the Osteoporosis Guidelines

Note 1

Clinical Risk Factors / Indicators of Low Bone Mass Density (BMD) [1]
These should be taken into account when assessing the patient.

Independent clinical risk factors as defined in NICE TA 160 are:

- Parental history of hip fracture
- Alcohol intake of 4 units or more per day
- Rheumatoid arthritis

Indicators of Low BMD as defined in NICE TA 160 are:

- Low body mass index (defined as <22kg/m$^{2)}$
- Medical conditions such as ankylosing spondylitis , Crohn's disease
- Conditions that result in prolonged immobility
- Untreated premature menopause

Other clinical risk factors include therapy with breast cancer drugs, coeliac disease / malabsorption syndromes, inflammatory arthritis. (NB this list provides examples of other risk factors not included within NICE ta 160, it is not an exhaustive list)

Note 2

FRAX® tool (Specific to Algorithm A)
Algorithms that integrate the weight of CRFs for fracture risk with or without information on BMD have been developed - FRAX®. The FRAX® tool (www.shef.ac.uk/FRAX) computes the 10-year probability of hip fracture or a major osteoporotic fracture (clinical spine, hip, forearm or humerus) for several European countries, including the UK. The tool has been externally validated in independent countries and widely used. The FRAX® tool is used and recommended by local specialists.

Limitations of using the Frax® tool are:

- When the absolute fracture risk in patients of extreme ages is calculated.
- Neck of Femur BMD used to assess risk of fracture, not lumbar spine.

QFracture2012 tool (Specific to Algorithm A)
NICE have recommended the use of fracture risk assessment tools FRAX or QFracture2012 (http://www.qfracture.org/) in the assessment of patients
Ref: NICE CG 146, Osteoporosis: Clinical Guideline for prevention and treatment (updated March 2014)) National Osteoporosis Guideline Group (NOGG)

Note 3

General Measures

- Recommend good nutrition esp. 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
- Reduce dose of glucocorticoid when possible (specific to algorithm B)
- Consider glucocorticoid sparing therapy if appropriate or consider alternative route of administration(specific to algorithm B)

Note 4

Investigations

- FBC, ESR
- Bone and liver function tests (Ca, P, 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, LH and SHBG
- Serum VitD
- 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

Note 5

Compliance Issues / Intolerance / Poor Response Definitions

Compliance – Emphasise administration advice specific to bisphosphonates (see BNF). If patient not willing to follow the timing schedule, consider alternative treatment**.**

Intolerance –. If oesophageal irritation occurs, consider prescribing a proton pump inhibitor unless contra-indicated. 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

Poor response– on-going rapid decline in BMD.

Note 6

DXA Scans

- **Following initiation of bisphosphonate (po or IV) or denosumab therapy:**
  - consider repeating DXA after 3-5 years*

- **Ongoing bisphosphonate / denosumab therapy:-**
  - consider repeating DXA every 2-3 years*

- **Patients receiving glucocorticosteroids (long term)**
  - Consider repeating DXA every 1-3 years*

- **Presence of a recent fracture**
  - Consider a repeat DXA after 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*

* . exact frequency will vary depending on clinical risk factors

DXA scan should also be considered in the following:

- Patients with osteopenia (T score -1 to -2.4)

Note 7 (Ref NICE TA 464)

Summary of Licensed Indications - Bisphosphonates

Drug , Dosage Form and dosage	Licensed Indication
Alendronic acid (generic) tablets, 10mg once a day	• **Treating postmenopausal osteoporosis** • **Preventing and treating corticosteroid- induced osteoporosis in postmenopausal woman not receiving hormone replacement therapy** • **Treating osteoporosis in men**
Alendronic acid (generic) tablets, 70mg once a week	• **Treating postmenopausal osteoporosis** **(*see footnote)**
Ibandronic acid (generic) tablets , 150mg once a month	• **Treating postmenopausal osteoporosis**
Ibandronic acid (generic) injection,3mg/3ml once every 3 months	• **Treating postmenopausal osteoporosis**
Risedronate sodium (generic) tablets , 5mg once a day	• **Treating postmenopausal osteoporosis to reduce risk of vertebral or hip fractures** • **Preventing osteoporosis (including corticosteroid-induced osteoporosis in postmenopausal women**
Risedronate sodium(generic) tablets , 35mg once a week	• **Treating postmenopausal osteoporosis to reduce risk of vertebral or hip fractures** • **Treating osteoporosis in men at high risk of fractures**
Zoledronic acid (generic) intravenous infusion, 50 micrograms/ml once a year	• **Treating postmenopausal osteoporosis and osteoporosis in men (including corticosteroid-induced osteoporosis**

*NB: local specialists have advised that the use of once weekly alendronic acid is commonly used in men (off label use)

Prescribing Points

- Clinicians should consult electronic BNF or Summary of Product Characteristics (SPC) for full prescribing details (e.g. licensed indications, contra-indications, use in elderly, renal, hepatic impairment, contraindications, counselling, adverse effects etc.)
- Compliance with oral bisphosphonates should be checked after the first month of therapy and rechecked periodically thereafter to ensure compliance.
- The choice of treatment should be made on an individual basis after discussion between the responsible clinician and the patient, or their carers, about the advantages and disadvantages of the treatment available. Where generic products available, start treatment with the least expensive formulation, taking into account administration costs, the dose needed and the cost per dose[13].
- Please note that oral bisphosphonates should be discontinued if patient is started on an IV bisphophonate / denosumab / teriparatide / romosozumab 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.

Safety Issues

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.

- **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).

  See http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON452540 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

Counselling Points for bisphosphonates and denosumab

- Refer to electronic BNF , individual SmPC , and relevant MHRA information

Duration Of Therapy / Stopping Criteria (Specific to algorithm A)

Bisphosphonates (Oral & IV)

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

Treatment Duration: 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 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

DENOSUMAB

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

Treatment Duration: 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' facility.
- 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
- **If the specialist advises to stop denosumab treatment, they will advise the GP as to what 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.

- 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 fractures).

Denosumab – Shared Care guideline
A BLMK wide shared care guideline for denosumab has been approved fy the BLMK Area Prescribing Committee which outlines induvial responsibilities and included specific drug information and monitoring information.
Click here

Teriparitide and Romosozumab

- Both of these treatments are specialist use only; no GP prescribing.
- Secondary care clinicians should notify the GP when either of these drugs is initiated to ensure the treatment is recorded on patients medical notes.
- Bisphosponate treatment should be discontinued if either teriparatide or romosozumab is prescribed,
- Secondary care clinician will advise GP on which **follow on bone therapy treatment** is required post use of teriparatide / romosozumab.

Glucocorticosteroid Induced Osteoporosis Stopping Criteria
(Specific to Algorithm B)

For patients on long term steroids:-

- **Continue bone protective therapy:-**
  - **Bisphosphonate therapy**- review treatment +/- DXA after 3- 5 years (duration of treatment is dependent on presence of risk factors)
  - **Denosumab therapy** - review treatment +/- DXA after 3-5 years **and** seek specialist advice regarding duration of therapy (NB:denosumab treatment should not be stopped without specialist review (MHRA advice)

For patients where steroid therapy has been discontinued:-

- **Bisphoshonates therapy** - review patient and consider stopping treatment when steroid therapy is stopped (as long as no other risk factors.)
- **Denosumab therapy –** seek specialist advice as denosumab should not be stopped without a specialist review

Background

In general, bisphosphonates should be stopped as soon as steroids are stopped (provided there are no other risk factors) as the evidence of rapid bone loss is in the first 3-6 months of treatment.). As per the MHRA advice , Denosumab should **not** be stopped without specialist review.

References:

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