Osteoporosis - Guidance for Fracture Risk Assessment and Prevention in Primary Care

NHS Oxfordshire Clinical Commissioning Group

Summary

NICE TA464 confirms that, if a patient is eligible for a risk assessment (see box below) then it is cost effective to treat patients with an oral bisphosphonate if 'total osteoporotic fracture' 10 year risk is ≥1%, however clinicians and patients must consider risks, benefits and individual patient factors when making a decision to treat and the NICE decision support tool should be used. **Clinicians may wish to consider SIGN 142 guidance . SIGN suggest that if 10 year risk ≥10% consider a DEXA scan and treatment if T-score ≤-2.5**

Primary Prevention: no previous fragility fracture

Consider assessing fracture risk:

- In women aged ≥65 years and men aged ≥75 years
- In women <65 years and men <75 years in the presence of risk factors, for example:
  - Long term use (> 3 weeks) or frequent use (3-4 course per year) of oral or systemic glucocorticoids
  - History of falls
  - Family history of hip fracture
  - Other causes of secondary osteoporosis
  - Low body mass index (BMI) (<18.5kg/m^2
  - Smoking
  - Alcohol intake of more than 14 units per week for women and more than 21 units per week for men
- Do not routinely assess fracture risk in people under 50 years unless they have major risk factors (for example, 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[1]

Patients aged under 40 years who have a major risk factor, such as history of multiple fragility fracture, major osteoporotic fracture, or current or recent use of high-dose oral or high-dose systemic glucocorticoids (more than 7.5 mg prednisolone or equivalent per day for 3 months or longer)[1] should be **referred to secondary care**.

Estimate 10 year probability of 'total osteoporotic fracture' using **QFracture** (a calculation tool is available in EMIS)

NICE confirms that treatment is cost effective if 10 year risk ≥1%, but must consider clinical risks/benefits and patient factors. SIGN 142 recommends if 10 year risk ≥10%, consider a DEXA scan and use this to guide decision along with patient specific factors

Consider DEXA scan and treat if T-score ≤-2.5 at spine or hip[2]

For those who do not reach treatment thresholds or decline treatment, consider Healthy Lifestyle[2] advice
Consider repeat risk assessment only after a minimum of 2 years, or when there has been a change in the patient's risk factors [1]

Consider offering treatment (see page 2)

Secondary Prevention: previous fragility fracture

Patient with previous fragility fracture, **not** under care of fracture clinic

If patient under care of the fracture clinic, follow advice given on when to treat

Aged 50 to 74 years

Aged 75 years and over

Patients taking Aromatase Inhibitors and GnRH Analogues

- Baseline BMD should be assessed by DEXA scan prior to or within three months of starting treatment
- NICE CG80 (breast cancer) advises that bone protection treatment should be offered to patients on aromatase inhibitors who have a T score of ≤-2 (post-menopausal) or ≤ -1 (premature menopause). Patients over 75 with 1 or more risk factors should be offered bone protection treatment and do not require a DEXA scan.
- NICE CG175 (prostate cancer) advises that bone protection should not be routinely offered to patients on GnRH analogues. Patients should be risk assessed as normal and offered treatment if the risk assessment shows it is indicated (as above)

NB. The doses in this guideline are recommended by local specialists. However, these are not licensed in all patient groups and situations - please refer to Summary of Product Characteristics (SPC) for full prescribing details.

Treatment pathway for patients at risk of fragility fracture (Primary and Secondary Prevention)

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Ensure patient is calcium and vitamin D replete (see page 4)

1st line: Oral alendronate 70 mg weekly

Check adherence at 4m and 12m after initiation of oral therapy.
If pre-existing indigestion, consider risedronate.
If abnormality of swallowing or other factors which delay oesophageal transit or emptying, consider denosumab.

2nd line: Oral risedronate 35mg weekly

****If fracture occurs on treatment see advice below**

Note: **Ibandronic acid** 150mg once a month is an alternative option if alendronate/risedronate is not suitable. However there is limited data available on hip fractures- See SPC for details.

Non steroid induced osteoporosis

3rd line: Denosumab 60mg S/C 6 monthly

If denosumab is contraindicated or not tolerated[a]

Steroid induced osteoporosis (denosumab not licensed for this indication)

If alendronate/risedronate are contraindicated or not tolerated[a]

Refer to secondary care for consideration of:

- IV zoledronic acid/ IV ibandronic acid (in line with NICE TA464)
- teriparatide (in line with NICE TA161)
- raloxifene (in line with NICE TA161)

<u>When to use denosumab?</u>

Denosumab 60mg subcutaneously 6 monthly is an alternative option in line with NICE TA204 and local guidance if unable to comply or intolerant of oral bisphosphonates. The FIT study suggests if > 4% BMD loss despite adherent therapy, then consider switching to denosumab[6].

Denosumab 60mg 6 monthly (in line with NICE TA 204) See local guidance. Near patient testing reimbursement available. Pre-dose testing: Creatinine Clearance (CrCl), serum Ca and 25OHD. If CrCl between 20 and 30 ml/min then must be calcium replete as higher risk of post dose hypocalcaemia.

If denosumab therapy is stopped without switching or at end of denosumab therapy, there is a high rebound risk of vertebral fractures[9] -discuss with secondary care before stopping.

<u>Alendronate70mg tablet/Risedronate 35mg tablet</u>

Swallow the tablet whole, once a week on an empty stomach with a full glass of water upon arising for the day, then remain upright for 30mins. It should be taken at least 30 minutes before the first food, other medicines or drink (other than plain water).

<u>Steroid Induced Osteoporosis</u>

Bone loss and increased fracture risk occur early after initiation of glucocorticoids. Bone-protective treatment should be started at the onset of therapy in patients at increased risk of fracture.[3] **Bone protection treatment can be stopped if steroids are stopped, unless there is another indication for treatment.**

NICE TA464 confirms that people risk assessed in line with CG146 who have a ≥10% 10year risk may be treated cost effectively with IV bisphosphonates. However it is recommended locally that IV agents are reserved, following consideration of patient factors and risk/benefits, for those for whom oral agents are not tolerated or are contraindicated.

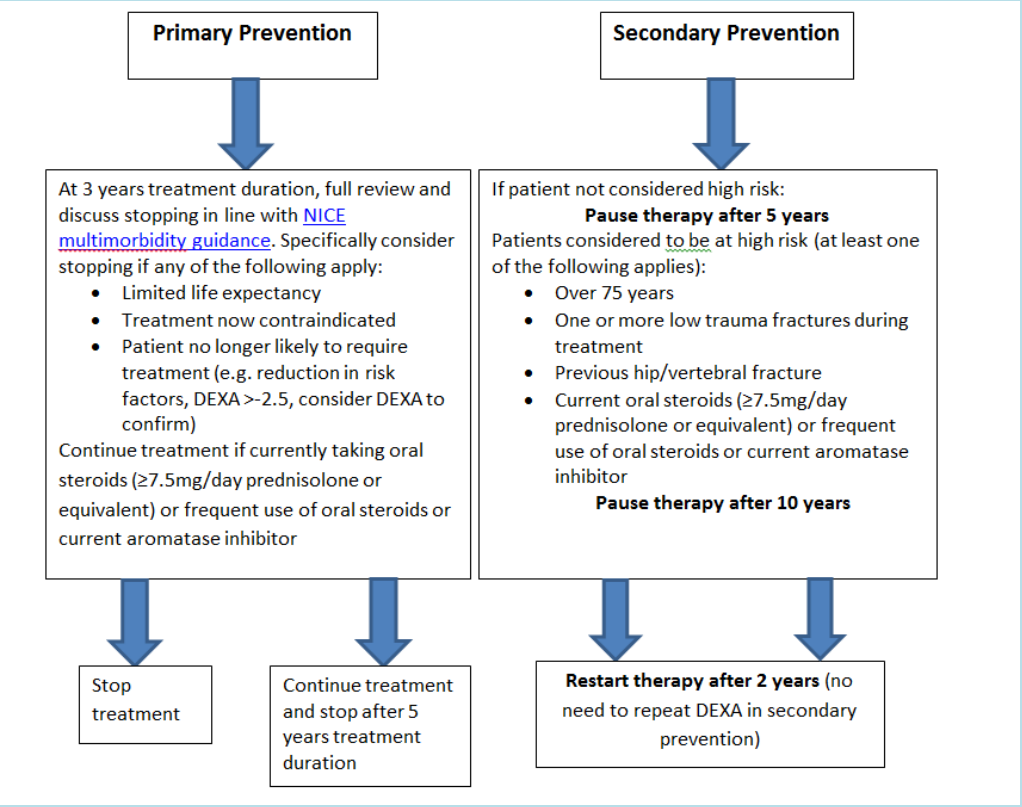
[a] Intolerance is defined as persistent side effects (incl. upper gastrointestinal disturbance) that are sufficiently severe to warrant discontinuation of treatment, and that occur even though the instructions for administration have been followed correctly. It is not advisable to initiate PPI treatment to manage GI side effects.

****If fragility fracture occurs after more than 6 months oral bisphosphonate therapy, check adherence, secondary causes (exclude atypical fracture – see pg 3) and calcium/ vit D intake (see pg 4). If adherent and Ca/vit D replete then consider discussion with secondary care (Ox.GPosteop@nhs.net) If more than 2 fractures and BMD <-3.5 refer to secondary care for consideration for teriparatide (in line with NICE TA 161)**

Duration of treatment

- NICE multimorbidity guidance (NG56) advises to:
  "Tell a person who has been taking bisphosphonate for osteoporosis for at least 3 years that there is no consistent evidence of:
  - further benefit from continuing bisphosphonate for another 3 years
  - harms from stopping bisphosphonate after 3 years of treatment.

  Discuss stopping bisphosphonate after 3 years and include patient choice, fracture risk and life expectancy in the discussion."
- SIGN 142 states that there is:
  "no published evidence was identified from randomised trials to suggest that drug holidays were effective in reducing the risk of skeletal adverse effects".



- Management of patients on treatment beyond 10 years should be considered on an individual basis. [3]

Denosumab - duration of treatment

- NICE TA204 states "The Committee accepted that the 5-year treatment duration assumption was appropriate and reflected clinical practice."
- The SPC states "The optimal total duration of antiresorptive treatment for osteoporosis (including both denosumab and bisphosphonates) has not been established. The need for continued treatment should be re-evaluated periodically based on the benefits and potential risks of denosumab on an individual patient basis, particularly after 5 or more

Take into account that risk assessment tools may underestimate fracture risk in certain circumstances, for example if a person:
•has a history of multiple fractures
•has had previous vertebral fracture(s)
•has a high alcohol intake
•is taking high-dose oral or high-dose systemic glucocorticoids (more than 7.5 mg prednisolone or equivalent per day for 3 months or longer)
•has other causes of secondary osteoporosis. [1]

Take into account that fracture risk can be affected by factors that may not be included in the risk tool, for example living in a care home or taking drugs that may impair bone metabolism (such as anti-convulsants, selective serotonin reuptake inhibitors, thiazolidinediones, proton pump inhibitors and anti-retroviral drugs).[1]

Risk of atypical femoral fracture with bisphosphonates:
During 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. Discontinuation of bisphosphonate therapy in patients suspected to have an atypical femur fracture should be considered while they are evaluated, and should be based on an assessment of the benefits and risks of treatment for the individual. See MHRA guidance for bisphosphonates full details.

Risk of atypical femoral fracture with denosumab:
During denosumab treatment, patients should be advised to report new or unusual thigh, hip, or groin pain; patients presenting with such symptoms should be evaluated for an incomplete femoral fracture. Discontinuation of denosumab treatment should be considered if an atypical femur fracture is suspected, while the patient is evaluated; an individual assessment of the benefits and risks should be performed.
See MHRA guidance for denosumab for full details.

Risk of osteonecrosis of the jaw:
Patients should be advised to maintain good oral hygiene, receive routine dental check-ups, and report any oral symptoms such as dental mobility, pain, or swelling. See MHRA guidance for bisphosphonates and denosumab for full details. Refer to 2◦ care if suspected.

Risk of osteonecrosis of the external auditory canal:
This should be considered in patients who present with ear symptoms including chronic ear infections or in those with suspected cholesteatoma. Patients should be advised to report any ear pain, discharge from the ear, or an ear infection. Possible risk factors include steroid use and chemotherapy, with or without local risk factors such as infection or trauma. See MHRA guidance for bisphosphonates and denosumab for full details.

Calcium and vitamin D Supplementation for bisphosphonates and other bone-sparing drugs

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Suggest improvements to dietary calcium[2]

Calculate dietary calcium - see here
For example:
1 pint milk (or equivalent) = 700mg
1 small matchbox of cheese = 200 mg
For more information see:
https://nos.org.uk/for-people-and-families/healthy-living-and-risk/

If on zoledronic, teriparatide or denosumab: also check serum 25OHD

> 50nmol/L

< 50 nmol/L

Initial load with
20,000-25,000 IU D3 weekly
OR 3,200 IU D3 daily
for 12 weeks then equivalent 800 IU/d unless already on calcium / vitamin D supplement. Check calcium 4 weeks after starting loading.

Patient receiving < 700 mg calcium per day

Encourage dietary sources of calcium and ensure patient receives 800-1000 IU/ day licensed dose of vitamin D

If cannot increase dietary calcium, ensure patient receives combined, chewable calcium and vitamin D supplement. If not tolerated due to taste, consider non-chewable/dispersible combined

Patient receiving > 700 mg calcium per day

Ensure patient receives 800-1000 IU/ day licensed dose of vitamin D

References
1. NICE CG146
2. SIGN 142 (March 2015)
3. NOGG 2017
4. Local Specialist recommendation
5. NICE Quality Standard Osteoporosis
6. FIT study
7. NICE TA 161.
8. NICE CKS Corticosteroids - oral (last revised in August 2015)
9. Cummings et al. J Bone Miner Res. 2017 Nov 4. doi: 10.1002/jbmr.3337
10. NICE NG53

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