Specialist Pharmacy Service

NICE Bites

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A summary of prescribing recommendations from NICE guidance

Osteoporosis: assessing the risk of fragility fracture

NICE CG146; 2012

This guideline offers best practice advice on the assessment of fragility fracture risk in adults.

Definition of terms

BMD	bone mineral density
BMI	body mass index
DXA	dual-energy x-ray absorptiometry
IV	intravenous

Targeting risk assessment

- Consider assessment of fracture risk in:
  - all women aged ≥65 years, **AND**
  - all men aged ≥75 years.
- Consider assessment of fracture risk in women <65 years and men aged <75 years in the presence of risk factors such as:
  - previous fragility fracture,
  - current use or frequent recent use of oral or systemic glucocorticoids,
  - history of falls,
  - family history of hip fracture,
  - other causes of secondary osteoporosis (see **Table 1**),
  - low BMI (<18.5 kg/m^2),
  - smoking,
  - alcohol intake above recommended limits.
- **Do NOT** routinely assess fracture risk in people aged <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.
- Measure BMD to assess fracture risk in people aged <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 systemic glucocorticoids.*
- Also see NICE pathway: Hip fracture

Methods of risk assessment

- Estimate absolute risk when assessing risk of fracture e.g. predicted risk of major osteoporotic or hip fracture over 10 years, expressed as a percentage.
- Use either FRAX® (without a BMD value if a DXA scan has not previously been undertaken) or QFracture®, within their allowed age ranges. Above the upper age limits defined by the tools, consider people to be at high risk.
- FRAX® can be used for people aged between 40 and 90 years, either with or without BMD values, as specified.
- QFracture® can be used for people aged between 30 and 84 years. BMD values cannot be included in the risk algorithm.
- Interpret the estimated absolute risk of fracture in people aged >80 years with caution, because predicted 10-year fracture risk may underestimate their short-term fracture risk.
- 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 systemic glucocorticoids*,
  - has other causes of secondary osteoporosis.

Table 1

Causes of secondary osteoporosis	
Endocrine	Hypogonadism including untreated premature menopause, treatment with aromatase inhibitors or androgen deprivation therapy hyperthyroidism, hyperparathyroidism, hyperprolactinaemia, Cushing's disease, diabetes
Gastrointestinal	Coeliac disease, inflammatory bowel disease, chronic liver disease, chronic pancreatitis, other causes of malabsorption
Rheumatological	Rheumatoid arthritis, other inflammatory arthropathies
Haematological	Multiple myeloma, haemoglobinopathies, systemic mastocytosis.
Respiratory	Cystic fibrosis, COPD, metabolic (homocystinuria)
Metabolic	Homocystinuria
Other	Chronic renal disease, immobility

- Take into account that fracture risk can be affected by factors that may not be included in the risk tool e.g. living in a care home, or taking drugs that may impair bone metabolism e.g. anti-convulsants, selective serotonin reuptake inhibitors, thiazolidinediones, proton pump inhibitors and anti-retrovirals.
- Following risk assessment with FRAX® (without a BMD value) or QFracture®, consider measuring BMD with DXA in people whose fracture risk is in the region of an intervention threshold** for a proposed treatment, and recalculate absolute risk using FRAX® with the BMD value.
- **Do NOT** routinely measure BMD without prior assessment using FRAX (without a BMD value) or QFracture.
- Also see NICE medtech innovation briefing; Bindex for investigating suspected osteoporosis.
- Consider measuring BMD with DXA before starting treatments that may have a rapid adverse effect on bone density e.g. sex hormone deprivation treatment for breast or prostate cancer.
- Consider recalculating fracture risk in the future:
  - if the original calculated risk was in the region of the intervention threshold** for a proposed treatment and only after a minimum of 2 years, **OR**
  - when there has been a change in the person's risk factors.

Assessment tools

FRAX®
Accessible at: https://www.sheffield.ac.uk/FRAX/tool.jsp

QFracture®
Accessible at: http://www.qfracture.org/
Note: QFracture does not include BMD in its algorithm.
These algorithms give the 10-year probability of fracture for:
- hip fracture
- major osteoporotic fracture (clinical spine, forearm, hip or shoulder fracture)

* >7.5mg prednisolone or equivalent per day for ≥3 months

**An intervention threshold is the level of risk at which an intervention Is recommended.

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Bisphosphonates for treating osteoporosis

NICE TA464; 2017

Preventing fragility fractures§

- **Oral** bisphosphonates (alendronic acid, ibandronic acid and risedronate sodium) are recommended as options for treating osteoporosis in adults only if the:
  - person is eligible for risk assessment, **AND**
  - 10-year probability of osteoporotic fragility fracture is at least 1%.
- **Intravenous** bisphosphonates (ibandronic acid and zoledronic acid) are recommended as options for treating osteoporosis in adults only if the:
  - person is eligible for risk assessment , **AND**
  - 10-year probability of osteoporotic fragility fracture is at least 10%, **OR**
  - 10-year probability of osteoporotic fragility fracture is at least 1% and the person has difficulty taking oral bisphosphonates or these drugs are contraindicated or not tolerated.
- Estimate the 10-year probability of fragility fracture using the FRAX® or QFracture® risk tools.
- Choice of treatment should be made on an individual basis after discussion between the responsible clinician and the patient and/or carers, about the advantages and disadvantages of treatments available.

§ Editorial note: the absolute risk level at which oral bisphosphonates are recommended as treatment options in this guidance are based on cost-effectiveness and are NOT clinical intervention thresholds. See www.nice.org.uk/guidance/ta464

Recommendations – wording used such as 'offer' and 'consider' denote the strength of the recommendation.

Drug recommendations – the guideline assumes that prescribers will use a drug's Summary of Product Characteristics (SPC) to inform treatment decisions.

- If several generic products are available, start treatment with the least expensive formulation, taking into account administration costs, the dose needed and the cost per dose.
- These recommendations are not intended to affect treatment with alendronic acid, ibandronic acid, risedronate sodium and zoledronic acid that was started in the NHS before this guidance was published. Adults having treatment outside these recommendations may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.
- For additional recommendations on the use of bisphosphonates in postmenopausal women, see also:
  NICE TA160: Primary prevention of fragility fractures in postmenopausal women
  NICE TA161: Secondary prevention of fragility fractures in postmenopausal women

MHRA (Medicines and healthcare regulatory agency) advice

Bisphosphonates: atypical femoral fractures
https://www.gov.uk/drug-safety-update/bisphosphonates-atypical-femoral-fractures

Bisphosphonates: osteonecrosis of the jaw
https://www.gov.uk/drug-safety-update/bisphosphonates-osteonecrosis-of-the-jaw

Bisphosphonates: very rare reports of osteonecrosis of external auditory canal
https://www.gov.uk/drug-safety-update/bisphosphonates-very-rare-reports-of-osteonecrosis-of-the-external-auditory-canal

Bisphosphonates: atrial fibrillation
https://www.gov.uk/drug-safety-update/bisphosphonates-atrial-fibrillation

Please go to www.nice.org.uk to check for any recent updates to this guidance

Table 2: Available bisphosphonate preparations

Drug	Formulation	Dose	Indication
Alendronic acid	10mg tablets	10mg once a day	• Postmenopausal osteoporosis[ab] • Prevention and treatment of corticosteroid-induced osteoporosis in postmenopausal women not receiving HRT[a] • Osteoporosis in **men**[ac]
	70mg tablets/effervescent tablets	70mg once a week	• Postmenopausal osteoporosis[b]
	Oral solution 70mg/100ml	70mg once a week	
Ibandronic acid	150mg tablets	150mg once a month	• Postmenopausal osteoporosis[d]
	IV injection 3mg/3ml	Once every 3 months	
Risedronate sodium	5mg tablets	5mg once a day	• Postmenopausal osteoporosis[b] • Prevention of osteoporosis (including corticosteroid-induced osteoporosis) in postmenopausal women
	35mg tablets	35mg once a week	• Postmenopausal osteoporosis[b] • Osteoporosis in **men**
Zoledronic acid	IV infusion (over at least 15 minutes) 5mg/100ml	5mg once a year	• Postmenopausal osteoporosis • Osteoporosis in **men** • Corticosteroid-induced osteoporosis

[a] check individual SPCs as indications differ for different preparations.
[b] to reduce risk of vertebral and hip fractures
[c] to reduce risk of vertebral fractures
[d] a reduction in risk of vertebral fractures has been demonstrated, efficacy on femoral neck fractures has not been established