NHS South of Tyne and Wear

serving Gateshead Primary Care Trust, South Tyneside Primary Care Trust and Sunderland Teaching Primary Care Trust

Prescribing guidelines for the Management of Osteoporosis

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NHS SOUTH OF TYNE AND WEAR

Prescribing Guidelines for the Management of Osteoporosis

Acknowledgement

NHS Clinical Knowledge Summaries (CKS) are producing a review titled “Osteoporosis - prevention of fragility fractures”. The guideline group are grateful to the CKS team for providing a draft review for consideration. The guideline group also wishes to acknowledge the North Tyneside Osteoporosis Guidelines which were used as a starting point for the development of this guideline.

INTRODUCTION

- 3 million people in UK have osteoporosis
- Almost half of the 10.6 million women aged over 50 in the UK will break a bone during their lifetime, mainly due to osteoporosis
- Only 480,000 women on bone fracture prevention
- 1 in 5 men will fracture a bone after the age of 50
- Prescribing of drugs for the prevention of osteoporosis cost £1 million in South of Tyne and Wear in 2009/10.
- Prescribing of drugs for the prevention of osteoporosis have increased by 9% in the last 12 months.

NICE produced Technology Appraisal (TA) 160 and TA161 for the primary and secondary prevention of osteoporotic fractures. This guidance is restricted to postmenopausal women with osteoporosis as defined by a bone mineral density T-score of ≤-2.5, and does not include men with osteoporosis or individuals treated with glucocorticoids.

An appraisal of denosumab has recently been released (TA204: October 2010) and NICE have completed a review of the position of strontium ranelate.

NICE has not produced a clinical guideline nor is one imminent. The National Osteoporosis Guideline (NOGG) was launched in October 2008 to address these deficits. The NOGG guidance includes a 10-year risk of fracture model which has been developed to identify those at highest risk (www.shef.ac.uk/FRAX). The NOGG guidance has been endorsed by many scientific and professional organisations including the National Osteoporosis Society and the Royal College of Physicians.

AIMS OF THIS GUIDELINE

The aim of the guideline is to support the management of osteoporosis patients in primary care, to ensure consistency of care across NHS SoTW and to ensure safe, evidence based, cost effective prescribing of medicines and best use of NHS resources. Implementation of the guideline will improve the overall management of patients with osteoporosis and will support the identification of at risk patients.

DEVELOPMENT

This guideline was developed by the NHS South of Tyne & Wear Osteoporosis Guideline Group. The membership consists of:-

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Further distribution for comment:-
Gateshead Medicines Management Committee
South Tyneside Medicines Management Group
Sunderland Primary Care Prescribing Sub-Group
SoTW Medicines Management Committee
Gateshead & South Tyneside LMC
Sunderland LMC
Gateshead & South Tyneside LDC
Sunderland LDC
Clinical Knowledge Summaries Team

Key Points Considered by the Guideline Group

Areas of agreement between NICE and NOGG include recommendations to treat elderly postmenopausal women with a fragility fracture and the use of generic alendronate as a first line option.

There is also agreement that bone mineral density measurements may be useful in reaching treatment decisions in younger postmenopausal women with a fragility fracture. However, whereas NICE requires a T-score ≤-2.5 in most women for either primary or secondary prevention, NOGG recognises the added contribution of independent clinical risk factors to fracture prediction and recommends the use of the WHO-supported fracture risk algorithm FRAX®. In addition, NICE guidance for second line options demands different combinations of bone density and risk factors for different treatments; not only is this complex to operate in a primary care setting, it also raises difficult ethical issues, since some patients who meet the criteria for alendronate treatment ,but are unable to take it, cannot have an alternative therapy until there is evidence of further disease progression. In contrast, NOGG adopts a more pragmatic approach and does not require different criteria for second-line treatments in those who are unable to tolerate alendronate.

In order to provide comprehensive and practical guidance for the management of osteoporosis in clinical practice, the following guideline suggests a combination of NICE and NOGG that retains the main principles of NICE guidance, but incorporates the greater workability and acceptability of NOGG in its approach to second line treatments. It also incorporates NOGG guidance for men with osteoporosis, individuals treated with glucocorticoids, and the use of more recently approved interventions.

Equality and Diversity Statement
This guideline will aim to be fair to all patients regardless of age, disability, gender, race, sexual orientation, religion/belief or any other factor that may result in unfair treatment or inequalities in health/employment.

This guideline is not exhaustive and does not override the individual responsibility of health professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

This guideline should be used in conjunction with the following guidelines:

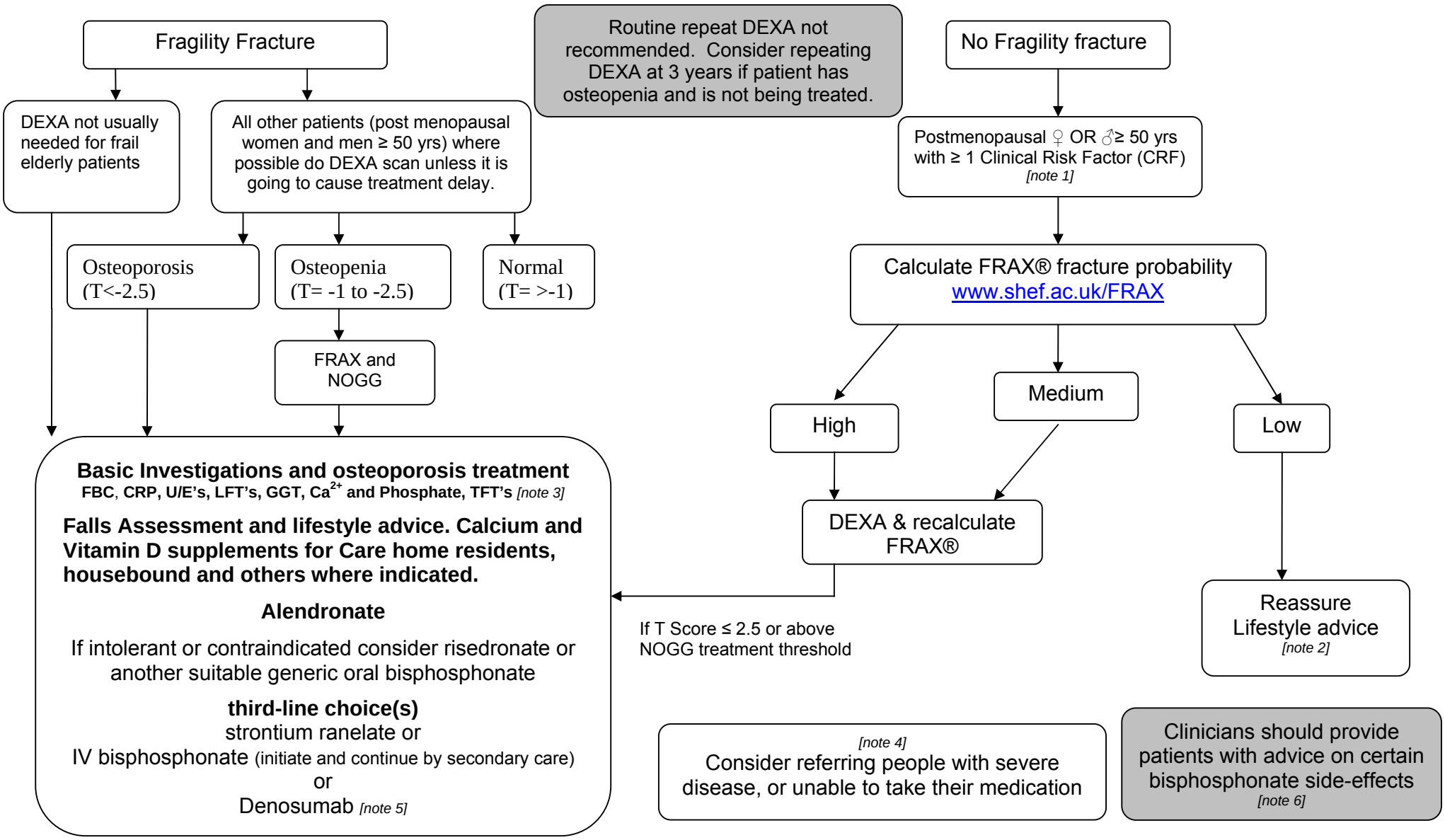
- **TA160: Alendronate, etidronate, risedronate, raloxifene and strontium ranelate for the primary prevention of osteoporotic fragility fractures in postmenopausal women.**
- **TA161: Alendronate, etidronate, risedronate, raloxifene, strontium ranelate and teriparatide for the secondary prevention of osteoporotic fragility fractures in postmenopausal women.**
- **TA204: Denosumab for the prevention of osteoporotic fractures in postmenopausal women.**
- **National Osteoporosis Guideline Group: Guideline for the diagnosis and management of osteoporosis in postmenopausal women and men from the age of 50 years in the UK.**

Full details of contra-indications and cautions for individual drugs are available in the BNF or in the Summary of Product Characteristics (available in the Electronic Medicines Compendium - www.emc.medicines.org.uk)

References

1. NICE. Alendronate, etidronate, risedronate, raloxifene and strontium ranelate for the primary prevention of osteoporotic fragility fractures in postmenopausal women. TA160. amended January 2010.
2. NICE. Alendronate, etidronate, risedronate, raloxifene, strontium ranelate and teriparatide for the secondary prevention of osteoporotic fragility fractures in postmenopausal women. TA161. amended January 2010.
3. NICE. Denosumab for the prevention of osteoporotic fractures in postmenopausal women. TA204. October 2010.
4. NOGG. Guideline for the diagnosis and management of osteoporosis in postmenopausal women and men from the age of 50 years in the UK. July 2010.
5. Cummings SR et al. Denosumab for Prevention of Fractures in Postmenopausal Women with Osteoporosis. N Engl J Med 2009;361:756-65.
6. Bisphosphonates. MHRA. December 2010 [www.MHRA.gov.uk]

Osteoporosis Treatment Algorithm



Osteoporosis Treatment Algorithm - Notes

Note 1:

***Clinical Risk Factors for FRAX®**
BMI<19, smoker, alcohol ≥3u day, previous fragility fracture,
parental fractured hip, steroids>3 months, rheumatoid arthritis, secondary osteoporosis (see below).
Secondary causes of osteoporosis include:

Untreated hypogonadism Premature Menopause<45, Prolonged immobility, Organ transplantation, Type I diabetes, Hyperthyroidism, Chronic malnutrition, Malabsorption, Chronic liver disease, Chronic Obstructive Pulmonary disease, and some drugs including antiepileptics, and antiandrogenic drugs

Note 2:

Lifestyle Advice

- Adequate nutrition especially with calcium
- Regular weight bearing exercise
- Avoidance of tobacco use and alcohol
- Care Home patients, housebound, frail elderly, and patients in sheltered accommodation should be considered for calcium & vitamin D therapy

Note 3:

Investigations to consider if Secondary Cause Suspected

Depending on the results from basic investigations, consider excluding secondary causes
TTG - (marked unexplained osteoporosis and/ or suspicion of coeliac disease)
PSA - (male vertebral or path. fractures)
Serum Vit D and PTH
Serum/urine electrophoresis - if vertebral fracture

Note 4:

Refer for the management of Secondary Care
• painful, acute vertebral fractures and multiple vertebral fractures.
• patients unable to take, tolerate or failing to respond to oral treatment.
• osteoporosis with complex medical problems.
• fragility fractures due to other bone disease.
• Young pre-menopausal women with osteoporosis
• Patients who fracture despite treatment

Note 5:

Denosumab

- Denosumab should only be initiated by a secondary care specialist. It will be initiated using the inclusion criteria of the FREEDOM study.
- Denosumab is currently not recommended for prescribing in primary care [*SoTW Medicines Management Committee statement, February 2011]*
- Secondary care will be responsible for continuing denosumab therapy until such time that prescribing is recommended in primary care.

Denosumab can be considered in:

- Patients with low eGFR, who previously could not fit with treatment.
- Patients whose cancer or anticancer hormonal treatment puts them at high risk of fragility fracture e.g., patients with breast or prostate cancer.
- Patients who receive frequent courses of steroids.

Note 6:

Bisphosphonate Side-effects:
Patients should be advised of the following dental recommendations when taking a bisphosphonate:

Dental examination, with appropriate preventative dentistry, should be considered before bisphosphonate treatment in patients with concomitant risk factors (e.g. cancer, chemotherapy, corticosteroids and poor oral hygiene).

During bisphosphonate treatment, patients with concomitant risk factors should avoid invasive dental procedures if possible. For patients who develop osteonecrosis of the jaw during bisphosphonate treatment, dental surgery may exacerbate the condition.

Whether discontinuation of bisphosphonate treatment in patients who need dental procedures reduces the risk of osteonecrosis of the jaw is not known. Clinical judgment should guide the management of every patient on the basis of an individual benefit-risk assessment.

Osteoporosis Treatment Formulary Choices

Formulary Choice	Osteoporosis Treatment	Reason	Dose	Side Effects *(refer to BNF or SPC more detail)*	Renal Impairment *(refer to BNF or SPC more detail)*	Notes
First-line	Alendronate (weekly)	Generic alendronate is the first line option for the majority of patients. In those in whom it is contraindicated or associated with side-effects, particularly upper gastrointestinal symptoms, the second-line choice should be chosen.	70mg once weekly	Upper gastrointestinal symptoms, bowel disturbance, headaches and musculoskeletal pain. Patients should be made aware of specific bisphopshonate related side-effects (see note 6).	Not recommended in patients with renal impairment (eGFR<35 ml/min).	**Alendronate** is contraindicated in the presence of abnormalities of the oesophagus that delay emptying, inability to stand or sit upright for at least 30 minutes and hypocalcaemia. It should be used with caution in patients with other upper gastrointestinal disorders. It should be taken after an overnight fast and 30 minutes before the first food or drink (other than water) of the day or any other oral medicinal products or supplementation (including calcium). Tablets should be swallowed whole with a glass of plain water (≥ 200 ml) while the patient is sitting or standing in an upright position. Patients should not lie down for 30 minutes after taking the tablet.

Formulary Choice	Osteoporosis Treatment	Reason	Dose	Side Effects *(refer to BNF or SPC more detail)*	Renal Impairment *(refer to BNF or SPC more detail)*	Notes
Second Line	Risedronate (weekly)	Risedronate is the second line option for those patients intolerant of or contraindicated to generic alendronate. Risedronates patent ended in late 2010 and decreases in price have already occurred.	35 mg once weekly	Upper gastrointestinal symptoms, bowel disturbance, headache and musculoskeletal pain. Patients should be made aware of specific bisphopshonate related side-effects (see note 6).	It is contraindicated in the presence of severe renal impairment (eGFR <30ml/min).	**Risedronate** is contraindicated in the presence of hypocalcaemia, pregnancy and lactation. It should be used with caution in patients with upper gastrointestinal disease. It should be taken after an overnight fast and 30 minutes before the first food or drink (other than water) of the day or any other oral medicinal products or supplementation (including calcium). Tablets should be swallowed whole with a glass of plain water (≥ 120 ml) while the patient is sitting or standing in an upright position. Patients should not lie down for 30 minutes hour after taking the tablet.

Formulary Choice	Osteoporosis Treatment	Reason	Dose	Side Effects *(refer to BNF or SPC more detail)*	Renal Impairment *(refer to BNF or SPC more detail)*	Notes
Third line	• Strontium ranelate • Denosumab • Intravenous bisphosphonate	The guideline group decided to provide clinicians with a range of third line options: **Strontium** ranelate provides an oral therapy option for patients, **Denosumab** is a new agent that is administered by a 6-monthly subcutaneous injection. Denosumab should be initiated and continued by secondary care. Secondary care may choose to give patients an **intravenous bisphosphonate** Choosing a product administered by injection (either subcutaneous or intravenous) may improve patient compliance.	2g daily 60mg s/c every 6 months Dose depends on product chosen.	Diarrhoea, headache, nausea and dermatitis. A small increase in the risk of venous thromboembolism was seen in the Phase III trials and, very rarely, hypersensitivity reactions may occur.	Strontium is contra-indicated in patients with severe renal impairment (creatinine clearance < 30 ml/min). Denosumab has an increased risk of hypocalcaemia if eGFR is less than 30ml/min.	**Strontium ranelate** is contra-indicated in patients with risk factors for venous thromboembolism. Strontium ranelate should be taken between meals and at least 2 hours after the last meal. It is usually taken at bedtime. Denosumab is contraindicated in patients with hypocalcaemia.

Formulary Choice	Osteoporosis Treatment	Reason	Dose	Side Effects *(refer to BNF or SPC more detail)*	Renal Impairment *(refer to BNF or SPC more detail)*	Notes
Calcium supplementation	Calcium and Vitamin D_3	Use the most cost-effective product available.	1-1.2g/day of calcium and 800-1000 IU/day of colecalciferol.	Gastrointestinal disturbances		**Calcium and vitamin D supplements** should be co-prescribed with these treatments unless there is evidence of an adequate dietary calcium intake. Calcium and vitamin D supplements should be routinely prescribed for frail elderly individuals who are housebound or in care homes .

Other Factors to Consider

Compliance

A number of studies have shown adherence with bone protection treatments to be low, with a recent systematic review showing persistence with treatment being as low as 17% in some patients. There is evidence to suggest that a low adherence is associated with smaller changes in bone mass density and increased fracture risk. From this research, the key factors that affect adherence to treatment are adverse events, lack of understanding of the condition/ disease being treated, lack of information about the treatment (including potential side effects) and lack of follow up.

The following measures could help improve adherence with treatment: ·

- Ensure patients understand what is being treated (fracture risk / osteoporosis)
- Give patient detailed information about the treatment (how it works, why they have to take it long term and potential side effects) ·
- Follow up the patient – a telephone follow up 3-6 months after starting treatment to ensure that they are experiencing no problems ·
- Encourage patients to contact practice if they have any side effects/ problems