



OSTEOPOROSIS

Top tips for MURs

- Advise patient to take medication regularly and confirm understanding of dosage regime
- Advise patient that drug treatment aims to improve bone repair and increase bone strength
- Counsel patient on reason for taking and advise them on how to take medication:
 - Alendronate, risedronate and ibandronic acid must be swallowed whole with a full glass of water, on an empty stomach, before breakfast. Patients should not eat or drink or take any other medicine and must remain upright for 30-60minutes after administration
 - Strontium should be taken at night without food
 - Avoid milk, antacids and other medications containing iron, calcium and magnesium during the stipulated time
- For patients taking calcium tablets, check the formulation is appropriate; chewable tablets, soluble tablets and ordinary tablets are available
- Check patients on vitamin D have had their plasma-calcium concentration checked at intervals and whenever nausea, vomiting or other symptoms of hypercalcaemia occur
- Counsel patient on signs and symptoms of complications that need referral (**see below**) and common side effects (**see overleaf**)
- Check that patients on bisphosphonates are:
 - Aware that they should not be taken in pregnancy and breastfeeding
 - Having regular dental check-ups, maintaining good oral hygiene and if using dentures to make sure they fit properly
 - Receiving adequate daily calcium of 1200mg daily through diet or supplements. Calcium is absorbed best when taken twice a day with food (with lunch and evening meal to avoid interactions with other foods / medicines taken first thing)
- Assess other medications as certain medications like glucocorticoids, PPIs, antidepressants, antiepileptics, aromatase inhibitors, glitazones, loop diuretics and large doses of levothyroxine, can increase the fracture risk through different mechanisms and should be used in caution in patients with osteoporosis
- Check patients on medication which often cause falls (hypnotics, antihypertensives, antidepressants, anticonvulsants, psychotropic drugs or polypharmacy), if they have had a falls assessment
- Report any relevant adverse drug reactions to the Yellow Card Scheme

Pathophysiology of osteoporosis

Osteoporosis is a progressive, systemic skeletal disorder which results from reduced bone mass and micro-architectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture. Osteoporosis is usually an age-related condition where bone resorption exceeds bone formation. In healthy bone there is a balance between the two processes, controlled by the parathyroid hormone which increases bone destruction, calcitonin which slows the destruction of bone by the osteoclasts and vitamin D which increases gastrointestinal absorption of calcium¹.

Bone strength primarily reflects the integration of bone density and bone quality². Severe osteoporosis (established osteoporosis) describes osteoporosis in the presence of one or more fragility fractures.³ Osteoporosis occurs most commonly in postmenopausal women and in those taking long-term oral corticosteroids.⁴

Lifestyle issues

- Counsel patient on reducing alcohol intake to within safe limits (up to 14 units a week, spread evenly over 3 or more days) – alcohol is known to be toxic to osteoblasts which rebuild bone
- Counsel patient on the importance of maintaining adequate calcium and vitamin D levels (lack of sunlight and/or low dietary intake can lead to low levels). Encourage a diet rich in milk or dairy products. Oily fish, nuts, mushrooms, some green vegetables and fortified breakfast cereals are a good source of vitamin D. Green leafy vegetables, nuts, sesame seeds, pulses, soya drinks, tofu and dairy products are good sources of calcium
- Advise patients who smoke the benefits of stopping smoking and how to access pharmacy smoking cessation services or Stop Smoking Wales
- Advise patient on the benefit of weight-bearing exercise (walking, aerobics) and exercises to strengthen muscles and maintain balance and co-ordination (swimming, gardening, tai chi). Recommend completing 30 minutes of aerobic exercise three to five times a week
- Counsel patients to try and get 10 minutes of sun exposure once or twice a day, without sunscreen and to try and get outside more between the months of May to September (taking care not to burn)

Red flags that need referral

- Any early signs of osteonecrosis of the jaw (loose tooth, exposed tooth, jaw pain with swelling and numbness) on bisphosphonate or denosumab treatment
- Any signs of osteonecrosis of the external auditory canal (ear pain, discharge from ear, ear infection) on bisphosphonate treatment
- Any symptoms of oesophageal irritation (dysphagia, pain on swallowing, retrosternal pain or heartburn)
- Any of the following symptoms in patients taking strontium ranelate: skin rash, fever, swollen glands and symptoms of a systemic allergic reaction. Tell patient to seek immediate medical attention
- Any symptoms of venous thromboembolism (painful or swollen legs, chest pain or feeling short of breath)
- Any signs of atypical stress fractures (pain in the thigh, hip or groin)
- Any symptoms of uncontrolled hypertension or ischaemic heart disease or cerebrovascular disease (if patient is on strontium)
- Any signs of hypocalcaemia on bisphosphonate / denosumab (muscle spasm, cramps, numbness or tingling in fingers, toes, seizures, altered mental status)
- Pregnancy and breastfeeding



How do drugs used to treat and prevent osteoporosis work?

Bisphosphonates (alendronic acid, etidronate, clodronate, risedronate, and ibandronic acid)	Inhibitors of bone resorption and increase bone mineral density by altering osteoclast activation and function. Absorbed onto hydroxyapatite crystals in bone, slowing the rate of bone growth and dissolution, therefore the rate of turnover is reduced, especially at site of active remodelling.
Recombinant parathyroid hormone (PTH: teriparatide)	A recombinant fragment of human PTH and an anabolic agent which stimulates new formation of bone and increases resistance to fracture.
Strontium ranelate	Has properties similar to calcium with dual effect on bone metabolism, it increases bone formation and decreasing bone resorption.
Denosumab	Human monoclonal antibody that inhibits osteoclast formation, function and survival, thereby decreasing bone resorption.
Hormone replacement therapy (HRT)	Inhibit bone resorption, most likely through the oestrogen-sensitive osteoblast. The osteoblast releases growth factors that inhibit the recruitment and differentiation of osteoclasts from their bone marrow precursors.
Selective oestrogen receptor modulators (SERMs)	Modify gene expression by binding to the alpha and beta isoforms of the oestrogen receptor. Appears to inhibit bone resorption induced by oestrogen deficiency.
Vitamin D analogues (calcitriol and alfacalcidol)	Increases serum calcium levels by promoting absorption of dietary calcium and stimulates release of calcium from bone - replacement therapy.
Calcitonin	Inhibits osteoclast activity, thereby decreasing bone resorption. No longer recommended for the prevention or treatment of postmenopausal osteoporosis.

What are the common side effects to look out for?

Common side effects	Recommendation
Upper gastrointestinal disturbance (bisphosphonates)	Counsel patient on correct administration. Consider recommending Gaviscon or equivalent (but avoid Gaviscon in the morning if taking bisphosphonate). Refer to prescriber if symptoms not tolerated. In people with oesophageal abnormalities and other factors that delay oesophageal transit or emptying, risedronate should be used cautiously and alendronate is contraindicated.
Nausea, vomiting, constipation or diarrhoea	Advise patient to get their calcium levels checked and to maintain adequate fluid intake. Advise to take calcium with food; refer if symptoms are persistent.
Headache (strontium ranelate), migraine headache (raloxifene)	Refer to prescriber. For headache, try a simple analgesic then refer if persistent. Refer symptoms of migraine.
Joint and/or muscle pain	Use simple analgesics and refer to prescriber if pain is persistent or fracture is suspected.
Throat irritation, rhinitis, urinary tract infection, inflammation or infection of vagina - more commonly seen with raloxifene	Refer to prescriber. With strontium, advise the patient to rinse mouth with water after swallowing.
Inflammation in the eye (eye pain, red eye or disturbed vision - sometimes seen with bisphosphonates)	Refer to prescriber

Potential serious drug interactions?

Drugs used to treat osteoporosis interact with many other medications including antacids, antibacterials, anticoagulants, calcium, cytotoxics, iron and lipid-regulating drugs - **see BNF Appendix 1: Interaction for more details.**

- Avoid taking calcium tablets at the same time of day as levothyroxine, iron, magnesium, bisphosphonates and quinolones (calcium tablets are best taken at lunch and with an evening meal)
- Certain medications e.g. PPIs and H2 receptor antagonists can reduce calcium levels

Where can you find more information?

- BNF sub-section 6.6 – Drugs affecting bone metabolism
- Musculoskeletal disorders – advancing your practice distance learning pack that can be found on the WCPPE website (<http://www.wcppe.org.uk>)
- NICE guidance: TA160 Osteoporosis - primary prevention; TA161 Osteoporosis - secondary prevention including strontium ranelate; Osteoporosis fragility fractures (CG146), TA204 Denosumab for prevention of osteoporotic fractures, can be found on NICE website (www.nice.org.uk)
- Clinical Knowledge Summary osteoporosis can be found on CKS website (<http://www.cks.nice.org.uk>)
- National Osteoporosis Society (NOS) (<http://www.patient.co.uk/support/national-osteoporosis-society>)
- Management of osteoporosis and the management of fragility fractures (<http://sign.ac.uk/guidelines/fulltext/142>)
- Management of osteoporosis. The Welsh approach. <http://www.equalityhumanrights.wales.nhs.uk/sitesplus/documents/1120/Stone.pdf>
- Vitamin D and bone health in adults. <https://nos.org.uk/media/2073/vitamin-d-and-bone-health-adults.pdf>
- Healthy eating for strong bones. <https://nos.org.uk/for-people-and-families/healthy-living-and-risk/healthy-eating-for-strong-bones/>

References

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2. Anonymous. Osteoporosis prevention, diagnosis and therapy. J Am Med Assoc, 285: 785–795, 2001
3. Kanis JA on behalf of the World Health Organization Scientific Group. Assessment of osteoporosis at the primary health-care level. Technical report. University of Sheffield, UK: WHO Collaborating Centre; 2008
4. Musculoskeletal disorders level 1, CPPE, distance learning pack