

REGIONAL DRUG AND THERAPEUTICS CENTRE

**THE USE OF TERIPARATIDE IN THE
MANAGEMENT OF OSTEOPOROSIS**

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SUMMARY

- Osteoporosis is a progressive systemic skeletal disease characterised by low bone mass and micro-architectural deterioration of bone tissue, leading to enhanced fragility and risk of fracture. Women are at greater risk of developing osteoporosis following the menopause mainly due to oestrogen deficiency. Osteoporosis is diagnosed by measurement of bone mineral density (BMD). If BMD is ≤ 2.5 standard deviations below the young normal adult mean value i.e. a T score of ≤ -2.5 then osteoporosis is present.
- An estimated 3 million people in the UK suffer from osteoporosis (5000 people per 100,000 population in England and Wales). The disease affects 1 in 3 women and 1 in 12 men over the age of 50. One third of adult women will sustain an osteoporotic fracture in their lifetime. Prospective studies show that the risk of fracture increases progressively with decreasing BMD.
- Teriparatide is a novel drug composed of a fragment of recombinant human parathyroid hormone (1-34) that acts by stimulating bone formation. It is administered by daily subcutaneous injection.
- Teriparatide is licensed for the treatment of established osteoporosis in postmenopausal women with duration of therapy restricted to 18 months. Teriparatide is not licensed for men in the UK.
- One trial has shown that teriparatide increases BMD significantly more than placebo in the spine and femoral neck. It also reduced new vertebral and non-vertebral fracture rates compared to placebo. However, teriparatide appears to reduce the BMD of the radius.
- Small trials suggest that there is a possibility of an increased effect when teriparatide is used in conjunction with HRT where indicated.
- At the licensed dose the most common adverse effects are limb pain, nausea, headache and dizziness. The licence restricts treatment duration to 18 months because of the development of osteosarcoma in rats. However a peer-reviewed study indicated that teriparatide is not likely to cause this in humans over this time period.
- Teriparatide is appropriate for patients with severe disease who either have an existing fracture or are at high risk of a fracture. Those patients intolerant of other therapies are also likely to benefit from treatment with teriparatide.
- Teriparatide is suitable to be prescribed under a shared care protocol between primary and secondary care with secondary care specialists responsible for initiation, follow up and discontinuation of treatment. The manufacturer intends to supply teriparatide directly to patients with other support around administration, however, this extra support is voluntary and may be withdrawn in the future.
- Teriparatide costs £272 per patient for 28 days treatment. On the basis of 5000 people per 100,000 population suffering from osteoporosis in England and Wales and hypothesising that around 10% progress to severe disease, increased prescribing costs to the NHS would amount to £136,000 per 100,000 population.
- Publication of a head to head trial of teriparatide and alendronate (FACT) is awaited which has examined changes in BMD of the lumbar spine and bone turnover markers. An oral version of teriparatide is currently in early development.

BACKGROUND

Osteoporosis is defined as a progressive systemic skeletal disease characterised by low bone mass and micro-architectural deterioration of bone tissue, leading to enhanced fragility and risk of fracture.¹ A diagnosis of osteoporosis is made if the bone mineral density (BMD) is ≤ 2.5 standard deviations below the young adult mean value i.e. a T score of ≤ -2.5 [WHO diagnostic criteria, appendix 1].¹ The disease affects 1 in 3 women and 1 in 12 men over the age of 50 in the UK, an estimated 3 million people.² More than one-third of adult women will sustain one or more osteoporotic fractures in their lifetime. In the UK, the disorder results in over 310,000 fractures each year causing significant disability and morbidity.^{3,4} Prospective studies show that risk of fracture increases progressively with decreasing BMD.⁵ Up to 14,000 people die each year as a result of osteoporotic hip fractures.³

Women are at greater risk of developing osteoporosis as they achieve a lower peak bone mass than men and bone loss is accelerated following the menopause mainly due to oestrogen deficiency.⁶ In age-related osteoporosis, which affects both men and women, loss of bone occurs due to nutritional factors (calcium, vitamin D and protein intake) and the ageing process. Genetic and lifestyle factors such as physical inactivity, smoking and excessive alcohol consumption also play a role. Secondary osteoporosis is caused by diseases such as rheumatoid arthritis and hypogonadism, immobilisation, and drugs such as corticosteroids.⁷

The main aim of the management of osteoporosis is to prevent the occurrence of fractures.⁸ Any underlying cause of secondary osteoporosis should be treated if possible such as hypogonadism, alcohol abuse, hyperthyroidism and glucocorticoid excess. Specific treatment of conditions such as hypogonadism increases BMD by up to 15%.^{9,10} Lifestyle changes including weight bearing exercise, reducing alcohol consumption and stopping smoking may be beneficial.⁸ Although BMD is an important determinant of fracture risk, other factors including susceptibility to falls and types of fall also contribute to the risk.⁸ The NSF for older people includes recommendations on reducing the risk of falls in susceptible people.³

The WHO definition of osteoporosis does not necessarily represent a threshold for treatment.¹¹ Drug treatment should be considered in patients with a T score below -2.5 and in those who have had previous fragility fractures with a T score between -1 and -2.5 however the decision to treat depends on overall fracture risk.⁹ Calcium and vitamin D supplements, tibolone, bisphosphonates, raloxifene, calcitriol, and calcitonin are currently used in the prevention and/or treatment of osteoporosis. HRT is now a last line agent in the prevention/treatment of osteoporosis since the CSM warning regarding its unfavourable risk/benefit ratio following the publication of the Women's Health Initiative trial and the UK Million Women Study.¹² All patients at risk of osteoporosis should maintain an adequate intake of calcium and vitamin D.¹³ The requirement for these supplements may be increased in the frail and elderly.¹⁰ Tibolone is an alternative synthetic steroid that is comparable to HRT in efficacy, however, there is no data regarding fracture prevention and patients taking tibolone must be at least 12 months post menopause.¹⁴

Three oral bisphosphonates are licensed for the prevention and treatment of postmenopausal osteoporosis or corticosteroid-induced osteoporosis; alendronate, etidronate and risedronate.¹³ Raloxifene is an alternative treatment for reducing the risk of vertebral fractures in postmenopausal women with a history of vertebral or non-vertebral fracture when a bisphosphonate is inappropriate or not tolerated.⁶ However, it should not be used by those at increased risk of venous thromboembolism.¹⁴ Calcitonin used intranasally with calcium and vitamin D supplements has been shown to reduce the incidence of vertebral fractures.⁶ Calcitriol and alfacalcidol decrease bone loss in women with osteoporosis but their effects differ between studies. Some studies have shown a decrease in vertebral fracture frequency.⁴ Calcitonin or calcitriol may be considered if other agents are unsuitable.¹³

