NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal

Denosumab for the prevention of osteoporotic fractures in postmenopausal women

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of denosumab within its licensed indication for the prevention of osteoporotic fractures in postmenopausal women.

Background

Osteoporosis is a progressive, systemic skeletal disorder characterised by low bone mass and deterioration of the structure of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture.

It is estimated that more than 2 million women have osteoporosis (that is, have a T-score of −2.5 standard deviations [SD] or below) in England and Wales. After the menopause, the prevalence of osteoporosis increases markedly with age, from approximately 2% at 50 years rising to more than 25% at 80 years.

Fragility fracture is often referred to as a low-trauma fracture; that is, a fracture sustained as the result of a force equivalent to the force of a fall from a height equal to, or less than, that of an ordinary chair. In the absence of fracture, osteoporosis is asymptomatic and often remains undiagnosed. It is estimated that annually there are 180,000 osteoporosis-related symptomatic fractures in England and Wales. Osteoporotic fragility fractures occur most commonly in the hip, vertebrae and wrist.

After a hip fracture, a high proportion of women are permanently unable to walk independently or to perform other activities of daily living and, consequently, many are unable to live independently. Vertebral fractures can be associated with curvature of the spine and loss of height and can result in pain, breathing difficulties, gastrointestinal problems and difficulties in performing activities of daily living. It is thought that the majority of vertebral fractures (50–70%) do not come to clinical attention. Both hip and vertebral fractures are also associated with increased mortality.

Drug treatments to treat osteoporosis may include calcium and vitamin D supplements, calcitriol, calcitonin, bisphosphonates (alendronate, etidronate, risedronate, ibandronate, zoledronate), parathyroid hormone (teriparatide), selective estrogen receptor modulators (raloxifene) and strontium ranelate.

NICE technology appraisal guidance No. 160 recommends alendronate as first-line treatment for the primary prevention of fragility fractures in postmenopausal women with osteoporosis who have specific levels of fracture risk as defined by their age, bone mineral density (BMD), and number of independent clinical risk factors for fracture or indicators of low BMD. Technology appraisal guidance No. 161 (secondary prevention, in women who have already sustained a fracture) recommends alendronate as first-line treatment for the secondary prevention of fragility fractures in post-menopausal women with confirmed osteoporosis. The other drugs included in the appraisals (risedronate, etidronate, raloxifene, strontium ranelate and teriparatide) are recommended for women who cannot take alendronate, at specified ages, BMD levels and number of independent clinical risk factors for fracture.

The technology

Denosumab (Amgen) is a fully human monoclonal antibody which inhibits osteoclasts (the cells responsible for bone resorption). It is administrated by subcutaneous injection. Denosumab does not hold a UK marketing authorisation. It has been studied in clinical trials for its effect on bone mineral density, bone turnover and fractures in postmenopausal women with low bone mineral density compared with placebo and alendronate.

Intervention	Denosumab
Population	Postmenopausal women at risk of having an osteoporotic fragility fracture
Comparators	Management strategies without the use of denosumab, which may include: • bisphosphonates (such as alendronate, etidronate, ibandronate, risedronate, zoledronate) • selective oestrogen receptor modulators (such as raloxifene) • strontium ranelate • parathyroid hormone analogues • calcitriol • calcitonin

Outcomes	The outcome measures to be considered include: • osteoporotic fragility fracture • bone mineral density • mortality • health-related quality of life • adverse effects of treatment.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. If the evidence allows, the following subgroups will be considered: • people with risk factors for fracture • site of fracture • women with a disability which prevents them from using specific technologies. Consideration should be given to: • approach fracture risk assessment • assessment of probability of fracture • cost of fracture risk assessment • continuation of treatment.

Related NICE recommendations	Related Technology Appraisals: Technology appraisal No. 160, Oct 2008. 'Alendronate, etidronate, risedronate, raloxifene and strontium ranelate for the primary prevention of osteoporotic fragility fractures in postmenopausal women'. Technology appraisal No. 161, Oct 2008. 'Alendronate, etidronate, risedronate, raloxifene, strontium ranelate and teriparatide for the secondary prevention of osteoporotic fragility fractures in postmenopausal women'. Related Guidelines: Clinical Guideline in preparation (currently 'suspended'), 'Osteoporosis: assessment of fracture risk and the prevention of osteoporotic fractures in individuals at high risk'. Earliest anticipated date of publication: to be confirmed.