NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal

Denosumab for the treatment of therapy-induced bone loss in non-metastatic breast cancer

Final scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of denosumab within its licensed indication for the treatment of therapy-induced bone loss in non-metastatic breast cancer.

Background

Breast cancer is the most common malignancy affecting women in the UK, accounting for 1 in 3 of all cancers in women. Breast cancer incidence rates have increased by more than 50% over the last twenty-five years. There were over 45,500 women newly diagnosed with breast cancer in England and Wales during 2005. In 2006, there were 10,916 deaths registered from breast cancer in England and Wales, an average rate of 42 deaths per 100,000 women and about 1 death per 100,000 men. Approximately two thirds of women diagnosed with breast cancer have hormone (oestrogen or progesterone) - receptor positive tumours. Approximately 80% of women presenting with breast cancer have non-metastatic disease.

Hormone-ablative therapies such as aromatase inhibitors (for hormone-receptor positive breast cancer), deprive tumour cells of the proliferative stimulus of oestrogen, but their use is also associated with accelerated bone loss and increased risk of fragility fracture. Bone loss that occurs with breast cancer therapy may be more rapid and severe than post-menopausal bone loss in women.

Patients receiving aromatase inhibitor therapy are encouraged to maintain a healthy lifestyle with an adequate intake of calcium and vitamin D supplements to prevent bone loss. Bisphosphonates (such as alendronic acid, sodium clodronate, disodium etidronate, risedronate sodium, ibandronic acid, zoledronic acid) may also be used to treat breast cancer therapy induced bone loss.

The technology

Denosumab (Amgen) is a fully human monoclonal antibody that specifically targets the receptor activator of nuclear factor kappa B ligand (RANKL). This results in inhibition of osteoclast differentiation, activation, and survival, consequently suppressing bone resorption.

Denosumab does not have a UK marketing authorisation. The drug is being studied in placebo-controlled clinical trials for its effect on bone mineral

density and fractures in people undergoing aromatase inhibitor therapy for non-metastatic breast cancer.

Intervention(s)	Denosumab
Population(s)	Women with non-metastatic breast cancer treated with hormone-ablative therapies
Standard comparators	• Bisphosphonates • Best supportive care
Outcomes	The outcome measures to be considered include: • bone mineral density • fragility fracture • adverse effects of treatment • health-related quality of life.
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 evidence allows, the appraisal will seek to identify subgroups (e.g people with high risk of fragility fracture associated with low bone mineral density) of individuals for whom the technology is particularly clinically and cost- effective.
Related NICE recommendations	Related Technology Appraisals: Technology appraisal, No. 112, Nov 2006, Hormonal therapies for the adjuvant treatment of early oestrogen-receptor-positive breast cancer. Related Guidelines: Clinical guideline in preparation, Breast cancer (early & locally advanced): diagnosis and treatment Earliest

	anticipated date of publication Feb 2009. NICE Cancer service guidance, Aug 2002, Improving outcomes in breast cancer.