NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Multiple Technology Appraisal

Denosumab for the treatment of bone metastases from solid tumours and multiple myeloma

Draft scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of denosumab within its licensed indication for the treatment of bone metastases from solid tumours and multiple myeloma.

Background

Metastatic cancer is cancer that has spread from the primary site to other parts of the body. When cancerous cells break away from the primary site, they can travel to other areas of the body through either the bloodstream or lymphaticsystem. Bone is one of the most common sites for these circulating cancer cells to settle and start growing. Metastases can occur in bones anywhere in the body, but the spine is commonly affected by bone metastasis, as well as the pelvis, hip, upper leg bones and the skull.

Although any type of cancer can spread to the bone, the most common are solid tumor cancers such as breast, prostate, lung, thyroid and kidney. Bone metastases from breast and prostate cancers account for more than 80% of all cases of metastatic bone disease. The incidence of bone involvement in advanced breast and prostate cancer is approximately 65-75%. Bone metastases can also occur in multiple myeloma, which is a cancer of a type of white blood cell that is found in the bone marrow. The incidence of bone metastases in people with advance multiple myeloma is 95-100%.

Survival rates for people with bone metastases vary depending on the primary tumour type. In breast cancer, median survival is 24 months with a 5-year survival rate of 20% and in prostate cancer there is a 5-year survival rate of 25% and a median survival of 40 months. The clinical course of bone metastases in multiple myeloma can be relatively short with a median survival time of 20 months and a 10% probability of surviving 5 years.

Bone metastasis results in bone destruction and increased tumour burden. Tumour cells in the bone secrete factors that activate cells (osteoclasts) responsible for bone resorption. In turn, resorption by osteoclasts releases growth factors from the bone that may stimulate tumour growth. Bone metastasis is one of the most frequent causes of pain in people with cancer. It can also cause bones to break, cause high calcium levels in the blood (hypercalcaemia), and spinal cord compression which may require surgery to the bone or radiation therapy to the bone.

Bisphosphonates are currently used for the treatment and prevention of skeletal-related events that result from bone metastases. Local radiotherapy and orthopaedic surgery may be required to treat bone pain and fractures that result from the bone damage.

The technology

Denosumab (Prolia, Amgen) is a fully human monoclonal antibody that specifically targets the receptor activator of nuclear factor kappa B ligand (RANKL). RANKL plays a role in bone destruction and tumour growth in metastatic cancers and multiple myeloma, by inhibiting osteoclast differentiation, activation, and survival, consequently suppressing bone resorption. It is administered by subcutaneous injection.

Denosumab does not have a UK marketing authorisation for the treatment of bone metastases from solid tumours and multiple myeloma. It has been studied in clinical trials compared with zoledronic acid (a bisphosphonate) in adults with bone metastases from solid tumours including breast and prostate cancer, and multiple myeloma.

Denosumab has a UK marketing authorisation for the treatment of osteoporosis in post menopausal women and for the treatment of bone loss associated with hormone ablation in men with prostate cancer.

Intervention(s)	Denosumab
Population(s)	Adults with bone metastases from solid tumours and adults with multiple myeloma
Comparators	Bisphosphonates such as sodium clodronate, disodium pamidronate, ibandronic acid and zoledronic acid
Outcomes	The outcome measures to be considered include: • Survival • Time to first skeletal related event • Incidence of skeletal related events including bone pain, fracture, hypercalcaemia and avoidance of other interventions such as surgical or radiation treatment • 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
Related NICE recommendations	Related Technology Appraisals: None Related Guidelines: Clinical Guideline No 75, November 2008, 'Metastatic spinal cord compression'

Questions for consultation

Have the most appropriate comparators for denosumab for the treatment of bone metastases from solid tumours and multiple myeloma been included in the scope? Are the comparators listed routinely used in clinical practice?

- Are the comparators different depending on the type of primary tumour?

Are there any subgroups of patients in whom the technology is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Please consider whether in the remit or the scope there are any issues relevant to equality. Please pay particular attention to whether changes need to be made to the remit or scope in order to promote equality, eliminate unlawful discrimination, or foster good relations between people who share a characteristic protected by the equalities legislation and those who do not share it, or if there is information that could be collected during the assessment process which would enable NICE to take account of equalities issues when developing guidance.

Do you consider the technology to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of the technology can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits