NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal

Denosumab for preventing bone metastases in castrate resistant prostate cancer

Draft scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of denosumab within its licensed indication for prolonging bone metastasis-free survival in castrate resistant prostate cancer.

Background

Prostate cancer is a disease in which tumours develop in the prostate, a gland in the male reproductive system. Its cause is thought to be multifactorial, involving both environmental and genetic factors. The incidence of prostate cancer increases with age and is higher in men of African-Caribbean family origin. In England and Wales, over 37,000 people were newly diagnosed with prostate cancer in 2009, and over 9600 people died from prostate cancer in 2010

Advanced prostate cancer often leads to bone metastases. The typical sites of involvement include the spine, pelvis and rib cage. The median survival of patients is around 3 years after the development of bone metastases. Bone metastases from prostate cancer are characterized by a predominance of osteoblastic lesions (inappropriate new bone formation). Bone metastases are a major cause of death, disability, decreased quality of life, and increased treatment cost in these patients.

NICE clinical guideline 58 ‘Prostate cancer’ states that people with localised disease should be managed with active surveillance, surgical prostatectomy (removal of the prostate) or high-dose radical radiotherapy. It also states that bisphosphonates should not be used for the prevention of bone metastases in men with prostate cancer.

The technology

Denosumab (XGEVA, Amgen) is a fully human monoclonal antibody that specifically targets the receptor activator of nuclear factor kappa B ligand (RANKL) which plays a role in bone destruction and tumour growth in metastatic cancers. It is intended to inhibit bone resorption. Denosumab is administered as a subcutaneous injection.

Denosumab does not hold a UK marketing authorisation for prolonging bone metastasis-free survival in people with castrate resistant prostate cancer. It has been studied in a clinical trial compared with placebo to prolong bone

metastasis-free survival in men with castrate resistant (androgen independent) non-metastatic prostate cancer who are considered to be at high risk for the development of bone metastases. Trials define people at high risk of developing bone metastases if their prostate specific antigen (PSA) level is greater than or equal to 8.0ng/mL, or their PSA level doubles within 10 months.

Intervention(s)	Denosumab
Population(s)	People with non-metastatic castrate resistant prostate cancer at high risk of developing bone metastases
Comparators	• Standard treatment without denosumab
Outcomes	The outcome measures to be considered include: • overall survival • bone metastasis free survival • time to first occurrence of bone metastasis • 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, subgroup analyses according to risk based on PSA scores or PSA doubling time may be considered.
Related NICE recommendations	Related Guidelines: Clinical Guideline No. 58, February 2008, 'Prostate Cancer: diagnosis and treatment'. Review date February 2011. Related Public Health Guidance: Cancer Service Guidance, September 2002.

	'Improving outcomes in urological cancers'.

Questions for consultation

Is standard treatment without denosumab an appropriate comparator? What does it include?

Should progression-free survival be included as an additional outcome measure in the scope?

Are there any subgroups of people 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.