NATIONAL INSTITUTE FOR CLINICAL EXCELLENCE

Health Technology Appraisal

Docetaxel for the treatment of hormone-refractory metastatic prostate cancer

Draft scope

Appraisal objective

To appraise the clinical and cost effectiveness of docetaxel (Taxotere®, Aventis Pharma Ltd) for hormone-refractory metastatic prostate cancer and to provide guidance to the NHS in England and Wales[1].

Background

Prostate cancer is the commonest cancer in men in the UK, with over 27,000 new cases diagnosed in 2000. It is also the second most common cause of male cancer mortality, with 9940 deaths in 2002. The number of diagnoses has been increasing in recent years, but it is thought that this is due to greater monitoring of prostate specific antigen (PSA) levels in the blood, which can indicate abnormal changes to the prostate. The causes of prostate cancer have not been adequately defined.

The incidence of prostate cancer increases with age and is rare in men under 50 years old. By the age of 80 years, over 50% of men have cancerous prostate changes. However, more than 95% of all prostate cancers begin as a hard mass in the peripheral portion of the gland and infiltration of the surrounding tissues takes place slowly. As a result of the slow rate of tumour growth, many men never know they have it and die from unrelated causes.

Prostate cancer growth is stimulated by androgens (male sex hormones) and men with the disease therefore may receive hormone therapy to reduce androgen levels. For men with metastatic disease (where the cancer has spread to other parts of the body, most commonly the bones), hormone therapy forms the cornerstone of treatment. Standard hormonal treatments for metastatic disease are orchidectomy (surgical removal of testes) or use of a gonadorelin analogue.

Around 80% of men with metastatic prostate cancer initially respond to hormone therapy. However, after around 12 to 18 months of treatment, the disease usually becomes androgen-independent, whereby it no longer requires androgen to progress. Alternative treatment strategies are therefore required and, although the cancer may respond to additional hormonal strategies (such as anti-androgen therapy and anti-androgen withdrawal), hormone-refractory prostate cancer (HRPC), whereby the cancer is unresponsive to further hormonal manipulation, ultimately develops. The

[1]The Department of Health and Welsh Assembly government remit to the Institute: To appraise the clinical and cost effectiveness of docetaxel for hormone-refractory prostate cancer.

options for the treatment of HRPC are limited; many chemotherapy regimes have been shown to be ineffective and associated with significant toxicity. More recently, alternative chemotherapy regimens, such as those based on mitoxantrone, estramustine and taxanes, have been identified and are increasingly used to control the cancer.

The technology

Docetaxel belongs to the taxane class of chemotherapy drugs. It works by inhibiting tubulin, a protein essential to cell division, thus preventing cancer cells from dividing and growing in number. It is currently licensed in the UK for locally advanced and metastatic breast cancer and non-small cell lung cancer but is not yet licensed for prostate cancer. The most recent information from the manufacturer indicates that they anticipate that docetaxel will gain marketing authorisation for hormone-refractory metastatic prostate cancer in combination with prednisone or prednisolone within the timelines of the appraisal. Docetaxel in combination with prednisone has already been approved by the U.S. Food and Drug Administration for the treatment of 'patients with androgen independent (hormone refractory) metastatic prostate cancer'.

Intervention(s)	Docetaxel
Population(s)	Men with hormone-refractory metastatic prostate cancer
Standard comparators	Comparison will be made with: • Chemotherapy regimens based on mitoxantrone or estramustine • Active supportive care.
Outcomes	The outcome measures to be considered include: • Overall survival • Progression-free survival • Response rate • PSA decline • Adverse effects of treatment • Health-related quality of life.
Economic analysis	Ideally, the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. Costs will be considered from an NHS and Personal Social Services perspective.

Other considerations	Where the evidence allows, the appraisal will identify subgroups of men with hormone-refractory metastatic prostate cancer for whom docetaxel is particularly appropriate or inappropriate. The intervention will be appraised according to its anticipated licensed indication. Guidance will only be issued in accordance with the marketing authorisation. Where judged appropriate, studies of the intervention and comparators in combination with other drugs may be considered.
Related NICE recommendations	Related Technology Appraisals: Atrasentan for hormone-refractory prostate cancer (to be scheduled). Related Guidelines: Prostate Cancer: Diagnosis and treatment. Anticipated launch to be confirmed.

Questions for consultation

Consultees are particularly asked to comment on the appropriateness of the listed comparators.