NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Cabazitaxel for the second line treatment of hormone refractory, metastatic prostate cancer

Final Scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of cabazitaxel within its licensed indication for the second line treatment of hormone refractory, metastatic prostate cancer that has progressed following or during docetaxel-based treatment.

Background

Prostate cancer is a disease in which tumours develop in the prostate, a gland in the male reproductive system. It is the most common cancer in men in England and Wales, with 32,188 new cases diagnosed in 2006. The incidence of prostate cancer increases with age, with around 80% of cases occurring in men over the age of 65 years. In 2007, 9222 deaths from prostate cancer were recorded in England and Wales.

The cause of prostate cancer is thought to be multifactorial, involving both environmental and genetic factors. Prostate cancer growth is stimulated by androgens (male sex hormones) and men with the disease therefore may receive hormone therapy to reduce androgen levels. Fifty-five to sixty percent of prostate cancers will become metastatic – that is, they will spread to other parts of the body (most commonly the bones). For men with metastatic disease, hormonal treatment forms the cornerstone of treatment. Standard hormonal treatments for metastatic disease are orchidectomy (surgical removal of testes) or use of a gonadotrophin releasing hormone analogue such as goserelin, leuprorelin or triptorelin.

Metastatic prostate cancer will initially respond to hormone therapy in around 80% of men. However, after around 12 to 18 months of treatment, the disease usually becomes androgen-independent, where the cancer no longer requires androgen to progress. Alternative treatment strategies are therefore required. The cancer may respond to additional hormonal strategies, but ultimately the cancer becomes unresponsive to further hormonal manipulation. This stage is called hormone refractory prostate cancer (HRPC). The prognosis is poor for patients with HRPC: survival is not expected to exceed between 7 and 15 months. The aim of treatment for HRPC is to alleviate symptoms, prolong life and slow progression of the disease.

NICE Technology Appraisal no. 101 recommends docetaxel as a treatment option for men with HRPC who have a Karnofsky performance-status score of 60% or more. Men with metastatic HRPC that has progressed during or after

a docetaxel-based treatment may receive a combination of palliative treatments. Management options include mitoxantrone with or without steroids such as prednisolone, and a variety of chemotherapy regimens such as 5-fluorouracil, cyclophosphamide and carboplatin/etoposide.

The technology

Cabazitaxel (Jevtana, Sanofi-aventis) is a taxane anti-neoplastic agent. It works by stopping the polymerisation of microtubules that are essential for mitotic and interphase cellular functions and thereby causes inhibition of cell division and cell death. It is administered by intravenous infusion.

Cabazitaxel does not currently have a UK marketing authorisation for the treatment of HRPC. It is being studied in clinical trials (in combination with prednisone) compared with mitoxantrone and prednisone in men with prostate cancer previously treated with docetaxel and with documented progression of disease.

Intervention(s)	Cabazitaxel in combination with prednisolone
Population(s)	Men who have hormone refractory metastatic prostate cancer that has progressed following or during docetaxel-based treatment
Comparators	• Mitoxantrone in combination with prednisolone • Chemotherapy without cabazitaxel (for example 5-fluorouracil, cyclophosphamide and carboplatin/etoposide)
Outcomes	The outcome measures to be considered include: • Overall survival • Progression-free survival • Response rate • Prostate-specific antigen level • 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	If evidence allows, consideration will be given to subgroups defined by • baseline performance status • duration of prior docetaxel exposure • time since docetaxel treatment Guidance will only be issued in accordance with the marketing authorisation.
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No. 101, Jun 2006, 'Docetaxel for the treatment of hormone refractory prostate cancer', Review date June 2013. Technology Appraisal No. 194, Jul 2010; 'Denosumab for the treatment of therapy-induced bone loss in non-metastatic prostate cancer'. Terminated appraisal. Technology Appraisal in Preparation, 'Dutasteride for reducing the risk of developing prostate cancer in men who are considered to be at increased risk of developing the disease', Earliest anticipated date of publication TBC. Suspended Technology Appraisal, 'Atrasentan for hormone refractory prostate cancer', Earliest anticipated date of publication TBC. Proposed Technology Appraisal, 'Abiraterone for the treatment of advanced metastatic castration resistant prostate cancer'. Earliest anticipated date of publication TBC. Proposed Technology Appraisal, 'Abiraterone for the treatment of advanced metastatic castration resistant prostate cancer in people who are chemotherapy-naive'. Earliest anticipated date of publication TBC. Related Guidelines: Cancer Service Guidance Urological Cancer, Sep 2002, Improving outcomes in urogenital cancers', Anticipated review date TBC, Clinical Guideline No. 58, Feb 2008, 'Prostate cancer: diagnosis and treatment', Anticipated review date Feb

	2011. Related Interventional Procedures: Interventional Procedure Guidance No. 258, Apr 2008, 'Intraoperative red blood cell salvage during radical prostatectomy or radical cystectomy'. Interventional Procedure Guidance No. 193, Nov 2006, 'Laparoscopic radical prostatectomy'. Interventional Procedure Guidance No. 174, May 2006, 'High dose rate brachytherapy in combination with external-beam radiotherapy for localised prostate cancer'. Interventional Procedure Guidance No. 145, Nov 2005, 'Crytotherapy as a primary treatment for prostate cancer'. Interventional Procedure Guidance No. 132, Jul 2005, 'Low dose rate brachytherapy for localised prostate cancer'. Interventional Procedure Guidance No. 119, May 2005, 'Crytotherapy for recurrent prostate cancer'. Interventional Procedure Guidance No. 118, Mar 2005, 'High-intensity focused ultrasound for prostate cancer'.