NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Proposed Health Technology Appraisal

Abiraterone for the treatment of chemotherapy naïve metastatic castration-resistant prostate cancer

Draft scope (Pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of abiraterone in combination with prednisolone within its licensed indication for the treatment of metastatic, castration-resistant prostate cancer in men who have not been previously treated with chemotherapy.

Background

Prostate cancer is a disease in which tumours develop in the prostate, a gland in the male reproductive system. In England and Wales, there were over 33,000 men newly diagnosed with prostate cancer and over 9,100 deaths from prostate cancer in 2008. The incidence of prostate cancer increases with age. The majority of men have histological evidence of prostatic cancer by age 80 but are more likely to die of unrelated causes. The cause of prostate cancer is thought to be multi-factorial, involving both environmental and genetic factors.

Prostate cancer growth is stimulated by androgens (male sex hormones, such as testosterone). NICE clinical guideline 58 ('Prostate cancer') states that men with localised disease should be managed with active surveillance, surgical removal of the prostate (known as prostatectomy) or high-dose radical radiotherapy. However, once the cancer has become metastatic (that is, once the cancer has spread to other parts of the body), it is unlikely that it will be able to be cured, though the progression of the cancer can be slowed with treatment. Stopping the body making testosterone can slow the growth of the cancer, or even shrink it. Men with prostate cancer may therefore receive hormonal therapy to reduce androgen levels. Standard hormonal treatments for metastatic disease are orchidectomy (surgical removal of the testes, also known as 'surgical castration') or use of a gonadotrophin-releasing hormone analogue such as goserelin, leuprorelin or triptorelin (also known as 'medical castration').

It is estimated that 55% to 65% of men with prostate cancer will go on to develop metastatic disease. More than 90% of men with metastatic prostate cancer initially respond to hormonal therapy. However, the disease will eventually become resistant to standard hormonal therapy and therefore alternative treatment strategies are required. This clinical condition is known variously as castration-resistant prostate cancer, androgen-independent

prostate cancer or hormone-refractory prostate cancer. Castration-resistant prostate cancer has become the preferred term within the clinical community.

NICE Technology Appraisal No. 101 recommends docetaxel as a treatment option for men with hormone-refractory prostate cancer who have a Karnofsky performance-status score of 60% or more. For men with metastatic hormone-refractory prostate cancer that has progressed during or after a docetaxel-based treatment, patients may receive a combination of palliative treatments. Management options include mitoxantrone with or without steroids such as prednisolone.

The technology

Abiraterone (Brand name unknown, Janssen) is a selective androgen biosynthesis inhibitor. Abiraterone blocks cytochrome P17 (an enzyme thought to play a role in the production of testosterone), thereby stopping the testes and other tissues in the body from making testosterone. It is administered orally.

Abiraterone does not have a UK marketing authorisation. It is has been studied in clinical trials in combination with prednisone/prednisolone in men with asymptomatic or mildly symptomatic metastatic castration-resistant prostate cancer who have not received prior cytotoxic chemotherapy or biologic therapy.

Intervention(s)	Abiraterone in combination with prednisolone
Population(s)	Men with metastatic, castration-resistant prostate cancer who have not received prior cytotoxic chemotherapy or biologic therapy.
Comparators	• Docetaxel • Best supportive care (this may include radiotherapy, radiopharmaceuticals, analgesics, bisphosphonates, further hormonal therapies, and mitoxantrone with or without steroids or steroids alone)
Outcomes	The outcome measures to be considered include: • Overall survival • Progression-free survival • Response rate • Prostate specific antigen (PSA) response

	• 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.
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No. 101, June 2006, 'Docetaxel for the treatment of hormone refractory prostate cancer'. Review date June 2013. Technology Appraisal in Preparation, 'Abiraterone (in combination with prednisolone) for the treatment of metastatic castrate resistant prostate cancer following previous cytotoxic chemotherapy'. Earliest anticipated date of publication TBC. Technology Appraisal in Preparation, 'Cabazitaxel for the second line treatment of hormone refractory, metastatic prostate cancer'. Earliest anticipated date of publication TBC. Related Guidelines: Cancer Service Guidance Urological Cancer, September 2002, Improving outcomes in urogenital cancers'. Anticipated review date TBC, Clinical Guideline No. 58, February 2008, 'Prostate cancer: diagnosis and treatment'. Anticipated review date February 2011.

Questions for consultation

Has the population been appropriately defined? For example, is the term 'castrate-resistant' more appropriate than 'castration-resistant'?

Have the most appropriate comparators for abiraterone for the treatment of chemotherapy naïve, metastatic, castration-resistant prostate cancer been included in the scope? In particular

- Should any other chemotherapy treatments be included?
- How should 'best supportive care' be defined?

Are docetaxel and best supportive care used in the same circumstances? Or are they used for particular patient groups? If so what are the characteristics of these patients groups?

Are there subgroups of men in whom abiraterone is expected to be more clinically effective and cost effective or other groups that should be examined separately? For instance, is abiraterone likely to be more effective in asymptomatic or mildly symptomatic men?

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

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp)