Proposed Health Technology Appraisal

Enzalutamide for the treatment of metastatic castration-resistant prostate cancer previously treated with a docetaxel-containing regimen

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of enzalutamide within its licensed indication for the treatment of metastatic castration-resistant prostate cancer previously treated with a docetaxel-containing regimen.

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 multi-factorial, 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, there were over 33,000 people newly diagnosed with prostate cancer and over 9100 deaths from prostate cancer in 2008.

Around 55–65% of people with prostate cancer develop metastatic disease (that is, the cancer spreads to other parts of the body). Over 90% of people with metastatic prostate cancer initially respond to hormonal therapy but eventually become resistant to it. This clinical condition is described as castration-resistant prostate cancer (but the terms 'androgen-independent prostate cancer' and' hormone-refractory prostate cancer' are also used).

NICE clinical guideline 58 'Prostate cancer: Diagnosis and treatment' recommends that people with localised disease should be offered active surveillance, prostatectomy (surgical removal of the prostate) or high-dose radical radiotherapy. Standard hormonal treatments for metastatic disease are orchidectomy (surgical removal of the testes) or use of a gonadotrophin-releasing hormone analogue such as goserelin, leuprorelin or triptorelin. For metastatic castration-resistant prostate cancer, NICE technology appraisal guidance 101 recommends docetaxel as a treatment option for men with metastatic hormone-refractory disease who have a Karnofsky performance-status score of 60% or more. In clinical practice, after progression during or after a docetaxel-based treatment, patients may receive a further chemotherapy treatment or a combination of palliative treatments. Management options include mitoxantrone with or without steroids such as prednisolone. NICE technology appraisal 259 recommends abiraterone in combination with prednisone or prednisolone as an option for the treatment of castration-resistant metastatic prostate cancer which has progressed on or after one docetaxel-containing chemotherapy. Cabazitaxel is not recommended for hormone-refractory metastatic prostate cancer previously

treated with a docetaxel-containing regimen (NICE technology appraisal guidance 255).

The technology

Enzalutamide (Brand name unknown, Astellas Pharma) is an androgen receptor antagonist which inhibits androgen receptor signalling through three mechanisms: inhibition of androgen receptor binding, inhibition of nuclear translocation, and inhibition of co-activator recruitment and DNA binding to the androgen receptor. It is administered orally.

Enzalutamide does not currently have a UK marketing authorisation for the treatment of prostate cancer. It has been studied in clinical trials compared with placebo in men with metastatic castration-resistant prostate cancer which has been treated with one or two prior chemotherapy regimens, with at least one regimen containing docetaxel.

Intervention	Enzalutamide
Population	Adults with metastatic castration-resistant prostate cancer which has been previously treated with a docetaxel-containing chemotherapy regimen
Comparators	• Abiraterone in combination with prednisone or prednisolone • Mitoxantrone alone or in combination with prednisolone • Best supportive care (this may include radiotherapy, radiopharmaceuticals, analgesics, bisphosphonates, further hormonal therapies, and corticosteroids).
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. 259, June 2012, 'Abiraterone for castration-resistant metastatic prostate cancer previously treated with a docetaxel-containing regimen'. Review proposal date April 2015. Technology Appraisal No. 255, May 2012, 'Cabazitaxel for the second-line treatment of hormone refractory, metastatic prostate cancer'. Review proposal date February 2015. Technology Appraisal No. 101, June 2006, 'Docetaxel for the treatment of hormone-refractory prostate cancer'. Moved to static guidance list. Technology Appraisal in preparation, 'Abiraterone in combination with prednisolone for the treatment of metastatic, castration-resistant prostate cancer in people who have not been previously treated with chemotherapy'. Earliest anticipated date of publication November 2013. Proposed Technology Appraisal, 'Sipuleucel-T for the first line treatment of metastatic castration resistant prostate cancer'. Related Guidelines: Cancer Service Guidance Urological Cancer, September 2002, Improving outcomes in urogenital cancers'. Clinical Guideline No. 58, February 2008, 'Prostate cancer: diagnosis and treatment'. Currently under review. Earliest anticipated date of publication November 2013. NICE pathway for prostate cancer. Available at http://pathways.nice.org.uk/pathways/prostate-cancer

Questions for consultation

Have the most appropriate comparators for enzalutamide for the treatment of previously treated metastatic castration-resistant prostate cancer been included in the scope? Are the comparators listed routinely used in clinical practice?

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? Should any subgroups be defined based on prior treatment exposure and/or duration of treatment?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which enzalutamide will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

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)