NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE
Health Technology Appraisal

Enzalutamide for treating non-metastatic hormone-relapsed prostate cancer

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of enzalutamide within its marketing authorisation for treating non-metastatic hormone-relapsed 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 multi-factorial, involving both environmental and genetic factors.[1,2]

The incidence of prostate cancer increases with age and is higher in men of black African-Caribbean family origin and people with a family history of the disease[1]. In England, about 40,300 people were diagnosed with prostate cancer in 2015[3] and about 9,500 people died from prostate cancer in 2014[4]. In 2015, 79% of patients diagnosed in England with prostate cancer had non-metastatic disease[5]. Non-metastatic prostate cancer is diagnosed when imaging studies show that the cancer has not spread to other parts of the body (for example, the bones). This includes both localised prostate cancer, where the cancer has not spread into the surrounding tissues or to other parts of the body, and locally advanced prostate cancer, where the cancer has spread to the area just outside the prostate.

NICE clinical guideline 175 classifies disease as low, intermediate or high risk based on prostate-specific antigen concentration, Gleason score (based on a biopsy) and clinical stage. People with intermediate or high risk non-metastatic prostate cancer may be offered hormone therapy. Prostate cancer may initially respond to hormonal therapy but eventually become resistant to it. This clinical condition is described as hormone-relapsed prostate cancer (but the terms ‘castration-resistant prostate cancer’, ‘hormone-refractory prostate cancer’ and ‘androgen-independent prostate cancer’ are also used). Hormone-relapsed prostate cancer is diagnosed by rising PSA levels.

In prostate cancer care, the term ‘radical’ means treatment that aims to cure the disease. Treatment options for non-metastatic hormone-relapsed prostate cancer may include further hormonal therapy, radical prostatectomy (surgical removal of the prostate) and radical radiotherapy or brachytherapy (radiation delivered inside the prostate gland).

The technology

Enzalutamide (Xtandi, Astellas Pharma and Pfizer) is an androgen receptor antagonist that acts on different steps in the androgen receptor signalling pathway to decrease proliferation of cancer cells and induce cancer cell death leading to tumour regression. Enzalutamide is administered orally.

Enzalutamide does not currently have a marketing authorisation in the UK for the treatment of non-metastatic prostate cancer. It is being studied in a clinical trial, compared with placebo, in adults with non-metastatic hormone-relapsed prostate cancer.

Enzalutamide has a marketing authorisation in the UK for the treatment of metastatic hormone-relapsed prostate cancer in adults following failure of androgen deprivation therapy or following progression after docetaxel therapy.

Intervention(s)	Enzalutamide
Population(s)	Adults with non-metastatic hormone-relapsed prostate cancer
Comparators	• Androgen deprivation therapy • Radical surgery • Radical radiotherapy • Androgen deprivation therapy in combination with radical radiotherapy or radical surgery
Outcomes	The outcome measures to be considered include: • disease-free survival • progression-free survival • prostate specific antigen (PSA) response • overall survival • adverse effects of treatment (for example, erectile dysfunction or incontinence) • 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. The availability of any patient access schemes for the intervention or comparator technologies will be taken into account.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations and NICE Pathways	**Related Interventional Procedures:** 'Laparoscopic radical prostatectomy' (2006). NICE interventional procedure guidance 193. 'High dose rate brachytherapy in combination with external-beam radiotherapy for localised prostate cancer' (2006). NICE interventional procedure guidance 174. 'Cryotherapy as a primary treatment for prostate cancer' (2005). NICE interventional procedure guidance 145. 'Low dose rate brachytherapy for localised prostate cancer' (2005). NICE interventional procedure guidance 132. 'Cryotherapy for recurrent prostate cancer' (2005). NICE interventional procedure guidance 119. 'High-intensity focused ultrasound for prostate cancer' (2005). NICE interventional procedure guidance 118. **Related Guidelines:** 'Prostate cancer: diagnosis and management' (2014) NICE Clinical Guideline No. 175 **Related Quality Standards:** Prostate cancer (2015) NICE quality standard QS91 https://www.nice.org.uk/guidance/QS91

	Related NICE Pathways: Prostate cancer (2014) NICE Pathway http://pathways.nice.org.uk/pathways/prostate-cancer
Related National Policy	NHS England (2017) Manual for Prescribed Specialised Services 2017/18. Specialist cancer services (adults) [section 105, pages 234-7 Department of Health, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1-2. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

Have all relevant comparators for enzalutamide been included in the scope?

Which treatments are considered to be established clinical practice in the NHS for high-risk non-metastatic hormone-relapsed prostate cancer?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom enzalutamide is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider enzalutamide will fit into the existing NICE pathway, 'Prostate cancer'?

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 enzalutamide 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 enzalutamide 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.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

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/article/pmg19/chapter/1-Introduction).

References

1. Cancer Research UK. About cancer. Prostate cancer risks and causes. Accessed January 2018. http://www.cancerresearchuk.org/about-cancer/type/prostate-cancer/about/prostate-cancer-risks-and-causes

2. Macmillan Cancer Support. Cancer information. Risk factors and causes of prostate cancer. Accessed January 2018. http://www.macmillan.org.uk/Cancerinformation/Cancertypes/Prostate/Aboutprostatecancer/Causes.aspx

3. Office for National Statistics. Cancer registration statistics, England, 2015. Accessed January 2018. https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/bulletins/cancerregistrationstatisticsengland/2015

4. Cancer Research UK. Cancer stats. Prostate cancer mortality statistics. Accessed January 2018. http://www.cancerresearchuk.org/cancer-info/cancerstats/types/prostate/mortality/

5. National Prostate Cancer Audit. Annual report 2015. Accessed January 2018. http://www.npca.org.uk/annual-report-2015/