

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**Health Technology Appraisal****Apalutamide for treating non-metastatic, hormone-relapsed prostate cancer****Final scope****Remit/appraisal objective**

To appraise the clinical and cost effectiveness of apalutamide within its marketing authorisation for treating adults with non-metastatic, hormone-relapsed prostate cancer.

Background

Prostate cancer is a condition in which tumours develop in the prostate, a gland in the male reproductive system. The exact cause is unknown but environmental and genetic factors are associated with an increased risk of developing prostate cancer.^{1,2}

The incidence of prostate cancer increases with age and is higher in people of black African-Caribbean family origin and people with a family history of the condition.¹ In England in 2016, about 40,500 people were diagnosed with prostate cancer³ and about 9,900 people died from the condition.⁴ Between 2015 to 2016, 84% of people diagnosed in England with prostate cancer had non-metastatic disease, that is, disease that has not spread to other parts of the body (for example, the bones).⁵ Non-metastatic disease includes localised prostate cancer, where the cancer is confined to the prostate, and locally advanced prostate cancer, where the cancer has spread to the area just outside the prostate.

NICE clinical guideline 175 classifies localised prostate cancer to be at low, intermediate or high risk of progression 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 hormone 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.^a Hormone-relapsed prostate cancer is diagnosed by rising prostate-specific antigen levels despite treatment with androgen-deprivation therapy or orchidectomy.

^aIn January 2013, NICE and the Department of Health and Social Care agreed that, following feedback received from stakeholders during scoping and appraisal consultations, the term 'castration resistant prostate cancer' should be replaced with 'hormone relapsed prostate cancer'. This has been implemented for all appraisals from January 2013.

There are currently no licensed treatments for non-metastatic, hormone-relapsed prostate cancer. The main treatment is continued androgen deprivation therapy which may include anti-androgens, such as, bicalutamide. This is because although some cancer cells may no longer respond to testosterone withdrawal, stopping hormone therapy completely would increase testosterone levels and decrease the likely time to metastatic disease. For people who have not had previous radiotherapy, they may also be offered this treatment with hormone therapy. Everyone is monitored for evidence of disease metastasis, at which point, other treatments are considered.

The technology

Apalutamide (Erleada, Janssen) 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. Apalutamide is administered orally.

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

Intervention(s)	Apalutamide with androgen deprivation therapy
Population(s)	Adults with non-metastatic, hormone-relapsed prostate cancer
Comparators	<ul style="list-style-type: none"> • androgen deprivation therapy • enzalutamide with androgen deprivation therapy (subject to ongoing NICE appraisal)
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • metastasis-free survival • time to symptomatic progression • time to prostate-specific antigen progression • progression free survival • overall survival • adverse effects of treatment • health-related quality of life

Economic analysis	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.</p>
Other considerations	<p>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.</p>
Related NICE recommendations and NICE Pathways	<p>Appraisals in Development</p> <p>‘Enzalutamide for treating non-metastatic hormone-relapsed prostate cancer’ NICE technology appraisals guidance [ID1359]. Publication date to be confirmed.</p> <p>Related Interventional Procedures</p> <p>‘Laparoscopic radical prostatectomy’ (2006) NICE interventional procedures guidance 193.</p> <p>‘High dose rate brachytherapy in combination with external-beam radiotherapy for localised prostate cancer’ (2006) NICE interventional procedures guidance 174.</p> <p>‘Cryotherapy as a primary treatment for prostate cancer’ (2005) NICE interventional procedures guidance 145.</p> <p>‘Low dose rate brachytherapy for localised prostate cancer’ (2005) NICE interventional procedures guidance 132.</p> <p>‘Cryotherapy for recurrent prostate cancer’ (2005) NICE interventional procedures guidance 119.</p> <p>‘High-intensity focused ultrasound for prostate cancer’ (2005) NICE interventional procedures guidance 118.</p> <p>Related Guidelines</p> <p>‘Prostate cancer: diagnosis and management’ (2014) NICE guideline 175. Update publication expected April</p>

	<p>2019.</p> <p>Related Quality Standards</p> <p>‘Prostate cancer’ (2015) NICE quality standard 91.</p> <p>Related NICE Pathways</p> <p>‘Prostate cancer’ (2018) NICE Pathway.</p>
<p>Related National Policy</p>	<p>NHS England (2018) Manual for Prescribed Specialised Services 2018/19. Specialist cancer services (adults): section 105.</p> <p>Department of Health (2016) NHS Outcomes Framework 2016-2017: Domains 1-2.</p>

References

1. Cancer Research UK (2015) [Prostate cancer risks and causes](#). Accessed November 2018.
2. Macmillan Cancer Support (2015) [Potential causes of prostate cancer](#). Accessed November 2018.
3. Office for National Statistics (2018) [Cancer registration statistics, England, 2016](#). Accessed November 2018.
4. Cancer Research UK (2018) [Prostate cancer mortality statistics](#). Accessed November 2018.
5. National Prostate Cancer Audit (2017) [Annual report 2017](#). Accessed November 2018.