

## NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Health Technology Appraisal

## Apalutamide for treating prostate cancer

## Final scope

**Remit/appraisal objective**

To appraise the clinical and cost effectiveness of apalutamide within its marketing authorisation for treating non-metastatic, hormone-relapsed prostate cancer and metastatic hormone-sensitive 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.<sup>1,2</sup>

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.<sup>1</sup> In England in 2017, about 41,200 people were diagnosed with prostate cancer, with an age-standardised mortality rate of 47.7 for every 100,000 persons.<sup>3</sup> Between 2017 to 2018, 83% 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).<sup>4</sup> 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. Between 2017 to 2018, 17% of people diagnosed in England with prostate cancer had metastatic disease, that is, disease that has spread to other parts of the body (for example, the bones).<sup>4</sup>

[NICE clinical guideline 131](#) 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.<sup>a</sup> Hormone-relapsed prostate

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<sup>a</sup>In 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.

cancer is diagnosed by rising prostate-specific antigen levels despite treatment with androgen-deprivation therapy or orchidectomy.

The main treatment for non-metastatic, hormone-relapsed prostate cancer 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.

For newly diagnosed metastatic prostate cancer, [NICE clinical guideline 131](#) recommends starting docetaxel chemotherapy within 12 weeks of starting androgen deprivation therapy. For metastatic prostate cancer, the guideline recommends offering bilateral orchidectomy (removal of the testicles) as an alternative to continuous luteinising hormone-releasing hormone agonist therapy. For people who are willing to accept the adverse impact on overall survival and gynaecomastia (breast swelling) in the hope of retaining sexual function, the guideline recommends offering anti-androgen monotherapy with bicalutamide. [NICE technology appraisal 404](#) recommends degarelix, a gonadotrophin-releasing hormone antagonist, for treating advanced hormone-dependent prostate cancer in people with spinal metastases. Metastatic, hormone-sensitive prostate cancer refers to a broader population that includes people with metastatic prostate cancer who are newly diagnosed and hormone naïve or are continuing to respond to androgen deprivation therapy.

### 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 has marketing authorisations for the treatment of non-metastatic castration-resistant prostate cancer in adults who are at high risk of developing metastatic disease and for the treatment of metastatic hormone-sensitive prostate cancer in combination with androgen deprivation therapy.

<b>Intervention(s)</b>	Apalutamide with androgen deprivation therapy
<b>Population(s)</b>	Adults with prostate cancer

<b>Comparators</b>	<p>For people with non-metastatic hormone-relapsed prostate cancer:</p> <ul style="list-style-type: none"> <li>• Androgen deprivation therapy</li> </ul> <p>For people with metastatic hormone-sensitive prostate cancer:</p> <ul style="list-style-type: none"> <li>• Androgen deprivation therapy alone (including orchidectomy, luteinising hormone-releasing hormone agonist therapy or monotherapy with bicalutamide)</li> <li>• Docetaxel with androgen deprivation therapy</li> <li>• Abiraterone with prednisone or prednisolone and androgen deprivation therapy (subject to ongoing NICE appraisal)</li> <li>• Enzalutamide with androgen deprivation therapy (subject to ongoing NICE appraisal)</li> </ul>
<b>Outcomes</b>	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> <li>• overall survival</li> <li>• progression-free survival</li> <li>• response rate</li> <li>• prostate specific antigen (PSA) response</li> <li>• adverse effects of treatment</li> <li>• health-related quality of life.</li> </ul>
<b>Economic analysis</b>	<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>

<p><b>Other considerations</b></p>	<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> <p>If the evidence allows, the following subgroups of people will be considered:</p> <ul style="list-style-type: none"> <li>• people with newly diagnosed metastatic prostate cancer</li> <li>• people with high-risk metastatic prostate cancer</li> </ul>
<p><b>Related NICE recommendations and NICE Pathways</b></p>	<p><b>Related Technology Appraisals:</b></p> <p><a href="#">‘Enzalutamide for treating non-metastatic hormone-relapsed prostate cancer’</a> NICE technology appraisals guidance 580. May 2019</p> <p><a href="#">‘Padeliporfin for untreated localised prostate cancer’</a> NICE technology appraisals guidance [TA546]. November 2018</p> <p><b>Appraisals in development (including suspended appraisals)</b></p> <p><a href="#">‘Abiraterone for treating newly diagnosed high risk metastatic hormone-naïve prostate cancer’</a> NICE technology appraisals guidance [ID945]. Publication TBC</p> <p><a href="#">‘Enzalutamide with androgen deprivation therapy for treating metastatic hormone-sensitive prostate cancer’</a> NICE technology appraisals guidance [ID1605]. Publication expected August 2020</p> <p><a href="#">‘Darolutamide with androgen deprivation therapy for treating non-metastatic hormone-relapsed prostate cancer’</a> NICE technology appraisals guidance [ID1443]. Publication expected November 2020</p> <p><b>Related Guidelines</b></p> <p><a href="#">‘Prostate cancer: diagnosis and management’</a> (2019) NICE guideline 131. Published May 2019.</p> <p><b>Related Quality Standards</b></p> <p><a href="#">‘Prostate cancer’</a> (2015) NICE quality standard 91.</p> <p><b>Related NICE Pathways</b></p> <p><a href="#">‘Prostate cancer’</a> (2018) NICE Pathway.</p>

<p><b>Related National Policy</b></p>	<p>The NHS Long Term Plan, 2019. <a href="#">NHS Long Term Plan</a>.  NHS England (2018/2019) <a href="#">NHS manual for prescribed specialist services (2018/2019)</a> Specialist cancer services (adults) [section 105].  Department of Health and Social Care (2016) <a href="#">Department of Health and Social Care, NHS Outcomes Framework 2016-2017</a> Domains 1-5.  NHS England (2013) <a href="#">NHS England B14/S/a 2013/14 NHS standard contract for cancer: specialised kidney, bladder and prostate cancer services (adult)</a>.  NHS England (2016) <a href="#">Clinical Commissioning Policy Statement: Docetaxel in combination with androgen deprivation therapy for the treatment of hormone naïve metastatic prostate cancer</a>.</p>
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**References**

1. Cancer Research UK (2015) [Prostate cancer risks and causes](#). Accessed February 2020.
2. Macmillan Cancer Support (2018) [Potential causes of prostate cancer](#). Accessed February 2020.
3. Office for National Statistics (2019) [Cancer registration statistics, England, 2017](#). Accessed February 2020.
4. National Prostate Cancer Audit (2019) [Annual report 2019](#). Accessed February 2020.