

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Enzalutamide with androgen deprivation therapy for treating metastatic hormone-sensitive prostate cancer

Draft scope

**Draft remit/appraisal objective**

To appraise the clinical and cost effectiveness of enzalutamide with androgen deprivation therapy within its marketing authorisation for treating 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 2015 to 2016, 16% 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>

For newly diagnosed metastatic prostate cancer, the [NICE 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.

The description 'metastatic, hormone-sensitive prostate cancer' refers to a 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

Enzalutamide (Xtandi, Astellas Pharma) 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 treating metastatic hormone-sensitive prostate cancer. Enzalutamide plus androgen deprivation therapy is being studied in a clinical trial, compared with placebo plus androgen deprivation therapy, in adults with metastatic hormone-sensitive prostate cancer.

Enzalutamide has a marketing authorisation in the UK for the treatment of:

- high-risk non-metastatic castration-resistant prostate cancer
- metastatic castrate-resistant prostate cancer that is asymptomatic or mildly symptomatic after failure of androgen deprivation therapy when chemotherapy is not yet clinically indicated and
- metastatic castrate-resistant prostate cancer that has progressed on or after docetaxel therapy.

<b>Intervention(s)</b>	Enzalutamide in combination with androgen deprivation therapy
<b>Population(s)</b>	People with metastatic hormone-sensitive prostate cancer
<b>Comparators</b>	<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> </ul>
<b>Outcomes</b>	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> <li>• Time to prostate-specific antigen progression</li> <li>• Progression free survival</li> <li>• Overall survival</li> <li>• Adverse effects of treatment</li> <li>• Health-related quality of life.</li> </ul>

<p><b>Economic analysis</b></p>	<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> (2019) NICE technology appraisal guidance 580.</p> <p><a href="#">Enzalutamide for treating metastatic hormone-relapsed prostate cancer before chemotherapy is indicated</a> (2016) NICE technology appraisal guidance 377.</p> <p><a href="#">Enzalutamide for metastatic hormone-relapsed prostate cancer previously treated with a docetaxel-containing regimen</a> (2014) NICE technology appraisal guidance 316.</p> <p><b>Appraisals in development (including suspended appraisals)</b></p> <p><a href="#">Apalutamide for treating metastatic hormone-sensitive prostate cancer</a> NICE technology appraisals guidance [ID1534]. Expected publication date TBC.</p>

	<p><a href="#">Abiraterone for treating newly diagnosed high risk metastatic hormone-naïve prostate cancer</a> NICE technology appraisals guidance [ID945]. Suspended.</p> <p><b>Related Guidelines</b></p> <p><a href="#">‘Prostate cancer: diagnosis and management’</a> (2019) NICE guideline.</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].</p> <p>Department of Health (2016) <a href="#">Department of Health and Social Care, NHS Outcomes Framework 2016-2017</a> Domains 1-5.</p> <p>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>.</p> <p>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>

### 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 prostate cancer?

Are the outcomes listed appropriate?

Are the subgroups suggested in ‘other considerations appropriate? Are there any other 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 (2015) [Prostate cancer risks and causes](#). Accessed June 2019.
2. Macmillan Cancer Support (2018) [Potential causes of prostate cancer](#). Accessed June 2019.

3. Office for National Statistics (2019) [Cancer registration statistics, England, 2017](#). Accessed June 2019.
4. National Prostate Cancer Audit (2017) [Annual report 2017](#). Accessed June 2019.