NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Apalutamide for treating metastatic hormone-sensitive prostate cancer

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of apalutamide 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.[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 cancer[3] and about 9,900 people died from the condition.[4] 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).[5]

For newly diagnosed metastatic prostate cancer, the updated draft NICE clinical guideline 175 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 for treating advanced hormone-dependent prostate cancer in people with spinal metastases.

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 metastatic, hormone-sensitive prostate cancer. Apalutamide 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.

Intervention(s)	Apalutamide with androgen deprivation therapy
Population(s)	Adults with metastatic hormone-sensitive prostate cancer
Comparators	• Androgen deprivation therapy alone (including orchidectomy, luteinising hormone-releasing hormone agonist therapy or monotherapy with bicalutamide) • Docetaxel with androgen deprivation therapy • Abiraterone with prednisone or prednisolone and androgen deprivation therapy (subject to ongoing NICE appraisal)
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. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment 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	**Appraisals in development (including suspended appraisals)** 'Apalutamide for treating non-metastatic, hormone-relapsed prostate cancer' NICE technology appraisals guidance [ID1174]. Publication expected October 2019. 'Abiraterone for treating newly diagnosed high risk metastatic hormone-naive prostate cancer' NICE technology appraisals guidance [ID945]. Suspended. **Related Guidelines** 'Prostate cancer: diagnosis and management' (2014) NICE guideline 175. Update publication expected April 2019. **Related Quality Standards** 'Prostate cancer' (2015) NICE quality standard 91. **Related NICE Pathways** 'Prostate cancer' (2018) NICE Pathway.
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan. NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Specialist cancer services (adults) [section 105]. Department of Health (2016) Department of Health and Social Care, NHS Outcomes Framework 2016-2017 Domains 1-5. NHS England (2013) NHS England B14/S/a 2013/14 NHS standard contract for cancer: specialised kidney, bladder and prostate cancer services (adult). NHS England (2016) Clinical Commissioning Policy Statement: Docetaxel in combination with androgen deprivation therapy for the treatment of hormone naïve metastatic prostate cancer.

Questions for consultation

Is the population for this appraisal defined appropriately?

- NICE understands that 'hormone-naive' refers to people who are about to start (or who have started within the last 12 weeks) androgen deprivation therapy. 'Hormone-sensitive' is a broader population that refers to all people with metastatic prostate cancer who are having androgen deprivation therapy. In which population is apalutamide expected to be used?

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

- NICE recommends degarelix as an option for treating advanced hormone-dependent prostate cancer in people with spinal metastases. Would degarelix and apalutamide be used in the same population?

Have all relevant comparators for apalutamide been included in the scope? Which treatments are considered to be established clinical practice in the NHS for metastatic hormone-sensitive prostate cancer?'

Are the outcomes listed appropriate?

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

Where do you consider apalutamide 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 apalutamide 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 apalutamide 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 apalutamide 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).

NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost comparison methodology for this topic?
- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?
- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?
- Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

1. Cancer Research UK (2015) Prostate cancer risks and causes. Accessed March 2019.
2. Macmillan Cancer Support (2018) Potential causes of prostate cancer. Accessed March 2019.
3. Office for National Statistics (2018) Cancer registration statistics, England, 2016. Accessed March 2019.
4. Cancer Research UK (2018) Prostate cancer mortality statistics. Accessed March 2019.

   National Prostate Cancer Audit (2017) Annual report 2017. Accessed March 2019.

