NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Darolutamide for treating non-metastatic hormone-relapsed prostate cancer

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of darolutamide within its marketing authorisation for treating 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 cancer[3] 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.[1] Hormone-relapsed prostate cancer is diagnosed by rising prostate-specific antigen levels.

[1]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.

Currently, the main treatment for non-metastatic, hormone-relapsed prostate cancer is 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

Darolutamide ("brand name unknown", Bayer) 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. Darolutamide is administered orally.

Darolutamide does not currently have a marketing authorisation in the UK for the treatment of non-metastatic hormone-relapsed prostate cancer. Darolutamide is being studied in a phase III trial, compared with placebo, in adults with non-metastatic hormone-relapsed prostate cancer; with prostate-specific antigen levels of more than 2ng/ml.

Intervention(s)	Darolutamide with androgen deprivation therapy
Population(s)	Adults with non-metastatic hormone-relapsed prostate cancer
Comparators	• Androgen deprivation therapy • Apalutamide with androgen deprivation therapy (subject to ongoing NICE appraisal)
Outcomes	The outcome measures to be considered include: • Metastasis-free survival • Time to prostate-specific antigen progression • Overall survival • 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 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 Technology Appraisals:** 'Apalutamide for treating non-metastatic, hormone-relapsed prostate cancer' NICE technology appraisal guidance [ID1174]. Publication expected date TBC. 'Enzalutamide for treating non-metastatic hormone-relapsed prostate cancer' NICE technology appraisals guidance [ID1359]. Publication expected May 2019. 'Padeliporfin for untreated localised prostate cancer' NICE technology appraisals guidance [TA546] **Related Guidelines:** 'Prostate cancer: diagnosis and management' (2014) NICE guideline 175. Reviewed October 2016. **Guidelines in development**: 'Prostate cancer: diagnosis and management (update) In development [GID-NG10057]' Publication expected April 2019. **Related Interventional Procedures:** 'Laparoscopic radical prostatectomy' (2006) NICE

	interventional procedures guidance 193. 'High dose rate brachytherapy in combination with external-beam radiotherapy for localised prostate cancer' (2006) NICE interventional procedures guidance 174. 'Cryotherapy as a primary treatment for prostate cancer' (2005) NICE interventional procedures guidance 145. 'Low dose rate brachytherapy for localised prostate cancer' (2005) NICE interventional procedures guidance 132. 'Cryotherapy for recurrent prostate cancer' (2005) NICE interventional procedures guidance 119. 'High-intensity focused ultrasound for prostate cancer' (2005) NICE interventional procedures guidance 118 **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) Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1-2. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

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

Are the outcomes listed appropriate?

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

Where do you consider darolutamide 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 darolutamide 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 darolutamide 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 darolutamide 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 March 2019.

2. Macmillan Cancer Support (2015) 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.

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