NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Darolutamide with androgen deprivation therapy and docetaxel for treating hormone-sensitive metastatic prostate cancer

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of darolutamide with androgen deprivation therapy and docetaxel within its marketing authorisation for treating hormone-sensitive metastatic 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, between 2019 and 2020, 43,330 people were diagnosed with prostate cancer. Of those, 13% of people diagnosed had metastatic disease, that is, disease that has spread to other parts of the body (for example, the bones).[3] The age standardised mortality rate for prostate cancer in 2019 was 45.5 for every 100,000 persons.[4]

NICE clinical guideline 131 (NG131) 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 (also called androgen deprivation 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.

For newly diagnosed metastatic prostate cancer, NG131 recommends starting docetaxel chemotherapy within 12 weeks of starting androgen deprivation therapy. For metastatic prostate cancer, the guideline recommends offering bilateral orchidectomy 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 (hormone-sensitive) prostate cancer in people with spinal metastases. In addition, NICE technology appraisal 712 recommends enzalutamide plus androgen deprivation therapy as an option for treating hormone-sensitive metastatic prostate cancer in adults, and NICE technology appraisal 741 recommends apalutamide plus androgen deprivation therapy as an option for treating hormone-sensitive metastatic prostate cancer in adults, if docetaxel is not suitable.

The description 'hormone-sensitive metastatic prostate cancer' refers to a population that includes people with metastatic prostate cancer who are newly diagnosed and have not had androgen deprivation therapy, or whose disease is continuing to respond to androgen deprivation therapy.

The technology

Darolutamide (Nubeqa, Bayer) does not currently have a marketing authorisation in the UK for treating hormone-sensitive metastatic prostate cancer. Darolutamide with androgen deprivation therapy and docetaxel is being studied in a clinical trial, compared with placebo plus androgen deprivation therapy and docetaxel, in adults with hormone-sensitive metastatic prostate cancer.

Darolutamide does have a marketing authorisation in the UK for treating hormone-relapsed prostate cancer in adults at high risk of developing metastatic disease.

Intervention(s)	Darolutamide with androgen deprivation therapy and docetaxel
Population(s)	People with hormone-sensitive metastatic prostate cancer
Subgroups	If the evidence allows, the following subgroups of people will be considered: • people with newly diagnosed metastatic prostate cancer • people with high-risk metastatic prostate cancer.
Comparators	• Androgen deprivation therapy alone (including orchidectomy, luteinising hormone-releasing hormone agonist therapy, degarelix, monotherapy with bicalutamide) • Docetaxel with androgen deprivation therapy • Apalutamide with androgen deprivation therapy • Enzalutamide with androgen deprivation therapy
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rate • prostate-specific antigen response • time to prostate-specific antigen progression • 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. If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost comparison may be carried out. 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. The availability and cost of biosimilar and generic products should 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	**Related Technology Appraisals:** 'Apalutamide with androgen deprivation therapy for treating hormone-sensitive metastatic prostate cancer' (2021). NICE Technology appraisal guidance [TA741]. Review date 2024. 'Abiraterone for treating newly diagnosed high-risk hormone-sensitive metastatic prostate cancer' (2021). NICE Technology appraisal guidance [TA721]. Review date 2024. 'Enzalutamide for treating hormone-sensitive metastatic prostate cancer' (2021). NICE Technology appraisal guidance [TA712]. Review date 2024. 'Darolutamide with androgen deprivation therapy for treating hormone-relapsed non-metastatic prostate cancer' (2020). NICE Technology appraisal guidance [TA660]. Review date 2023. **Related Guidelines:** 'Prostate cancer: diagnosis and management' (2019). NICE guideline [NG131]. **Related Quality Standards:** 'Prostate cancer' (2015). NICE quality standard [QS91].

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) NHS England (2021) Clinical Commissioning Policy: External beam radiotherapy for patients presenting with hormone sensitive, low volume metastatic prostate cancer at the time of diagnosis NHS England (2016) Clinical Commissioning Policy Statement: Docetaxel in combination with androgen deprivation therapy for the treatment of hormone naïve metastatic prostate cancer NHS England (2013) 2013/14 NHS standard contract for cancer: chemotherapy (adult)

Questions for consultation

Where do you consider darolutamide with androgen deprivation therapy and docetaxel will fit into the existing care pathway for hormone-sensitive metastatic prostate cancer?

Would degarelix be considered a comparator?

Would darolutamide with androgen deprivation therapy and docetaxel be a candidate for managed access?

Do you consider darolutamide with androgen deprivation therapy and docetaxel 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 with androgen deprivation therapy and docetaxel can result in any potential 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 committee to take account of these benefits.

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 the treatment 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.

NICE intends to evaluate this technology through its Single Technology Appraisal process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

NICE's health technology evaluations: the manual 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 (2022) Prostate cancer risks and causes. Accessed April 2022.
2. Macmillan Cancer Support (2022) Potential causes of prostate cancer. Accessed April 2022.
3. National Prostate Cancer Audit (2021) Annual report 2021. Accessed April 2022.
4. NHS Digital (2022). Cancer registration statistics, England 2019. Accessed April 2022