NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

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

Final scope

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.[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 2017, about 41,200 people were diagnosed with prostate cancer, with an age-standardised mortality rate of 47.7 for every 100,000 persons.[3] 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).[4]

For newly diagnosed metastatic prostate cancer, 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 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.

Intervention(s)	Enzalutamide in combination with androgen deprivation therapy
Population(s)	People 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 For people with newly diagnosed high-risk disease: • Abiraterone with prednisone or prednisolone and androgen deprivation therapy (subject to ongoing NICE appraisal)
Outcomes	The outcome measures to be considered include: • Time to prostate-specific antigen progression • Progression free survival • 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 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. 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.
Related NICE recommendations and NICE Pathways	**Related Technology Appraisals:** Enzalutamide for treating non-metastatic hormone-relapsed prostate cancer (2019) NICE technology appraisal guidance 580. Enzalutamide for treating metastatic hormone-relapsed prostate cancer before chemotherapy is indicated (2016) NICE technology appraisal guidance 377. Enzalutamide for metastatic hormone-relapsed prostate cancer previously treated with a docetaxel-containing regimen (2014) NICE technology appraisal guidance 316. **Appraisals in development (including suspended appraisals)** Apalutamide for treating metastatic hormone-sensitive prostate cancer NICE technology appraisals guidance [ID1534]. Expected publication date TBC.

	Abiraterone for treating newly diagnosed high risk metastatic hormone-naive prostate cancer NICE technology appraisals guidance [ID945]. Expected publication date TBC. **Related Guidelines** 'Prostate cancer: diagnosis and management' (2019) NICE guideline. **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.