NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

177Lu-PSMA-617 for treating PSMA-positive hormone-relapsed metastatic prostate cancer after 2 or more therapies

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of 177Lu-PSMA-617 within its marketing authorisation for treating prostate-specific membrane antigen (PSMA) positive, hormone-relapsed metastatic prostate cancer previously treated with androgen receptor directed therapy (ARDT) and taxane based chemotherapy.

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 family origin and people with a history of the condition.[1] In England between April 2018 and April 2019, around 52,580 people were diagnosed with prostate cancer and in 2018 10,068 died from the condition.[3,4] Around 13% had metastatic disease, that is disease that has spread to other parts of the body (for example, the bones).[4]

Prostate cancers can express a transmembrane protein called prostate-specific membrane antigen (PSMA). PSMA expression is further increased in poorly differentiated, metastatic, and hormone-refractory prostate cancers.[5]

NICE clinical guideline 131 recommends androgen deprivation therapy (luteinising hormone-releasing hormone agonist therapy, bicalutamide or bilateral orchidectomy) for people whose prostate cancer is sensitive to such hormonal therapy. Docetaxel can be added to luteinising hormone-releasing hormone agonist therapy if the prostate cancer is metastatic.

Hormone-relapsed prostate cancer (also known as hormone-resistant, hormone-refractory and castrate-resistant) refers to prostate cancer which has progressed on androgen deprivation therapy. Abiraterone in combination with prednisone or prednisolone is recommended for treating metastatic hormone-relapsed prostate cancer in people who have no or mild symptoms after androgen deprivation therapy has failed, and before chemotherapy is indicated (TA387). Similarly, enzalutamide is recommended for treating metastatic hormone-relapsed prostate cancer in people who have no or mild symptoms after androgen deprivation therapy has failed, and before chemotherapy is indicated (TA377).

NICE guideline 131 and TA101 recommends chemotherapy (docetaxel) as a treatment option for people with metastatic hormone-relapsed prostate cancer if their Karnofsky performance-status score is 60% or more.

Abiraterone in combination with prednisone or prednisolone and enzalutamide are also recommended for metastatic hormone-relapsed prostate cancer if it has progressed on a docetaxel-containing chemotherapy regimen (TA259 and TA317 respectively).

Radium-223 dichloride is recommended for treating hormone-relapsed prostate cancer with bone metastases in people who already had a docetaxel, or for whom docetaxel is contraindicated or unsuitable (TA412).

Cabazitaxel in combination with prednisone or prednisolone is recommended as an option for treating people whose disease has progressed during or after docetaxel therapy (TA391).

The technology

177Lu-PSMA-617 (brand name unknown, Novartis) is a human PSMA targeted ligand that is conjugated to the beta-emitting radioisotope lutetium (117Lu). It is delivered by intravenous infusion. It works by releasing an energetic beta particle to precisely deliver radiation to kill prostate cancer cells.

177Lu-PSMA-617 does not currently have a market authorisation in the UK for the treatment of metastatic hormone relapsed prostate cancer. 177Lu-PSMA-617 is being studied in a Phase III clinical trial compared with best standard of care alone, in adult male patients with progressive prostate-specific membrane antigen positive metastatic hormone relapsed prostate cancer. The study included people who had received at least one novel androgen axis drug (also referred to as androgen receptor directed therapy, such as enzalutamide or abiraterone) and 1 to 2 previous taxane based chemotherapies.

Intervention(s)	Lutetium-177 prostate-specific membrane antigen-617 (177Lu-PSMA-617)
Population(s)	Adults with prostate-specific membrane antigen (PSMA) positive, hormone-relapsed metastatic prostate cancer previously treated with androgen receptor directed therapy (ARDT) and taxane based chemotherapy.
Comparators	• Cabazitaxel • Docetaxel (for people who have had docetaxel in combination with ADT previously) • Radium-223 dichloride (for people with bone metastases) • Olaparib (for people with BRCA1/2- mutations, subject to ongoing NICE technology appraisal) • Best supportive care The different positions that these comparators could be used in the treatment pathway will be considered in the appraisal.

Outcomes	The outcome measures to be considered include: • radiographic progression free survival • overall survival • time to a first symptomatic skeletal event • 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. The availability of any managed access arrangement for the intervention 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: Radium-223 dichloride for treating hormone-relapsed prostate cancer with bone metastases (2016) NICE technology appraisal guidance 412 Cabazitaxel for hormone-relapsed metastatic prostate cancer treated with docetaxel (2016) NICE technology appraisal guidance 391 Abiraterone for treating metastatic hormone-relapsed prostate cancer before chemotherapy is indicated (Last updated 2016) NICE technology appraisal guidance 387 Enzalutamide for treating metastatic hormone-relapsed prostate cancer before chemotherapy is indicated (2016) NICE technology appraisal guidance 377 Abiraterone for castration-resistant metastatic prostate cancer

	previously treated with a docetaxel-containing regimen (Last updated 2016) NICE technology appraisal guidance 259 Enzalutamide for metastatic hormone-relapsed prostate cancer previously treated with a docetaxel-containing regimen (2014) NICE technology appraisal guidance 316 Docetaxel for the treatment of hormone-refractory metastatic prostate cancer (2006) NICE technology appraisal guidance 101 Appraisals in development (including suspended appraisals) Niraparib for previously treated hormone-relapsed metastatic prostate cancer with DNA-repair anomalies [ID3782]. NICE medical technologies guidance. Suspended Abiraterone for treating newly diagnosed high risk metastatic hormone-naive prostate cancer NICE technology appraisal guidance ID 945. Publication date: TBC Apalutamide for treating metastatic hormone-sensitive prostate cancer. NICE technology appraisal guidance ID 1534. Publication expected 26 May 2021 Apalutamide with abiraterone acetate and prednisone for treating metastatic hormone-relapsed prostate cancer. NICE technology appraisal guidance ID 1480. Publication date: TBC Enzalutamide with androgen deprivation therapy for untreated metastatic hormone-sensitive prostate cancer. NICE technology appraisal guidance ID 1605. Publication date TBC Nivolumab in combination for treating hormone-relapsed metastatic prostate cancer after chemotherapy NICE technology appraisal guidance ID 1621. Publication date: TBC Olaparib for previously treated, hormone-relapsed metastatic prostate cancer with homologous recombination repair gene mutations NICE technology appraisal guidance ID 1640. Publication expected 10 February 2021 Related Guidelines: Prostate cancer: diagnosis and management (2019) NICE guideline 131 Hormone-sensitive metastatic prostate cancer: docetaxel. (2016) NICE evidence summary 50 Prostate cancer (2019) NICE pathway

Related National Policy	Department of Health (2009) Cancer commissioning guidance The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) 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 prostate specific membrane antigen expression currently tested in UK clinical practice? How will people with PSMA-positive hormone relapsed metastatic prostate cancer be identified in clinical practice?

Is there a cut-off threshold of PSMA expression for being PSMA-positive?

Have all relevant comparators for 177Lu-PSMA-617 been included in the scope?

Which treatments are considered to be established clinical practice in the NHS for hormone relapsed metastatic prostate cancer previously treated with androgen receptor directed therapy (ARDT) and taxane based chemotherapy?

How should best supportive care be defined?

What treatments used in UK clinical practice are classed as androgen receptor directed therapies?

Is it appropriate to exclude abiraterone and enzalutamide as potential comparators because patients can only receive them once in UK clinical practice and it is expected that 177Lu-PSMA-617 will be used after androgen receptor directed therapy?

Subject to the ongoing NICE technology appraisal of olaparib [ID1640], would 177Lu-PSMA-617 be used as a treatment option for the subgroup of people with BRCA1/2-mutations if a targeted treatment for this group such as olaparib was available?

If a person had previously had off-label docetaxel in combination with ADT for treating hormone-sensitive prostate cancer and an ARDT is it anticipated that they would be eligible for treatment with 177Lu-PSMA-617? Or, is it anticipated that 177Lu-PSMA-617 would only be used after docetaxel, when docetaxel is used according to its marketing authorisation?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom 177Lu-PSMA-617 is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider 177Lu-PSMA-617 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 177Lu-PSMA-617 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 177Lu-PSMA-617 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 177Lu-PSMA-617 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 (2020) Prostate cancer risks and causes. Accessed April 2021.

2. Macmillan Cancer Support (2018) Potential causes of prostate cancer. Accessed May 2021.

3. Cancer Research UK (2018) Prostate cancer mortality statistics. Accessed April 2021.

4. National Prostate Cancer Audit (2021) Annual Report 2020. Accessed May 2021

5. Bouchelouche K, Choyke PL, Capala J. Prostate specific membrane antigen- a target for imaging and therapy with radionuclides. Discov Med. 2010 Jan;9(44):55-61.