Health Technology Briefing
December 2025

Lutetium 177Lu vipivotide tetraxetan for previously treated progressive metastatic castrate resistant prostate cancer

Company/Developer	Novartis Pharmaceuticals UK Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 41012	NICE ID: Not Available	UKPS ID: 674904

Licensing and Market Availability Plans

Currently in phase III clinical development.

Summary

Lutetium-177 PSMA-617 is in development for the treatment of advanced prostate cancer that has spread to other parts of the body and is no longer responding to standard hormone therapy. This stage of the disease is known as metastatic castration-resistant prostate cancer. The prostate is a small gland located below the bladder that helps make semen in males. Prostate cancer develops when cells in this gland start to grow uncontrollably. Once prostate cancer stops responding to hormone-lowering treatments, options become limited. However, not all patients can receive certain chemotherapies that involve drugs called taxanes, which are often offered at this stage. This may be due to age, side effects or other health conditions, leaving a need for new, effective, and better-tolerated treatment options.

Lutetium-177 PSMA-617 is given by injection into the vein. It is a targeted form of radiotherapy that delivers a small, controlled dose of radiation directly to prostate cancer cells. The medicine attaches to a protein found in high amounts on prostate cancer cells, called prostate-specific membrane antigen (PSMA), and releases radiation that damages the cancer's DNA, leading to the death of cancer cells while limiting harm to nearby healthy tissue. If licensed, lutetium-177 PSMA-617 could provide an additional treatment option for men with advanced prostate cancer whose disease has worsened after hormone therapy but who have not yet received taxane chemotherapy.

This briefing reflects the evidence available at the time of writing and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes or commissioning without additional information. A version of the briefing was sent to the company for a factual accuracy check. The company was available to comment.
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Proposed Indication

Treatment of patients with progressive metastatic castrate resistant prostate cancer (mCRPC) previously treated with an alternate androgen receptor-directed therapy (also known as androgen receptor pathway inhibitors (ARPI) which is the term used here), and not exposed to a taxane-containing regimen in the castration-resistant prostate cancer or metastatic hormone sensitive prostate cancer (mHSPC) settings.[1]

Technology

Description

177Lu-PSMA-617 (Pluvicto) is a radiopharmaceutical. The active moiety of lutetium-177 prostate-specific membrane antigen-617 (177Lu-PSMA-617) is the radionuclide lutetium-177 which is linked to a targeting moiety that binds with high affinity to prostate-specific membrane antigen (PSMA), a transmembrane protein that is highly expressed in prostate cancer, including mCRPC.[1,2] Upon the binding of 177Lu-PSMA-617 to PSMA-expressing cancer cells, the beta-minus emission from lutetium-177 delivers therapeutic radiation to the targeted cell, as well as to surrounding cells, and induces DNA damage which can lead to cell death. [2]

177Lu-PSMA-617 is currently in clinical development for the treatment of patients with progressive mCRPC previously treated with ARPI and not exposed to a taxane-containing regimen. In the phase III trial PSMAfore (NCT04689828) 177Lu-PSMA-617 is administered intravenously (IV) once every six weeks for six cycles.[1]

Key Innovation

Despite multiple available therapies, mortality in mCRPC remains high, and treatment options after progression on ARPIs are limited.[3] Although guidelines recommend taxane-based chemotherapy, some patients cannot easily receive them due to age or comorbidities and are therefore candidates for a second ARPI.[4] Because many patients are unable or unwilling to receive taxane-based chemotherapy, there is an unmet need for new, effective, and well-tolerated therapies in this setting.[3]

PSMAfore (NCT04689828) is the first phase 3 trial to assess the efficacy and safety of 177Lu-PSMA-617 in a taxane-naïve mCRPC population. The results of the primary analysis show that 177Lu-PSMA-617 is an effective alternative to a change of ARPI for delaying both disease progression and deterioration of quality of life in patients with mCRPC who have initially progressed on an ARPI, and for whom it was considered appropriate to delay taxane-based chemotherapy. The results of PSMAfore complement those of VISION (NCT03511664), which found that 177Lu-PSMA-617 prolonged imaging-based progression-free survival and overall survival when added to standard care in patients with advanced PSMA-positive mCRPC.[3,5]

Regulatory & Development Status

Lutetium 177Lu vipivotide tetraxetan currently has Marketing Authorisation in the EU/UK for the treatment of adult patients with PSMA-positive mCRPC who have been treated with ARPI and taxane-based chemotherapy or who are not medically suitable for taxanes.[2]

Lutetium 177Lu vipivotide tetraxetan is also in phase II/III clinical development for renal cell carcinoma.[6]

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Patient Group

Disease Area and Clinical Need

Prostate cancer affects the prostate gland under the bladder.[7] Prostate cancer usually starts to grow on the outer part of the prostate. This means it does not press on the tube that carries urine from the bladder to the penis (urethra) and cause symptoms, until the cancer has grown or spread. Once symptoms present, they include difficulty urinating, needing to urinate urgently, needing to urinate often, having a week flow of urine. Other symptoms can include erectile dysfunction, blood in the urine or semen and lower back pain.[8] Prostate cancer mainly affects men over 50, and the risk increases with age. Black men are twice as likely to develop prostate cancer.[9] The disease can be considered to be castrate-resistant when androgen deprivation therapy or combined androgen blockade no longer control prostate-specific antigen levels or symptoms of the disease, or when there is radiological evidence of progression.[10] Prostate cancer can also spread to any part of the body and become metastatic.[11]

Prostate cancer is the most common cancer in men in the UK. More than 63,000 men are diagnosed every year and around 510,000 men are living with or after prostate cancer. More than 12,000 men die from prostate cancer every year in the UK alone. In the UK, about 1 in 8 men will get prostate cancer in their lifetime.[10,11] Black men are more likely to get prostate cancer than other men and it is estimated that in the UK 1 in 4 Black men will get prostate cancer in their lifetime.[11] One- and five-year survival rates for stage 4 prostate cancer are 89.8% and 53.2%, respectively.[12] In England (2024-25) there were 103,730 finished consultant episodes (FCEs) and 99,126 admissions for malignant neoplasm of prostate (ICD-10 code C61), which resulted in 77,624 day cases and 75,822 FCE bed days.[13]

Recommended Treatment Options

There are no specific guidelines by The National Institute for Health and Care Excellence (NICE) for patients with mCRPC previously treated with ARPIs and not exposed to a taxane-containing regimen in the castration-resistant prostate cancer or mHSPC settings.

NICE currently recommends the following therapies for the treatment of patients with progressive mCRPC/metastatic hormone-resistant prostate cancer/ metastatic hormone-refractory prostate cancer:

- Abiraterone[14,15]
- Docetaxel[16]
- Enzalutamide[19,20]
- Cabazitaxel[21]
- Radium 223[22]

Clinical Trial Information

Trial	**PSMAfore;** NCT04689828; 2023-507772-50-00; A Phase III, Open-label, Multi-Center, Randomized Study Comparing 177Lu-PSMA-617 vs. a Change of Androgen Receptor-Directed Therapy in the Treatment of Taxane Naïve Men With Progressive Metastatic Castrate Resistant Prostate Cancer **Phase III**: Active, Not Recruiting **Locations:** USA, UK, Canada, Switzerland and 10 EU countries **Primary Completion Date:** October 2022
Trial Design	Randomised, parallel assignment, open label

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Population	N=469 (actual); Patients with progressive mCRPC who have progressed only once on prior second-generation ARPI; adults aged 18 years
Intervention(s)	177LuPSMA617, administered intravenously once every 6 weeks for 6 cycles with 68Ga-PSMA-11 (single intravenous dose of approximately 150 MBq). Administered dose must not be lower than 111 MBq or higher than 185 MBq
Comparator(s)	ARPI administered orally on a continuous basis, as per package insert and guidelines and 68GaPSMA11 (single intravenous dose of approximately 150 MBq)
Outcome(s)	**Primary outcome measure:** radiographic progression free survival (rPFS) See trial record for full list of all outcomes.
Results (efficacy)	In the primary analysis, 177Lu-PSMA-617 prolonged rPFS with a median of 9.30 months versus 5.55 months with ARPI change (hazard ratio 0.41, 95% CI 0.29–0.56). At the time of third interim overall survival (OS) analysis with more mature data, the updated median rPFS was 11.60 months with ^{177}Lu-PSMA-617 versus 5.59 months with ARPI change (hazard ratio 0.49, 95% CI 0.39–0.61). In the final OS analysis, it was not statistically significantly different between the ^{177}Lu-PSMA-617 and ARPI change arms based on the intention to treat principle. The Inverse Probability of Censoring Weighting crossover-adjusted analyses suggested that crossover confounded the OS analysis.[4]
Results (safety)	The safety profile of 177Lu-PSMA-617 was acceptable and consistent with previous reports, with no new safety signals identified.[4]

Estimated Cost

The list price of lutetium-177 vipivotide tetraxetan is £20,000 per 7,400 MBq single dose vial per treatment cycle (excluding VAT; company submission). The company has a commercial arrangement, which would have applied if the technology had been recommended.[23]

Relevant Guidance

NICE Guidance

- NICE technology appraisal guidance. Docetaxel for the treatment of hormone-refractory metastatic prostate cancer (TA101). August 2017.
- NICE technology appraisal guidance. Radium-223 dichloride for treating hormone-relapsed prostate cancer with bone metastases (TA412). September 2016.
- NICE technology appraisal guidance. Cabazitaxel for hormone-relapsed metastatic prostate cancer treated with docetaxel (TA391). August 2016
- NICE technology appraisal guidance. Abiraterone for castration-resistant metastatic prostate cancer previously treated with a (TA259). July 2016.
- NICE technology appraisal guidance. Abiraterone for treating metastatic hormone-relapsed prostate cancer before chemotherapy is indicated (TA387). April 2016.
- NICE technology appraisal guidance. Enzalutamide for treating metastatic hormone-relapsed prostate cancer before chemotherapy is indicated (TA377). January 2016.

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- NICE technology appraisal guidance. Enzalutamide for metastatic hormone-relapsed prostate cancer previously treated with a docetaxel-containing regimen (TA316). July 2014.

NHS England (Policy/Commissioning) Guidance

- NHS England. Clinical Commissioning Policy: The use of Stereotactic Ablative Radiotherapy (SABR) in the treatment of Prostate Cancer. 16031/P. July 2016.
- NHS England. Clinical Commissioning Policy: Proton Beam Therapy for Cancer of the Prostate. 16020/P. July 2016.
- NHS England. 2013/14 NHS Standard Contract for Cancer: Specialised Kidney, Bladder and Prostate Cancer Services (Adult). B14/S/a.

Other Guidance

- European Association of Urology (UAU). Guidelines on prostate cancer. 2024.[24]
- European Urology. EAU-EANM-ESTRO-ESUR-SIOG Guidelines on Prostate Cancer. Part II—2024 Update: Treatment of Relapsing and Metastatic Prostate Cancer. 2024.[25]
- European Society for Medical Oncology. Clinical Practice Guidelines – Prostate Cancer. 2020.[26]

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