Medicines & Healthcare products Regulatory Agency

MHRA

Early Access to Medicines Scientific Opinion - Public Assessment Report	
Product	**lutetium (^{177}Lu) vipivotide tetraxetan**
EAMS indication	Lutetium (^{177}Lu) vipivotide tetraxetan is indicated for the treatment of adult patients with prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer (mCRPC) who have been treated with androgen receptor (AR) pathway inhibition and taxane-based chemotherapy or who are not medically suitable for taxanes.
Company	**Advanced Accelerator Applications**
EAMS number	**35903/0001**
EAMS Scientific Opinion date	**05/04/2022**

Introduction
The aim of the Early Access to Medicines Scheme (EAMS) is to provide earlier availability of promising new unlicensed medicines and medicines used outside their licence, to UK patients that have a high unmet clinical need. The MHRA scientific opinion provides benefit and risk information to physicians who may wish to prescribe the EAMS medicine under their own responsibility. More information about the scheme can be found here:
http://www.mhra.gov.uk/Howweregulate/Innovation/EarlyaccesstomedicinesschemeEAMS/index.htm

The scientific opinion is based on assessment of the information supplied to the MHRA on the benefits and risks of the medicine. As such this is a scientific opinion and should not be regarded as a medicine licensed by the MHRA or a future commitment by the MHRA to license such a medicine, nor should it be regarded as an authorisation to sell or supply such a medicine. A positive scientific opinion is not a recommendation for use of the medicine and should not be interpreted as such. Under EAMS the risk and legal responsibility for prescribing a 'special' remains with the physician, and the opinion and EAMS documentation published by the MHRA are intended only to inform physicians' decision making and not to recommend use. An EAMS scientific opinion does not affect the civil liability of the manufacturer or any physician in relation to the product.

The General Medical Council's guidance on prescribing unlicensed medicines can be found here:
https://www.gmc-uk.org/guidance/ethical_guidance/14327.asp

What is lutetium (177Lu) vipivotide tetraxetan?
Lutetium (^{177}Lu) vipivotide tetraxetan (otherwise known as [^{177}Lu]Lu-PSMA-617) is a radiopharmaceutical product for therapy only.

What is lutetium (^{177}Lu) vipivotide tetraxetan used to treat?
Lutetium (^{177}Lu) vipivotide tetraxetan is used to treat adults with a certain type of advanced prostate cancer (called prostate-specific membrane antigen-positive metastatic castration-resistant prostate cancer [PSMA-positive mCRPC]) (otherwise known as metastatic hormone-refractory prostate cancer [mHRPC]) that has spread to other parts of the body (metastatic) and that has already been treated with other anticancer treatments.

How is lutetium (^{177}Lu) vipivotide tetraxetan used?
Tests will be performed to see if PSMA is present on the surface of the cancer cells. The cancer is likely to respond to treatment with lutetium (^{177}Lu) vipivotide tetraxetan if the test result is positive.

The use of lutetium (^{177}Lu) vipivotide tetraxetan involves exposure to radioactivity. There are strict laws on the use, handling and disposal of radiopharmaceutical products. Lutetium (^{177}Lu) vipivotide tetraxetan will only be used in special controlled areas in hospital. This product will only be handled and given by people who are trained and qualified to use it safely.

The recommended dose is 7400 MBq (megabecquerel, the unit used to express radioactivity). Lutetium (^{177}Lu) vipivotide tetraxetan is given approximately every 6 weeks for up to a total of 6 doses. Lutetium (^{177}Lu) vipivotide tetraxetan is administered directly into a vein.

Blood tests will be taken before and during treatment to monitor the condition and to detect any side effects as early as possible. Based on the results, it may be decided to delay, modify, or stop treatment with lutetium (^{177}Lu) vipivotide tetraxetan if necessary.

How does lutetium (^{177}Lu) vipivotide tetraxetan work?
Lutetium (^{177}Lu) vipivotide tetraxetan binds to a protein called PSMA (known as prostate specific membrane antigen) that is found on the surface of prostate cancer cells. Once bound, radiation is emitted from the ^{177}Lu causing prostate cancer cells to die.

How has lutetium (^{177}Lu) vipivotide tetraxetan been studied?
A total of 831 adult male patients with confirmed prostate cancer with progressive, metastatic, castrate resistant disease; and had a positive test (a ^{68}Ga-PSMA-11 PET/CT scan) for PSMA, were enrolled in a study that compared, the use of lutetium (^{177}Lu) vipivotide tetraxetan combined with current best standard of care, against best standard of care treatment alone. .

The main measures of effectiveness (how well the medicine worked) was the improvement in overall survival and an improvement in the time taken for the disease to progress (as evaluated or detected by radiological scans).

What are the benefits and risks of lutetium (^{177}Lu) vipivotide tetraxetan?
Benefits
In the 551 patients treated with lutetium (^{177}Lu) vipivotide tetraxetan combined with current best standard of care, there was a 12.5 month delay in the time to progression of the disease (as seen with radiological scans) and a 4 month improvement in overall survival, compared to patients treated with best standard of care alone.

At 6 months since start of treatment, 65% of patients, treated with lutetium (^{177}Lu) vipivotide tetraxetan combined with current best standard of care, had no worsening of the disease detected in their scans. This compared to 28% of patients treated with the best standard of care alone who had no worsening of the disease.

62% and 43% of patients, treated with lutetium (^{177}Lu) vipivotide tetraxetan combined with current best standard of care, were alive at 12 months and 18 months, respectively, since start of treatment. 49% and 29% of patients, treated with current best standard of care alone, were alive at 12 months and 18 months, respectively, since start of treatment.

Risks

The most common are tiredness, weakness, pale skin or shortness of breath (possible signs of low level of red blood cells); bleeding or bruising more easily than normal or difficulty to stop bleeding and frequent infections with signs such as fever, sore throat or mouth ulcers (possible signs of low level of white blood cells); passing urine less often than usual or passing much smaller amounts of urine than usual (possible sign of kidney problems); changes in bowel movements (constipation or diarrhoea), vomiting, urinary tract infection, abdominal pain, weight loss.

Why has lutetium (^{177}Lu) vipivotide tetraxetan been given a positive Early Access to Medicine Scientific opinion?
Metastatic castration-resistant prostate cancer (mCRPC) is a disease that has a major impact on quality of life and is life threatening. Presence of prostate-specific membrane antigen on the prostate cancer cells is considered to be a sign of a poorer prognosis (PSMA-positive mCRPC).

In patients who have exhausted available treatments and have PSMA positive mCRPC, lutetium (^{177}Lu) vipivotide tetraxetan, offers a treatment option through targeting and binding to the PSMA protein on the surface of prostate cancer cells. In these patients, treatment with lutetium (^{177}Lu) vipivotide tetraxetan shows meaningful improvement survival and delays progression of disease.

The risks associated with lutetium (^{177}Lu) vipivotide tetraxetan can be managed and do not outweigh the benefits.

What are the uncertainties?
Patients with mild or moderate kidney impairment may be at greater risk of developing side effects. These patients should have blood tests more frequently to monitor their kidney function and to check for died effects.

The safety of lutetium (^{177}Lu) vipivotide tetraxetan have not been studied in patients with severe kidney disease or end-stage kidney disease.

Any long-term effects as a result of radiation exposure from treatment with lutetium (^{177}Lu) vipivotide tetraxetan is not known at present.

The company that makes lutetium (^{177}Lu) vipivotide tetraxetan will provide additional information when it becomes available.

Are there on-going clinical studies?
There is no on-going study of lutetium (^{177}Lu) vipivotide tetraxetan in the EAMS indication.

What measures are in place to monitor and manage risks? (RMP)
A risk management plan has been developed to ensure that lutetium (^{177}Lu) vipivotide tetraxetan is used as safely as possible. Based on this plan, the company that make lutetium (^{177}Lu) vipivotide tetraxetan must ensure that all healthcare professionals expected to use the medicine, as well as patients, are provided with information on the medicine including the side effects and recommendations for minimising these side effects.

Information will be collected about patients before they enter the scheme. Healthcare professionals will be asked by the company to report side effects experienced by patients receiving lutetium (^{177}Lu) vipivotide tetraxetan through the scheme. They will receive comprehensive training prior to commencement of patient treatment. Safety data will be reviewed and reported to the MHRA on a regular basis by the company.

Other information about Lutetium (^{177}Lu) vipivotide tetraxetan – see EAMS Treatment Protocol