Medicines & Healthcare products Regulatory Agency

MHRA

Early Access to Medicines Scheme – Treatment protocol – Information for healthcare professionals

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 medicinal products included in the scheme are those that are intended to treat, diagnose or prevent seriously debilitating or life-threatening conditions where there are no adequate treatment options. More information about the scheme can be found here: http://www.mhra.gov.uk/Howweregulate/Innovation/EarlyaccesstomedicinesschemeEAMS/index.htm

This information is intended for healthcare professionals and is provided by the pharmaceutical company that manufactures the EAMS medicine. This medicine does not yet have a licence (marketing authorisation) in this indication and the information is provided to assist physicians in prescribing this unlicensed medicine. Guidance on prescribing unlicensed medicines can be found on the GMC webpage:
https://www.gmc-uk.org/guidance/ethical_guidance/14327.asp

The scientific opinion is based on assessment of the information supplied to the MHRA on the benefits and risks of this promising new 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.

Healthcare professionals should also refer to the summary information on the pharmacovigilance system which is provided in the document 'Early Access to Medicines Scheme – Treatment protocol – Information on the pharmacovigilance system'.

Scientific opinion period: The MHRA will withdraw the EAMS positive scientific opinion when a marketing authorisation (drug licence) is issued for the EAMS product covering the EAMS indication, or if following scientific assessment, the EAMS criteria are considered to be no longer met.

Treatment protocol update(s): In case of substantial new efficacy or safety data, the treatment protocol may need to be updated.

Contact information regarding queries on using this EAMS medicine can be found at the end of this document.

Information for the healthcare professionals

1. NAME OF THE MEDICINAL PRODUCT

Lutetium (^{177}Lu) vipivotide tetraxetan (otherwise known as [^{177}Lu]Lu-PSMA-617) 1000 MBq/mL solution for injection/infusion.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One mL of solution contains 1000 MBq of lutetium (^{177}Lu) vipivotide tetraxetan at the date and time of calibration.

The total amount of radioactivity per single-dose vial is 7400 MBq at the date and time of administration. Given the fixed volumetric activity of 1000 MBq/mL at the date and time of calibration, the volume of the solution in the vial is adjusted between 7.5 mL and 12.5 mL in order to provide the required amount of radioactivity at the date and time of administration.

Physical characteristics

Lutetium (^{177}Lu) has a half-life of 6.647 days. Lutetium (^{177}Lu) decays by β- emission to stable Hafnium (^{177}Hf) with the most abundant β- (79.3%) having a maximum energy of 0.497 MeV. The average beta energy is approximately 0.13 MeV. Low gamma energy is also emitted, for instance at 113 keV (6.2%) and 208 keV (11%).

Excipient with known effect

Each mL of solution contains up to 0.312 mmol (7.1 mg) of sodium.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection/infusion.

Clear, colourless to slightly yellow solution.

pH: 4.5 to 7.0.

4. CLINICAL PARTICULARS

4.1 EAMS therapeutic 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.

Taxane-ineligibility (including the identification of patients not medically suitable for taxanes) is to be determined by the treating physician.

4.2 Posology and method of administration

Lutetium (^{177}Lu) vipivotide tetraxetan should be administered only by persons authorised to handle radiopharmaceuticals in designated clinical settings (see section 6.6) and after evaluation of the patient by a qualified physician.

Radiopharmaceuticals, including lutetium (^{177}Lu) vipivotide tetraxetan, should be used by or under the control of healthcare professionals who are qualified by specific training and experience in the safe use and handling of radiopharmaceuticals, and whose experience and training have been approved by the appropriate governmental agency authorised to license the use of radiopharmaceuticals.

Lutetium (^{177}Lu) vipivotide tetraxetan is a radiopharmaceutical and should be handled with appropriate safety measures to minimise radiation exposure (see section 4.4). Waterproof gloves and effective radiation shielding should be used when handling lutetium (^{177}Lu) vipivotide tetraxetan.

Patient identification

Patients should be identified by PSMA imaging using PET/CT.

Posology
The recommended lutetium (^{177}Lu) vipivotide tetraxetan dose is 7400 MBq every 6 weeks (±1 week) for a total of 6 doses.

Treatment monitoring

Laboratory tests should be performed before and during treatment with lutetium (^{177}Lu) vipivotide tetraxetan.

- Haematology (haemoglobin, white blood cell count, absolute neutrophil count, platelet count)
- Kidney function (serum creatinine or calculated creatinine clearance)
- Liver function (alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, blood serum albumin, total blood bilirubin)

Dose modifications for adverse drug reactions (ADRs)

Recommended dose modifications of lutetium (^{177}Lu) vipivotide tetraxetan for ADRs are provided in Table 1. Management of severe or intolerable ADRs may require temporary dose interruption (extending the dosing interval from 6 weeks up to 10 weeks), dose reduction or permanent discontinuation of treatment with lutetium (^{177}Lu) vipivotide tetraxetan.

Table 1. Recommended dose modifications of lutetium (^{177}Lu) vipivotide tetraxetan for ADRs

ADR	Severity[a]	Dose modification
Dry mouth	Grade ≥3	Reduce lutetium (^{177}Lu) vipivotide tetraxetan dose by 20%.
Gastrointestinal toxicity	Grade ≥3 (not amenable to medical intervention)	Withhold lutetium (^{177}Lu) vipivotide tetraxetan until improvement to grade 2 or baseline. Reduce lutetium (^{177}Lu) vipivotide tetraxetan dose by 20%.
Anaemia, thrombocytopenia, leukopenia, neutropenia, pancytopenia	Grade ≥2	Withhold lutetium (^{177}Lu) vipivotide tetraxetan until improvement to grade 1 or baseline. Manage as deemed appropriate. The use of growth factors is permitted but should be discontinued once improved to grade 1 or baseline. Checking haematinic levels (iron, B12 and folate) and providing supplementation is advocated. Transfusions may be given as clinically indicated.

Renal toxicity	Defined as: • Confirmed serum creatinine increase (grade ≥2) • Confirmed creatinine clearance < 30 mL/min; calculate using Cockcroft-Gault with actual body weight	Withhold lutetium (^{177}Lu) vipivotide tetraxetan until improvement.
	Defined as: • Confirmed ≥40% increase from baseline serum creatinine, and • Confirmed 40% decrease in baseline creatinine clearance; calculate using Cockcroft-Gault with actual body weight	Withhold lutetium (^{177}Lu) vipivotide tetraxetan until improvement or return to baseline. Reduce lutetium (^{177}Lu) vipivotide tetraxetan dose by 20%.
	Recurrent renal toxicity grade ≥3	Permanently discontinue lutetium (^{177}Lu) vipivotide tetraxetan.
Spinal cord compression		Withhold lutetium (^{177}Lu) vipivotide tetraxetan until the compression has been adequately treated and any neurological sequela have stabilised and ECOG performance status has been stabilised.
Fracture in weight-bearing bones		Withhold lutetium (^{177}Lu) vipivotide tetraxetan until the fracture has been adequately stabilised/treated and ECOG performance status has stabilised.
AST or ALT >5 times ULN in the absence of liver metastases		Permanently discontinue lutetium (^{177}Lu) vipivotide tetraxetan.

Abbreviations: CLcr, creatinine clearance; ECOG, Eastern Cooperative Oncology Group; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ULN, upper limit of normal.
Grading according to most current Common Terminology Criteria for Adverse Events (CTCAE).
[a] The same thresholds are also applicable to baseline values at the time of treatment initiation with lutetium (^{177}Lu) vipivotide tetraxetan.

Elderly
No dose adjustment is recommended in patients aged 65 years or older (see section 5.2).

Renal impairment
No dose adjustment is recommended for patients with mild (baseline creatinine clearance [Clcr] 60 to 89 mL/min by Cockcroft-Gault) to moderate (CLcr 30 to 59 mL/min) renal impairment. The pharmacokinetic profile and safety of lutetium (^{177}Lu) vipivotide tetraxetan have not been studied in patients with severe (CLcr 15 to 29 mL/min) renal impairment or end-stage renal disease (see sections 4.4 and 5.2).

Hepatic impairment
No dose adjustment is recommended for patients with hepatic impairment.

Paediatric population
There is no relevant use of lutetium (^{177}Lu) vipivotide tetraxetan in the paediatric population in the indication of treatment of PSMA-expressing prostate cancer.

Method of administration

Lutetium (^{177}Lu) vipivotide tetraxetan is a ready-to-use radiopharmacetuical medicinal product for single use only.

Preparation instructions

- Aseptic technique and radiation shielding should be used when handling or administering lutetium (^{177}Lu) vipivotide tetraxetan, using tongs as needed to minimise radiation exposure.
- The vial should be visually inspected under a shielded screen for particulate matter and discoloration prior to administration. The lutetium (^{177}Lu) vipivotide tetraxetan vial should be discarded if particulates or discoloration are present.
- The lutetium (^{177}Lu) vipivotide tetraxetan solution should not be injected directly into any other intravenous solution.
- The amount of radioactivity delivered to the patient should be confirmed with an appropriately calibrated dose calibrator prior to and after lutetium (^{177}Lu) vipivotide tetraxetan administration.

Administration instructions

Lutetium (^{177}Lu) vipivotide tetraxetan may be administered intravenously as an injection using a disposable syringe fitted with a syringe shield (with or without a syringe pump), as an infusion using the gravity method (with or without an infusion pump), or as an infusion using the vial (with a peristaltic infusion pump).

Prior to administration, flush the intravenous catheter used exclusively for lutetium (^{177}Lu) vipivotide tetraxetan administration with ≥10 mL of 0.9% sterile sodium chloride solution to ensure patency and to minimise the risk of extravasation. In the event of extravasation, the injection must be stopped, the site of injection changed and the affected area irrigated with sodium chloride solution.

Intravenous methods of administration

Instructions for the syringe method (with or without a syringe pump)

- After disinfecting the vial stopper, withdraw an appropriate volume of lutetium (^{177}Lu) vipivotide tetraxetan to deliver the desired radioactivity by using a disposable syringe fitted with a syringe shield and a disposable sterile needle.
- Administer lutetium (^{177}Lu) vipivotide tetraxetan to the patient by slow intravenous push (either with a syringe pump or manually without a syringe pump) via an intravenous catheter that is pre-filled with 0.9% sterile sodium chloride solution and that is used exclusively for lutetium (^{177}Lu) vipivotide tetraxetan administration to the patient.
- Once the desired radioactivity has been administered, perform an intravenous flush of ≥10 mL of 0.9% sterile sodium chloride solution through the intravenous catheter to the patient.

Instructions for the gravity method (with or without an infusion pump)

- Insert a 2.5 cm, 20 gauge needle (short needle) into the lutetium (^{177}Lu) vipivotide tetraxetan vial and connect via a catheter to 500 mL 0.9% sterile sodium chloride solution (used to transport the lutetium (^{177}Lu) vipivotide tetraxetan solution during the infusion). Ensure that the short needle does not touch the lutetium (^{177}Lu) vipivotide tetraxetan solution in the vial and do not connect the short needle directly to the patient. Do not allow the sodium chloride solution to flow into the lutetium (^{177}Lu) vipivotide tetraxetan vial prior to the initiation of the lutetium (^{177}Lu) vipivotide tetraxetan infusion and do not inject the lutetium (^{177}Lu) vipivotide tetraxetan solution directly into the sodium chloride solution.
- Insert a second needle that is 9 cm, 18 gauge (long needle) into the lutetium (^{177}Lu) vipivotide tetraxetan vial, ensuring that the long needle touches and is secured to the bottom of the lutetium (^{177}Lu) vipivotide tetraxetan vial during the entire infusion. Connect the long needle to the patient by an intravenous catheter that is pre-filled with 0.9% sterile sodium chloride solution and that is used exclusively for the lutetium (^{177}Lu) vipivotide tetraxetan tetraxetan infusion into the patient.
- Use a clamp or an infusion pump to regulate the flow of the sodium chloride solution via the short needle into the lutetium (^{177}Lu) vipivotide tetraxetan vial at a rate of approximately 400 mL/h (the sodium chloride solution entering the vial through the short needle will carry the lutetium (^{177}Lu) vipivotide tetraxetan solution from the vial to the patient via the intravenous catheter connected to the long needle over a total duration of 30 to 40 minutes).

- During the infusion, ensure that the level of solution in the lutetium (^{177}Lu) vipivotide tetraxetan vial remains constant.
- Disconnect the vial from the long needle line and clamp the saline line once the level of radioactivity is stable for at least five minutes.
- Follow the infusion with an intravenous flush of ≥10 mL of 0.9% sterile sodium chloride solution through the intravenous catheter to the patient.

Instructions for the vial method (with a peristaltic infusion pump)
- Insert a 2.5 cm, 20 gauge needle (short venting needle) into the lutetium (^{177}Lu) vipivotide tetraxetan vial. Ensure that the short needle does not touch the lutetium (^{177}Lu) vipivotide tetraxetan solution in the vial and do not connect the short needle directly to the patient or to the peristaltic infusion pump.
- Insert a second needle that is 9 cm, 18 gauge (long needle) into the lutetium (^{177}Lu) vipivotide tetraxetan vial, ensuring that the long needle touches and is secured to the bottom of the lutetium (^{177}Lu) vipivotide tetraxetan vial during the entire infusion. Connect the long needle and a 0.9% sterile sodium chloride solution to a 3-way stopcock valve via appropriate tubing.
- Connect the output of the 3-way stopcock valve to tubing installed on the input side of the peristaltic infusion pump following the pump manufacturer's instructions.
- Pre-fill the line by opening the 3-way stopcock valve and pumping the lutetium (^{177}Lu) vipivotide tetraxetan solution through the tubing until it reaches the exit of the valve.
- Pre-fill the intravenous catheter which will be connected to the patient by opening the 3-way stopcock valve to the 0.9% sterile sodium chloride solution and pumping the 0.9% sterile sodium chloride solution until it exits the end of the catheter tubing.
- Connect the pre-filled intravenous catheter to the patient and set the 3-way stopcock valve such that the lutetium (^{177}Lu) vipivotide tetraxetan solution is in line with the peristaltic infusion pump.
- Infuse an appropriate volume of lutetium (^{177}Lu) vipivotide tetraxetan solution at approximately 25 mL/h to deliver the desired radioactivity.
- When the desired lutetium (^{177}Lu) vipivotide tetraxetan radioactivity has been delivered, stop the peristaltic infusion pump and then change the position of the 3-way stopcock valve so that the peristaltic infusion pump is in line with the 0.9% sterile sodium chloride solution. Restart the peristaltic infusion pump and infuse an intravenous flush of ≥10 mL of 0.9% sterile sodium chloride solution through the intravenous catheter to the patient.

For patient preparation, see section 4.4.

4.3 Contraindications

Hypersensitivity to the active substance, or any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Risk from radiation exposure

Lutetium (^{177}Lu) vipivotide tetraxetan contributes to a patient's overall long-term cumulative radiation exposure. Long-term cumulative radiation exposure is associated with an increased risk for cancer.

Radiation exposure to patients, medical personnel, and household contacts should be minimised during and after treatment with lutetium (^{177}Lu) vipivotide tetraxetan consistent with institutional good radiation safety practices, patient management procedures, and instructions to the patient for follow-up radiation protection at home. Patients with uncontrolled urinary incontinence and/or patients that use urinary catheter bags should not enrol in the lutetium (^{177}Lu) vipivotide tetraxetan EAMS programme.

Patient preparation
Patients should be encouraged to increase oral fluids and urged to void as often as possible to reduce bladder radiation, especially after high activities e.g. for radionuclide therapy.

After the procedure
Before the patient is released, the nuclear medicine physician should explain the necessary radioprotection precautions that the patient should follow to minimise radiation exposure to others. Following administration of lutetium (^{177}Lu) vipivotide tetraxetan, patients should be advised to limit close contact (less than 1 metre) with household contacts for 2 days or with children and pregnant women for

7 days. Following administration of lutetium (^{177}Lu) vipivotide tetraxetan, patients should be advised to sleep in a separate bedroom from household contacts for 3 days, from children for 7 days, or from pregnant women for 15 days.

Individual benefit/risk justification

For each patient, the radiation exposure must be justifiable by the likely benefit. The radioactivity administered should in every case be as low as reasonably achievable to obtain the required therapeutic effect.

Myelosuppression

In the VISION study, myelosuppression occurred more frequently in patients who received lutetium (^{177}Lu) vipivotide tetraxetan plus SoC compared to patients who received SoC alone (see section 4.8).

Haematology laboratory tests, including haemoglobin, white blood cell count, absolute neutrophil count, and platelet count, should be performed before and druring treatment with lutetium (^{177}Lu) vipivotide tetraxetan. Lutetium (^{177}Lu) vipivotide tetraxetan should be withheld and patients should be clinically managed as deemed appropriatediscontinued based on the severity of myelosuppression (see section 4.2).

Renal toxicity

In the VISION study, renal toxicity occurred more frequently in patients who received lutetium (^{177}Lu) vipivotide tetraxetan plus SoC compared to patients who received SoC alone (see section 4.8).

Patients should be advised to remain hydrated and to urinate frequently before and after administration of lutetium (^{177}Lu) vipivotide tetraxetan. Kidney function laboratory tests, including serum creatinine and calculated creatinine clearance, should be performed. Lutetium (^{177}Lu) vipivotide tetraxetan should be withheld, dose reduced, or permanently discontinued based on the severity of renal toxicity (see section 4.2).

Renal/Hepatic impairment

Careful consideration of the benefit risk ratio in these patients is required since an increased radiation exposure is possible.

Exposure (AUC) of lutetium (^{177}Lu) vipivotide tetraxetan increased with decreasing creatinine clearance, however CLcr ≥ 54 mL/min (Cockcroft-Gault) did not have a clinically meaningful effect on the pharmacokinetics of lutetium (^{177}Lu) vipivotide tetraxetan. Patients with mild or moderate renal impairment may be at greater risk of toxicity. Frequently monitor renal function and adverse drug reactions in patients with mild to moderate renal impairment. The pharmacokinetic profile and safety of lutetium (^{177}Lu) vipivotide tetraxetan have not been studied in patients with severe (CLcr 15 to 29 mL/min) renal impairment or end-stage renal disease.

Specific warnings

This medicinal product contains up to 3.9 mmol (88.75 mg) sodium per dose, equivalent to 4.4% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

Precautions with respect to environmental hazard see section 6.6.

4.5 Interaction with other medicinal products and other forms of interaction

No clinical drug interaction studies were required.

CYP450 enzymes

Lutetium (^{177}Lu) vipivotide tetraxetan is not a substrate of cytochrome P450 (CYP450) enzymes. It does not induce cytochrome P450 (CYP) 1A2, 2B6 or 3A4, and it does not inhibit cytochrome P450 (CYP) 1A2, 2B6, 2C8, 2C9, 2C19, 2D6 or 3A4/5 *in vitro*.

Transporters

Lutetium (^{177}Lu) vipivotide tetraxetan is not a substrate of BCRP, P-gp, MATE1, MATE2-K, OAT1, OAT3 or OCT2, and it is not an inhibitor of BCRP, P-gp, BSEP, MATE1, MATE2-K, OAT1, OAT3, OATP1B1, OATP1B3, OCT1 or OCT2 *in vitro*.

4.6 Fertility, pregnancy and lactation

Contraception in males

Based on its mechanism of action, male patients should be advised to use condoms for intercourse during treatment with lutetium (^{177}Lu) vipivotide tetraxetan and for 14 weeks after the last dose.

Pregnancy

The safety and efficacy of lutetium (^{177}Lu) vipivotide tetraxetan have not been established in females as lutetium (^{177}Lu) vipivotide tetraxetan is not indicated for use in females.. No animal studies using lutetium (^{177}Lu) vipivotide tetraxetan have been conducted to evaluate its effect on female reproduction and embryo-foetal development; however, all radiopharmaceuticals, including lutetium (^{177}Lu) vipivotide tetraxetan, have the potential to cause foetal harm. Based on its mechanism of action, lutetium (^{177}Lu) vipivotide tetraxetan can cause foetal harm when administered to a pregnant woman (see section 5.1).

Breast-feeding

The safety and efficacy of lutetium (^{177}Lu) vipivotide tetraxetan have not been established in females as lutetium (^{177}Lu) vipivotide tetraxetan is not indicated for use in females. There are no data on the presence of lutetium (^{177}Lu) vipivotide tetraxetan in human milk or its effects on the breast-fed newborn/infant or on milk production.

Fertility

No studies were conducted to determine the effects of lutetium (^{177}Lu) vipivotide tetraxetan on fertility. The recommended cumulative dose of 44400 MBq of lutetium (^{177}Lu) vipivotide tetraxetan results in a radiation absorbed dose to the testes within the range where lutetium (^{177}Lu) vipivotide tetraxetan may cause infertility.

In addition, patients must not donate sperm for 6 months after administration of lutetium (^{177}Lu) vipivotide tetraxetan.

4.7 Effects on ability to drive and use machines

Lutetium (^{177}Lu) vipivotide tetraxetan has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of safety profile

The safety of lutetium (^{177}Lu) vipivotide tetraxetan was evaluated in the phase III VISION study in patients with progressive, PSMA-positive mCRPC. Of the 831 patients randomised, 734 patients received at least one dose of randomised treatment. Patients received at least one dose of either lutetium (^{177}Lu) vipivotide tetraxetan 7400 MBq administered every 6 to 10 weeks plus SoC (n=529) or SoC alone (n=205).

Among patients who received lutetium (^{177}Lu) vipivotide tetraxetan plus SoC, the median number of doses was 5 (range: 1 to 6), with 67.7% of patients who received at least 4 doses or lutetium (^{177}Lu) vipivotide tetraxetan, and 46.5% of patients who received a total of 6 doses of lutetium (^{177}Lu) vipivotide tetraxetan. The median cumulative dose was 37500 MBq (range: 7000 to 48300). The median duration of exposure was 7.8 months (range: 0.3 to 24.9) for patients who received lutetium (^{177}Lu) vipivotide tetraxetan plus SoC and 2.1 months (range: 0.0 to 26.0) for patients who received SoC alone.

Table 2 summarises the incidence of ADRs. The most common ADRs (≥20%) occurring at a higher incidence in patients who received lutetium (^{177}Lu) vipivotide tetraxetan plus SoC compared with SoC alone include: fatigue (43.1%), dry mouth (39.3%), nausea (35.3%), anaemia (31.8%), decreased appetite (21.2%) and constipation (20.2%). The most common grade ≥3 to 4 ADRs (≥5%) occurring at a higher incidence in patients who received lutetium (^{177}Lu) vipivotide tetraxetan plus SoC compared to SoC alone include: anaemia (12.9%), thrombocytopenia (7.9%), lymphopenia (7.8%) and fatigue (5.9%).

Tabulated list of ADRs

ADRs (Table 2) are listed by MedDRA system organ class. Within each system organ class, the ADRs are ranked by frequency, with the most frequent reactions first. In addition, the corresponding frequency category for each ADR is based on the following convention (CIOMS III): very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000).

Table 2. ADRs occurring at a higher incidence in patients who received lutetium (^{177}Lu) vipivotide tetraxetan plus SoC compared to SoC alone in VISION[a]

ADRs	Frequency category	All grades n (%)	Grades 3 to 4[b] n (%)
Blood and lymphatic system disorders			
Anaemia	Very common	168 (31.8)	68 (12.9)
Thrombocytopenia	Very common	91 (17.2)	42 (7.9)
Leukopenia[c]	Very common	83 (15.7)	22 (4.2)
Lymphopenia	Very common	75 (14.2)	41 (7.8)
Pancytopenia[d]	Common	9 (1.7)	7 (1.3) [b]
Nervous system disorders			
Dizziness	Common	44 (8.3)	5 (0.9)
Headache	Common	37 (7.0)	4 (0.8)
Dysgeusia[e]	Common	37 (7.0)	0 (0.0)
Eye disorders			
Dry eye	Common	16 (3.0)	0 (0.0)
Ear and labyrinth disorders			
Vertigo	Common	11 (2.1)	0 (0.0)
Gastrointestinal disorders			
Dry mouth[f]	Very common	208 (39.3)	0 (0.0)
Nausea	Very common	187 (35.3)	7 (1.3)
Constipation	Very common	107 (20.2)	6 (1.1)
Vomiting[g]	Very common	101 (19.1)	5 (0.9)
Diarrhoea	Very common	100 (18.9)	4 (0.8)
Abdominal pain[h]	Very common	59 (11.2)	6 (1.1)
Renal and urinary disorders			
Urinary tract infection[i]	Very common	61 (11.5)	20 (3.8)
Acute kidney injury[j]	Common	45 (8.5)	17 (3.2)
General disorders and administration site conditions			
Fatigue	Very common	228 (43.1)	31 (5.9)
Decreased appetite	Very common	112 (21.2)	10 (1.9)
Weight decreased	Very common	57 (10.8)	2 (0.4)
Oedema peripheral[k]	Common	52 (9.8)	2 (0.4)
Pyrexia	Common	36 (6.8)	2 (0.4)

Abbreviation: SoC, standard of care

[a] National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) Version 5.0.

[b] Only includes grades 3 to 4 ADRs, with the exception of pancytopenia. Grade 5 (fatal) pancytopenia was reported in 2 patients who received lutetium (^{177}Lu) vipivotide tetraxetan plus SoC.

[c] Leukopenia includes leukopenia and neutropenia.

[d] Pancytopenia includes pancytopenia and bicytopenia.

[e] Dysgeusia includes dysgeusia and taste disorder.

[f] Dry mouth includes dry mouth, aptyalism and dry throat.

[g] Vomiting includes vomiting and retching.

[h] Abdominal pain includes abdominal pain, abdominal pain upper, abdominal discomfort, abdominal pain lower, abdominal tenderness and gastrointestinal pain.

[i] Urinary tract infection includes urinary tract infection, cystitis and cystitis bacterial.

[j] Acute kidney injury includes blood creatinine increased, acute kidney injury, renal failure and blood urea increased.

[k] Oedema peripheral includes oedema peripheral, fluid retention and fluid overload.

Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects. The radiation dose resulting from therapeutic exposure may result in higher incidence of cancer and mutations. In all cases it is necessary to ensure that the risks of the radiation are less than from the disease itself.

Description of selected ADRs

Myelosuppression
In the VISION study, myelosuppression occurred more frequently in patients who received lutetium (^{177}Lu) vipivotide tetraxetan plus SoC compared to patients who received SoC alone (all grades/grade ≥3): anaemia (31.8%/12.9%) versus (13.2%/4.9%); thrombocytopenia (17.2%/7.9%) versus (4.4%/1.0%); leukopenia (12.5%/2.5%) versus (2.0%/0.5%); lymphopenia (14.2%/7.8%) versus (3.9%/0.5%); leukopenia (12.5%/2.5%) versus (2.0%/0.5%); neutropenia (8.5%/3.4%) versus (1.5%/0.5%); pancytopenia (1.5%/1.1%) versus (0%/0%) including two fatal events of pancytopenia in patients who received lutetium (^{177}Lu) vipivotide tetraxetan plus SoC; and bicytopenia (0.2%/0.2%) versus (0%/0%).

Myelosuppression ADRs that led to permanent discontinuation in ≥0.5% of patients who received lutetium (^{177}Lu) vipivotide tetraxetan plus SoC included: anaemia (2.8%), thrombocytopenia (2.8%), leukopenia (1.3%), neutropenia (0.8%), and pancytopenia (0.6%). Myelosuppression ADRs that led to dose interruptions/dose reductions in ≥0.5% of patients who received lutetium (^{177}Lu) vipivotide tetraxetan plus SoC included: anaemia (5.1%/1.3%), thrombocytopenia (3.6%/1.9%), leukopenia (1.5%/0.6%), and neutropenia (0.8%/0.6%).

Renal toxicity
In the VISION study, renal toxicity occurred more frequently in patients who received lutetium (^{177}Lu) vipivotide tetraxetan plus SoC compared to patients who received SoC alone (all grades/grades 3 to 4): blood creatinine increased (5.3%/0.2%) versus (2.4%/0.5%); acute kidney injury (3.6%/3.0%) versus (3.9%/2.4%); renal failure (0.2%/0%) versus (0%/0%); and blood urea increased (0.2%/0%) versus (0%/0%).

Renal ADRs that led to permanent discontinuation in ≥0.2% of patients who received lutetium (^{177}Lu) vipivotide tetraxetan plus SoC included: blood creatinine increased (0.2%). Renal ADRs that led to dose interruptions/dose reductions in ≥0.2% of patients who received lutetium (^{177}Lu) vipivotide tetraxetan plus SoC included: blood creatinine increased (0.2%/0.4%) and acute kidney injury (0.2%/0%).

Reporting of suspected adverse reactions

Reporting of suspected adverse reactions during the EAMS is important, to monitor the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the MHRA Yellow Card scheme and to Novartis by completing the EAMS Adverse Event Report form provided in the physician pack. The contact details for the Novartis Patient Safety Department are: uk.patientsafety@novartis.

A Drug Exposure in Pregnancy Form must also be completed in situations where the partner of a male patient treated with lutetium (^{177}Lu) vipivotide tetraxetan is pregnant or becomes pregnant. The completed form must also be returned to the Novartis Patient Safety Department: uk.patientsafety@novartis.com.

4.9 Overdose

In the event of administration of a radiation overdose with lutetium (^{177}Lu) vipivotide tetraxetan, the radiation absorbed dose to the patient should be reduced where possible by increasing the elimination of the radionuclide from the body by frequent micturition or by forced diuresis and frequent bladder voiding. It might be helpful to estimate the effective radiation dose that was applied.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: not yet assigned. ATC code: not yet assigned.

Mechanism of action

The active moiety of lutetium (^{177}Lu) vipivotide tetraxetan is a radioligand therapy that is comprised of the therapeutic radionuclide ^{177}Lu which is linked to a targeting moiety that binds with high affinity to PSMA, a transmembrane protein that is highly expressed in prostate cancer, including mCRPC. Upon the binding of lutetium (^{177}Lu) vipivotide tetraxetan to PSMA-expressing cancer cells, the beta-minus emission from ^{177}Lu delivers therapeutic radiation to the targeted cell, as well as to surrounding cells, and induces DNA damage which can lead to cell death.

Pharmacodynamic effects

There are no data regarding lutetium (^{177}Lu) vipivotide tetraxetan exposure-efficacy relationships and the time course of pharmacodynamic response.

There are limited data regarding lutetium (^{177}Lu) vipivotide tetraxetan exposure-safety relationships and the time course of pharmacodynamic response.

Unlabelled vipivotide tetraxetan does not have any pharmacodynamic activity.

Clinical efficacy and safety

The efficacy of lutetium (^{177}Lu) vipivotide tetraxetan in patients with progressive, PSMA-positive mCRPC was established in VISION, a randomised, multicentre, open-label phase III study. Eight hundred and thirty-one (N=831) patients were randomised (2:1) to receive either lutetium (^{177}Lu) vipivotide tetraxetan 7 400 MBq every 6 weeks for up to a total of 6 doses plus SoC (N=551) or SoC alone (N=280).

Eligible patients were required to have PSMA-positive mCRPC, Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 0 to 2, at least one metastatic lesion present on computed tomography (CT), magnetic resonance imaging (MRI) or bone scan imaging, and adequate renal, hepatic and haematological function. Eligible patients were also required to have received at least one AR pathway inhibitor such as abiraterone acetate or enzalutamide and 1 or 2 prior taxane-based chemotherapy regimens (with a regimen defined as a minimum exposure of 2 cycles of a taxane). Patients with untreated, unstable, symptomatic central nervous system metastases or symptomatic or clinically/radiologically impending spinal cord compression were not eligible for the study.

Patients underwent a gallium (^{68}Ga) gozetotide positron emission tomography (PET) scan to evaluate PSMA expression defined by central read criteria. Eligible patients were required to have at least one PSMA-positive lesion identified by this scan, and no CT/MRI measurable lesions that showed poor or no gallium (^{68}Ga) gozetotide uptake on the PET scan.

SoC administered at the physician's discretion included: supportive measures including pain medications, hydration, blood transfusions, etc.; ketoconazole; radiation therapy (including seeded form or any external beam radiotherapy [including stereotactic body radiotherapy and palliative external beam]) to localised prostate cancer targets; bone-targeted agents including zolendronic acid, denosumab and any

bisphosphonates; androgen-reducing agents including any corticosteroid and 5-alpha reductases; AR pathway inhibitors. SoC excluded investigational agents, cytotoxic chemotherapy, immunotherapy, other systemic radioisotopes, and hemi-body radiotherapy treatment.

Patients continued randomised treatment until evidence of tumour progression (based on investigator assessment per Prostate Cancer Working Group 3 [PCWG3] criteria), unacceptable toxicity, use of prohibited treatment, non-compliance or withdrawal, or lack of clinical benefit.

The alternate primary efficacy endpoints were overall survival (OS) and radiographic progression-free survival (rPFS) by blinded independent central review (BICR) per PCWG3 criteria. Additional key secondary efficacy endpoints were overall response rate (ORR) by BICR per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 and time to first symptomatic skeletal event (SSE) defined as first new symptomatic pathological bone fracture, spinal cord compression, tumour-related orthopaedic surgical intervention, requirement for radiation therapy to relieve bone pain, or death from any cause, whichever occurred first.

Demographic and baseline disease characteristics were balanced between the treatment arms. The median age was 71 years (range: 40 to 94 years); 86.8% White; 6.6% Black or African American; 2.4% Asian; 92.4% had ECOG PS0-1; 7.6% had ECOG PS2. Randomisation was stratified by baseline lactase dehydrogenase (LDH), presence of liver metastases, ECOG PS score and inclusion of an AR pathway inhibitor as part of SoC at the time of randomisation. At randomisation, all patients (100.0%) received at least one prior taxane-based chemotherapy regimen and 41.2% of patients received two. At randomisation, 51.3% of patients received one prior AR pathway inhibitor, 41.0% of patients received 2, and 7.7% of patients received 3 or more. During the randomised treatment period, 52.6% of patients in the lutetium (^{177}Lu) vipivotide tetraxetan plus SoC arm and 67.8% of patients in the SoC alone arm received at least one AR pathway inhibitor.

Efficacy results for VISION are presented in Table 3 and Figures 1 and 2. The final analyses of OS and rPFS were event-driven and conducted after the occurrence of 530 deaths and 347 events, respectively.

Treatment with lutetium (^{177}Lu) vipivotide tetraxetan plus SoC demonstrated a statistically significant improvement in OS and rPFS by BICR compared to treatment with SoC alone. The primary efficacy results are supported by a statistically significant difference between the treatment arms in the time to first SSE (p<0.001) and ORR (p<0.001), and DCR (p<0.001). There was an estimated 38% risk reduction of death, an estimated 60% risk reduction of radiographic disease progression or death, and an estimated 50% risk reduction of SSE or death based on hazard ratios in favour of lutetium (^{177}Lu) vipivotide tetraxetan plus SoC treatment.

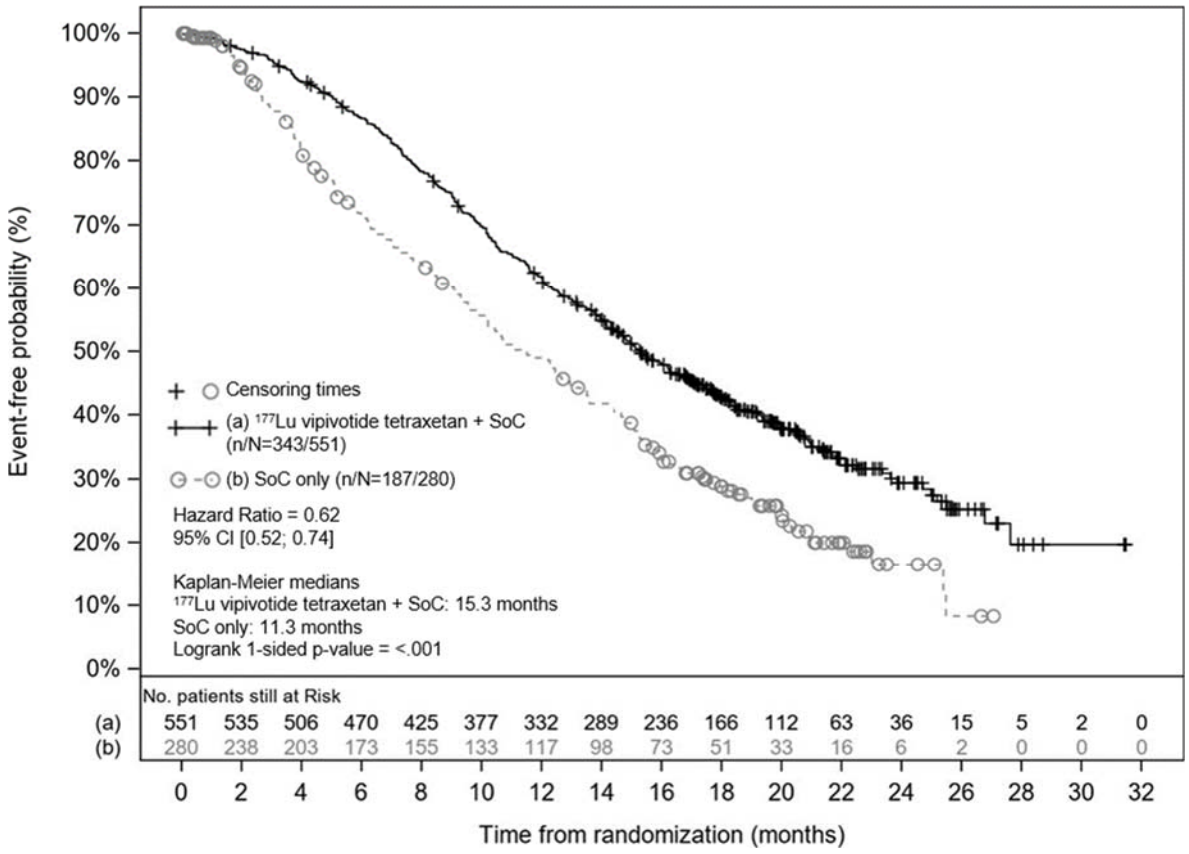
Table 3. Efficacy results in VISION

Efficacy parameters	**Lutetium (^{177}Lu) vipivotide tetraxetan plus SoC**	**SoC**
Alternate primary efficacy endpoints		
Overall survival (OS)	N=551	N=280
Deaths, n (%)	343 (62.3%)	187 (66.8%)
Median, months (95% CI)[a]	15.3 (14.2; 16.9)	11.3 (9.8; 13.5)
Hazard ratio (95% CI)[b]	0.62 (0.52; 0.74)	
P-value[c]	<0.001	
Radiographic progression-free survival (rPFS)	N=385	N=196
Events (progression or death), n (%)	254 (66.0%)	93 (47.4%)
Radiographic progressions, n (%)	171 (44.4%)	59 (30.1%)
Deaths, n (%)	83 (21.6%)	34 (17.3%)
Median, months (99.2% CI)[a]	8.7 (7.9; 10.8)	3.4 (2.4; 4.0)
Hazard ratio (99.2% CI)[b]	0.40 (0.29; 0.57)	
P-value[c]	<0.001	

CI: Confidence interval; NE: Not evaluable; BICR: Blinded independent central review; PCWG3: Prostate Cancer Working Group 3; RECIST: Response Evaluation Criteria in Solid Tumors; SoC: Standard of care;

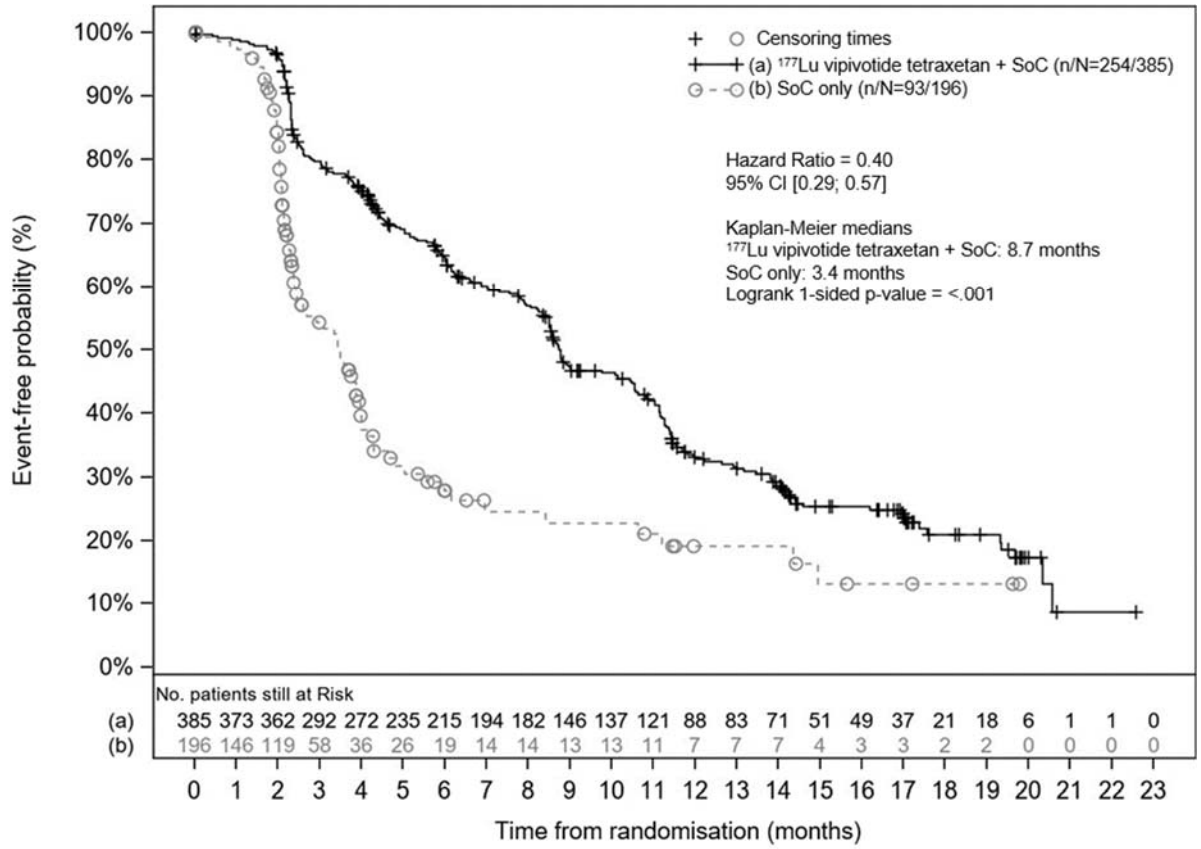
[a] Based on Kaplan-Meier estimate
[b] Hazard ratio based on the stratified Cox PH model. Hazard ratio <1 favours lutetium (^{177}Lu) vipivotide tetraxetan plus SoC
[c] Stratified log-rank test one-sided p-value
[d] By BICR per PCWG3 criteria

Figure 1. Kaplan-Meier plot of overall survival in VISION



Stratified log-rank test and stratified Cox model using strata per IRT defined by LDH level, presence of liver metastases, ECOG score and inclusion of an AR pathway inhibitor in SoC at time of randomisation.
n/N: Number of events/number of patients in treatment arm.

Figure 2. Kaplan-Meier plot of BICR-assessed radiographic progression-free survival (rPFS) in VISION



Stratified log-rank test and stratified Cox model using strata per IRT defined by LDH level, presence of liver metastases, ECOG score and inclusion of an AR pathway inhibitor in SoC at time of randomisation.
n/N: Number of events/number of patients in treatment arm.

Paediatric population

The European Medicines Agency has waived the obligation to submit the results of studies with lutetium (^{177}Lu) vipivotide tetraxetan in all subsets of the paediatric population in the treatment of PSMA-expressing prostate cancer (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

The pharmacokinetics of lutetium (^{177}Lu) vipivotide tetraxetan have been characterised in 30 patients in the phase III VISION sub-study.

Absorption

Lutetium (^{177}Lu) vipivotide tetraxetan is administered intravenously and is immediately and completely bioavailable.

The geometric mean blood exposure (area under the curve [AUC_{inf}]) for lutetium (^{177}Lu) vipivotide tetraxetan at the recommended dose is 52.3 ng.hr/mL (geometric mean coefficient of variation [CV] 31.4%). The geometric mean maximum blood concentration (C_{max}) for lutetium (^{177}Lu) vipivotide tetraxetan is 6.58 ng/mL (CV 43.5%).

Distribution

The geometric mean volume of distribution (V_z) for lutetium (^{177}Lu) vipivotide tetraxetan is 123 L (CV 78.1%).

Unlabelled vipivotide tetraxetan and non-radioactive lutetium (^{175}Lu) vipivotide tetraxetan are each 60% to 70% bound to human plasma proteins.

Organ uptake

The biodistribution lutetium (^{177}Lu) vipivotide tetraxetan shows how primary update in lacrimal glands, salivary glands, kidneys, urinary bladder wall, liver, small intestine and large intestine (left and right colon).

Elimination

The geometric mean clearance (CL) for lutetium (^{177}Lu) vipivotide tetraxetan is 2.04 L/h (CV 31.5%).

Lutetium (^{177}Lu) vipivotide tetraxetan is primarily eliminated renally.

Half-life

Lutetium (^{177}Lu) vipivotide tetraxetan shows a bi-exponential elimination with a geometric mean terminal elimination half-life ($T_{½}$) of 41.6 hours (CV 68.8%).

Biotransformation

Lutetium (^{177}Lu) vipivotide tetraxetan does not undergo hepatic or renal metabolism.

Elderly

Of the 529 patients who received at least one dose of lutetium (^{177}Lu) vipivotide tetraxetan plus SoC in the VISION study, 386 patients (73%) were aged 65 years or older and 143 patients (27%) were aged 75 years or older.

Effects of age, body weight and renal impairment

No clinically significant effects on the pharmacokinetic parameters of lutetium (^{177}Lu) vipivotide tetraxetan were identified for the following covariates assessed in 30 patients in the phase III VISION sub-study: age (median: 67 years; range: 52 to 80 years), body weight (median: 88.8 kg; range: 63.8 to 143.0 kg), mild to moderate renal impairment (baseline CLcr 30 to 89 mL/min by Cockcroft-Gault). The effect of severe renal impairment (baseline CLcr 15 to 29 mL/min) or end-stage renal disease on lutetium (^{177}Lu) vipivotide tetraxetan pharmacokinetics has not been studied.

Cardiac electrophysiology

The ability of lutetium (^{177}Lu) vipivotide tetraxetan to prolong the QTc interval at the recommended dose was assessed in 30 patients in the phase III VISION sub-study. Lutetium (^{177}Lu) vipivotide tetraxetan did not prolong the QT/QTc interval.

5.3 Preclinical safety data

No toxicological effects were observed in safety pharmacology or single-dose toxicity studies in rats and minipigs administered a non-radioactive formulation containing unlabelled vipivotide tetraxetan and lutetium (^{175}Lu) vipivotide tetraxetan or in repeat-dose toxicity studies in rats administered unlabelled vipivotide tetraxetan.

Mutagenicity and long-term carcinogenicity studies have not been carried out with lutetium (^{177}Lu) vipivotide tetraxetan; however, radiation is a carcinogen and mutagen.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Acetic acid
Sodium acetate
Gentisic acid
Sodium ascorbate
Pentetic acid
Water for injections

6.2 Incompatibilities

This medicinal product must not be mixed with other products except those mentioned in section 4.2.

6.3 Shelf life

120 hours (5 days) from the date and time of calibration.

6.4 Special precautions for storage

Store below 30°C. Do not freeze. Store in the original package to protect from ionising radiation (lead shielding).

Storage of radiopharmaceuticals should be in accordance with national regulations on radioactive materials.

6.5 Nature and contents of container

Clear, colourless, type I glass vial, closed with a bromobutyl rubber stopper and aluminium seal.

Each vial contains a volume varying from 7.5 mL to 12.5 mL of solution corresponding to a radioactivity of 7400 MBq at the date and time of administration.

The vial is enclosed within a lead container for protective shielding.

6.6 Special precautions for disposal and other handling

General warnings

Radiopharmaceuticals should be received, used and administered only by authorised persons in designated clinical settings. Their receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licences of the competent official organisation.

Radiopharmaceuticals should be prepared in a manner which satisfies both radiation safety and pharmaceutical quality requirements. Appropriate aseptic precautions should be taken.

For instructions on preparation of the medicinal product before administration, see section 4.2.

If at any time in the preparation of this product the integrity of this vial is compromised it should not be used.

Administration procedures should be carried out in a way to minimise risk of contamination of the medicinal product and irradiation of the operators. Adequate shielding is mandatory.

The administration of radiopharmaceuticals creates risks for other persons from external radiation or contamination from spill of urine, vomiting, etc. Radiation protection precautions in accordance with national regulations must therefore be taken.

This preparation is likely to result in a relatively high radiation dose to most patients. The administration of lutetium (^{177}Lu) vipivotide tetraxetan may result in significant environmental hazard. This may be of

concern to the immediate family of those individuals undergoing treatment or the general public depending on the level of radioactivity administered, hence radioprotection rules should be followed (section 4.4). Suitable precautions in accordance with national regulations should be taken concerning the radioactivity eliminated by the patients in order to avoid any contaminations.

The surface dose rates and the accumulated dose depend on many factors. Measurements on the location and during work are critical and should be practiced for more precise and instructive determination of overall radiation dose to the staff. Healthcare personnel are advised to limit the time of close contact with patients injected with lutetium (^{177}Lu) vipivotide tetraxetan. The use of television monitor systems to monitor the patients is recommended. Given the half-life of ^{177}Lu it is specially recommended to avoid internal contamination. It is necessary to use protective high quality (latex/nitrile) gloves to avoid direct contact with the radiopharmaceutical (vial/syringe). For minimising radiation exposure, always use the principles of time, distance and shielding (reducing the manipulation of the vial and using the material already supplied par the manufacturer).

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

^{177}Lu is prepared using two different sources of stable isotopes (either lutetium-176 or ytterbium-176) that require different waste management. The product batch release certificate should be consulted to identify the source of stable isotopes used and the appropriate waste management should be applied.

7. SCIENTIFIC OPINION HOLDER
Advanced Accelerator Applications UK & Ireland Ltd.
Edison House
223-231 Old Marylebone Road
Marylebone, London
NW1 5QT

8. EAMS NUMBER
35903/0001

9. DATE OF SCIENTIFIC OPINION
<Date of first authorisation: {DD month YYYY}>
<Date of latest renewal: {DD month YYYY}>

Additional information

The prescribing physician should carefully read the information provided in the rest of this document.

This EAMS will provide access to lutetium (^{177}Lu) vipivotide tetraxetan treatment for eligible patients with PSMA-positive mCRPC. Potentially eligible patients at participating National Health Service (NHS) sites will be identified by their prescribing physician.

Each prescribing physician interested in enrolling a patient in the programme should submit an initial request via the Novartis Grants, External Studies and Managed Access System (GEMS) via https://www.novartis.com/our-focus/healthcare-professionals/managed-access-programs. The prescribing physician will be required to register with Novartis Managed Access Programme Portal and patient details will need to be entered into the portal for each individual application. A unique initial request ID will be assigned to each eligible patient enrolled onto EAMS. This unique initial request ID will be used for future drug re-supply requests and adverse event reporting.

Novartis will request the baseline demographics data at the time of initial application and additional information at the time of re-supply request. The purpose of this data collection (registry) is to ensure the safe and effective use of the product in line with the EAMS Treatment protocols and EAMS scientific opinion.

The prescribing physician will be requested to provide the following information by completing an Initial Application and Drug Supply Request for each patient to be enrolled on to the programme for eligibility assessment:

- Year of birth
- Gender
- Disease/condition to be treated
- Additional information e.g. previous treatment history and concomitant medication

Novartis will review the application for eligibility. If a patient is deemed eligible for EAMS, Novartis will assign a unique EAMS number and communicate it to the requesting physician.

An EAMS Agreement Letter with Novartis will be required to be signed by the prescribing Physician, the Trust and Novartis. The MAP Agreement Letter will be signed either on a per patient basis or on a Trust basis. Drug supply will only be shipped once a fully executed MAP Agreement Letter and attestation has been completed.

For patients approved under this scheme and requiring ongoing drug supply, healthcare professionals will be required to complete the Re-supply Form on GEMS to request further cycles of treatment (until patients have received a maximum of 6 cycles of treatment in total). The healthcare professionals will be asked for confirmation that they understand and agree to comply with their obligations to report all adverse events and special situations to Novartis and that they are complying with this requirement. They will be also asked to confirm that all adverse events and special situations experienced since the last re-supply request have been reported or there are no new adverse events to report.

As part of the requirement of the EAMS, data on the safety of EAMS lutetium (^{177}Lu) vipivotide tetraxetan will be collected via uk.patientsafety@novartis.com and entered into the Argus database and the demographics and clinical characteristics of the patients enrolled in the EAMS will be collected using MACRO™.

Healthcare professionals should also report all known and suspected ADRs (i.e., adverse events which are thought to be related to the use of lutetium (^{177}Lu) vipivotide tetraxetan, in that a causal relationship is at least a possibility and cannot be ruled out) to the MHRA via the Yellow Card scheme, www.mhra.gov.uk/yellowcard. In addition, the EAMS patient ID number should be provided in the report narrative to help the MHRA identify that the adverse events is related to EAMS product and to help Novartis link the adverse events report to the correct EAMS patient. A 3-monthly periodic safety report will be submitted to the MHRA to summarise data on safety and usage of lutetium (^{177}Lu) vipivotide tetraxetan under the scheme.

For NHS England only - additional requirement for registering a patient:

Following notification from Novartis of eligibility approval, the physician must complete a Blueteq form online and register their patient with NHS England, which is located at https://www.blueteq-secure.co.uk/Trust/default.aspx. Once the Blueteq form has been completed, an approval email will be received by the user and pharmacy stating the request has been approved, also stating an EAMS number. This EAMS number must be communicated back to Novartis.

Contact information

Adverse event reporting:
Tel: 0845 601 1387
Email: uk.patientsafety@novartis.com

Contact details for medical information:
Tel: +44 (0)20 7258 5200
Email: infomed@adacap.com