Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986
This medicine is dispensed with a doctor's prescription only

Pluvicto
Solution for injection/infusion

Active ingredient
One mL of solution contains 1,000 MBq of lutetium (^{177}Lu) vipivotide tetraxetan at the date and time of calibration.

Inactive ingredients and allergens in the medicine - see section 2 under 'Important information about some of this medicine's ingredients', and section 6 'Additional information'.
Read the entire leaflet carefully before you start using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or the healthcare provider.

1. What is this medicine intended for?
Pluvicto is used to treat adults with a certain type of prostate cancer that is metastatic castration resistant [mCRPC] which is prostate specific membrane antigen positive (PSMA-positive) and that has already been treated with androgen receptor pathway inhibition and taxane based chemotherapy or who are not medically suitable for taxanes.

Therapeutic group: radiopharmaceutical product for therapy only

How Pluvicto works
Pluvicto binds to a protein called PSMA that is found on the surface of prostate cancer cells. Upon binding, the radioactive component in Pluvicto, lutetium-177, emits radiation to the cancer cells. The radiation induces DNA damage which can lead to cell death.

Tests will be performed to see if PSMA protein is present on the surface of the cancer cells.

The use of Pluvicto involves exposure to radioactivity. Your doctor and the healthcare providers treating you have considered that the clinical benefit that you will obtain from the procedure with the radiopharmaceutical outweighs the risk due to radiation.

If you have any questions about how Pluvicto works or why this medicine has been prescribed for you, ask your doctor and the healthcare provider treating you.

2. Before using this medicine
Do not use this medicine if:

- You are sensitive (allergic) to the active ingredient lutetium (^{177}Lu) vipivotide tetraxetan or to any of the other ingredients in this medicine (see section 6).

Special warnings about using this medicine
Before starting treatment with Pluvicto, tell your doctor and your healthcare provider about all your medical conditions, including if:

- You have low levels of blood cell counts (hemoglobin, white blood cell count, absolute neutrophil count, platelet count).
- You have or have had tiredness, weakness, pale skin, shortness of breath, bleeding or bruising more easily than normal or difficulty to stop bleeding, or frequent infections with

signs such as fever, chills, sore throat or mouth ulcers (possible signs of myelosuppression).
- You have or have had kidney problems.
- You are sexually active and are planning to have children.
- You have or have had other types of cancer other than prostate cancer and its metastases. If you have been treated in the past with cancer treatment or radioactive radiation therapy. The use of Pluvicto contributes to exposure to long-term cumulative radioactive radiation. Long-term exposure to cumulative radiation is linked to an increased risk of cancer.

See section 4 'Side effects' and section 2 'Pregnancy, breast-feeding and fertility' and "Tests and follow-up".

Before administration of Pluvicto you should
- Drink plenty of water in order to urinate as often as possible during the first hours after administration to reduce bladder radiation.

Children and adolescents
The safety and effectiveness of Pluvicto in children and adolescents under the age of 18 years have not been established.

Tests and follow-up
Your doctor will perform blood tests and renal function tests before and during the treatment to evaluate your condition and to diagnose adverse reactions as soon as possible. Based on the results, the doctor can decide to withhold, reduce dose, or permanently discontinue Pluvicto if necessary.

Pregnancy, breast-feeding and fertility
Pregnancy
The safety and efficacy of Pluvicto have not been established in females. Pluvicto can cause fetal harm.
If your partner is of reproductive potential, you should use effective contraception during treatment with Pluvicto and for 14 weeks after the last dose.

Breast-feeding
There are no data on the presence of lutetium (^{177}Lu) vipivotide tetraxetan in breast milk or its effects on the breastfed child or on breast milk production.

Fertility
Pluvicto may cause temporary or permanent infertility in men.

Important information about some of this medicine's ingredients
Each vial contains up to 88.75 mg of sodium. equivalent to 4.4% of the recommended maximum daily intake of 2 g sodium for an adult.

3. How to use this medicine?
Always use this medicine according to your doctor's instructions. Check with your doctor or healthcare provider if you are not sure about your dose or about how to take this medicine. Only your doctor will determine your dose and how you should take this medicine. **Do not change the recommended dose.**

The recommended dosage is 7.4GBq (GBq is the radiation unit) Pluvicto will be administered intravenously every 6 weeks for up to 6 doses, or until disease progression, or unacceptable toxicity.
Pluvicto is a radioactive medicine. The use of this medicine will be by healthcare providers who are qualified and experience in the safe use and handling of radiopharmaceuticals and in a location suitable to radioactive treatment.

After administration of Pluvicto, you should

- Remain hydrated and urinate frequently in order to eliminate the product from your body.
- Limit close contact (less than 1 meter) with others in your household for 2 days or with children and pregnant women for 7 days**.**
- Avoid sexual activity for 7 days**.**
- Sleep in a separate bedroom from others in your household for 3 days, from children for 7 days, or from pregnant women for 15 days.

Your doctor and healthcare provider treating you will inform you if you need to take any special precautions after receiving this medicine. This may include special precautions for you or your caregiver with regard to toilet use, showering, laundry, waste disposal, emergency medical assistance, unplanned hospitalization or traveling. Contact your doctor if you have any questions.

If you have accidentally received a higher dose
An overdose is unlikely. However, if you have received an overdose, you will be treated to reduce the radioactive radiation dose by frequent micturition or by forced diuresis which will result in bladder voiding and additional supportive care measures as clinically indicated.

If you forget to take the medicine
If you missed an appointment, reach out to your doctor in order to schedule a new appointment as soon as possible.
The treatment should be continued as recommended by the doctor. Even if there is an improvement in your health, you should not stop taking the medicine without consulting your doctor.

If you have any further questions about using Pluvicto, consult your doctor or the healthcare provider treating you.

4. Side effects

Like with all medicines, using Pluvicto may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

Contact your doctor immediately if you experience any of the following side effects.
Pluvicto may cause serious side effects, including:

- **Myelosuppression.** Pluvicto may cause low red blood cell counts (anemia), low platelet counts (thrombocytopenia) and low white blood cell counts (leukopenia and neutropenia). Your doctor will perform blood tests to determine blood counts before and during treatment with Pluvicto.
- **Renal problems.** Pluvicto may cause sever renal problem which expressed in acute kidney injury and increased creatinine levels (passing urine less often than usual or passing much smaller amounts of urine than usual). You should drink a lot of water and urinate as often as

possible before and during treatment with Pluvicto. Your doctor will perform kidney function tests before and during treatment with Pluvicto.

Additional side effects
Additional side effects are listed below. If these side effects become severe or serious, tell your doctor right away.

Very common side effects include (affect one or more in 10 users):
- Fatigue
- Dry mouth
- Nausea
- Low red blood cells count (anemia)
- Decreased appetite
- Constipation
- Vomiting
- Diarrhea
- Low platelet counts (thrombocytopenia)
- Urinary tract infection
- Weight decreased
- Abdominal pain

Laboratory Abnormalities
Hematology
- Decreased immune system cells (lymphocytes, leukocytes, platelets and neutrophils), decreased hemoglobin

Biochemistry
- Decrease: calcium, sodium
- Increased: aspartate aminotransferase, creatinine, potassium and sodium

Common side effects (affect up to 1-10 in 100 people) include:
- Swelling in the hands, ankles or feet (peripheral edema)
- Acute kidney injury
- Dizziness
- Headache
- Change in sense of taste
- Pyrexia
- Dry eye
- Vertigo
- Decreased blood cell count (Pancytopenia)

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects. You can also use this link: https://sideeffects.health.gov.il
In addition, you can report to Novartis via the following e-mail address:
Safetydesk.israel@novartis.com

5. How to store the medicine?

You will not have to store this medicine. This medicine is stored under the responsibility of the specialist in appropriate premises at the medical center where you are staying. Storage of radiopharmaceuticals will be carried out in accordance with national regulations on radioactive materials.

The following information is intended for the specialist only.

- Keep this medicine out of the sight and reach of children.
- Do no freeze.
- Store in the original package to protect from ionizing radiation (lead shielding).
- Store Pluvicto in accordance with local laws on radioactive materials.
- Do not use Pluvicto after the expiration date and time which are stated on the label.
- Dispose of any unused medicinal product or waste material in accordance with local laws.

6. Additional information

In addition to the active ingredient, this medicine also contains:
sodium ascorbate, sodium acetate, gentisic acid, acetic acid, pentetic acid, water for injections
See section 2 under 'Important information about some of this medicine's ingredients'.

What the medicine looks like and contents of the pack:
Pluvicto is a clear, colorless to slightly yellow, free from visible particle solution supplied in a colorless glass vial closed with rubber stopper with aluminium seal.
Each vial contains solution volume in the range from 7.5 mL to 12.5 mL in order to provide a total of 7.4GBq of radioactivity at the date and time of administration.
The vial is in a lead shielded container.

Registration holder and importer and its address: Novartis Israel Ltd., P.O.B. 7126, Tel Aviv.
Revised in May 2024.

Registration number of the medicine in the National Drug Registry of the Ministry of Health:
172-79-37413-99