

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 healthcare providers.

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 your healthcare providers.

2. Before using this medicine

Do not use this medicine if:

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| <ul style="list-style-type: none">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). |
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Special warnings about using this medicine

Before starting treatment with Pluvicto, tell your doctor and your healthcare providers about all your medical conditions, including if:

- You have low levels of blood cell counts (red blood cells, hemoglobin, white blood cells, absolute neutrophil count, platelets).

- You have or have had tiredness, weakness, pale skin, shortness of breath, bleeding or bruising more easily than normal, difficulty stopping 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 efficacy of this medicine 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, change or discontinue the treatment with Pluvicto if necessary.

Pregnancy, breast-feeding and fertility

Pregnancy

This medicine is not intended for women. 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. Inform your doctor immediately in the event of pregnancy during this period.

Breast-feeding

There are no data on the presence of lutetium (¹⁷⁷Lu) 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.

Driving and using machines

It is unlikely that Pluvicto will affect your ability to drive or use machines.

Important information about some of this medicine's ingredients

Each vial of Pluvicto contains up to 88.75 mg of sodium. This is 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 providers 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 exceed 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 experienced in the safe use and handling of radiopharmaceuticals and in a location suitable for radioactive treatment.

After administration of Pluvicto, you should

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

Your doctor and healthcare providers treating you will provide you with clear instructions regarding special precautions you need to take 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 or healthcare providers 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 or healthcare providers as soon as possible in order to schedule a new appointment.

Adhere to the treatment as recommended by your 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 your healthcare providers.

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 severe renal problems which are 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 frequently 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 (effects that appear in more than one in ten users):

- Tiredness (fatigue)
- Dry mouth
- Nausea
- Low red blood cell count (anemia)
- Back pain
- Joint pain
- Decreased appetite
- Constipation
- Vomiting
- Diarrhea
- Urinary tract infection
- Abdominal pain
- Weight loss
- Bone pain
- Swollen hands, ankles or feet (peripheral edema)

Laboratory abnormalities

Hematology

- Decreased immune system cells (lymphocytes, neutrophils), decreased platelets, decreased hemoglobin

Biochemistry

- Decrease in kidney function index
- Decrease in calcium and sodium levels
- Increase in aspartate aminotransferase (AST), potassium and sodium levels

Common side effects (effects that appear in 1-10 in 100 users):

- Less frequent urination than normal or passing much smaller amounts of urine than usual (possible signs of kidney problems [acute kidney injury])
- Dizziness
- Change in sense of taste
- Headache
- Fever (pyrexia)
- Dry eyes
- Oral fungal infection
- Vertigo

- Gastroesophageal reflux
- Sores in the mouth (stomatitis)
- Tiredness, weakness, pale skin, shortness of breath, bleeding or bruising more easily than normal or bleeding for longer than normal, or frequent infections with signs such as fever, chills, sore throat or mouth ulcers (possible signs of low blood cell levels [pancytopenia])
- Dry skin
- Difficulty swallowing and/or heartburn (esophageal disorders)
- Esophagitis
- Bone marrow failure

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 being treated. 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 not 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 solution, free from visible particles, supplied in a colorless glass vial closed with rubber stopper with aluminum seal.
Each vial contains a solution volume that can range from 7.5 mL to 12.5 mL corresponding to a radioactivity of 7.4 GBq 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 April 2025

Registration number of the medicine in the National Drug Registry of the Ministry of Health:

172-79-37413-99

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