Package leaflet: Information for the user

VELETRI 0.5 mg, Powder for Solution for Infusion
VELETRI 1.5 mg, Powder for Solution for Infusion

epoprostenol

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What VELETRI is and what it is used for

VELETRI contains the active substance epoprostenol, which belongs to a group of medicines called prostaglandin, which stops blood from clotting and widens the blood vessels.

VELETRI is used to treat a lung condition called ‘pulmonary arterial hypertension’. This is where the pressure is high in the blood vessels in the lungs. VELETRI widens the blood vessels to lower the blood pressure in the lungs.

VELETRI is used to prevent blood clotting during kidney dialysis when heparin cannot be used.

2. What you need to know before you use VELETRI

Do not use VELETRI
- **if you are allergic** to VELETRI or any of the other ingredients of this medicine (listed in section 6).
- if you have **heart failure**.
- if you start to develop a build-up of fluid in your lungs causing breathlessness after starting this treatment.

If you think any of these apply to you, **don’t take VELETRI** until you have checked with your doctor.

Warnings and precautions
Talk to your doctor before using VELETRI.

Before you are given VELETRI your doctor needs to know:
- if you have any problems with **bleeding**.

Skin damage at the injection site

VELETRI is injected into a vein. It is important that the medicine does not leak out of the vein into the surrounding tissue. If it does, the skin could be damaged. The symptoms of this are:

- tenderness
- burning
- stinging
- swelling
- redness.

This may be followed by blistering and shedding of the skin. While you are being treated with VELETRI, it is important that you check the injection area.

Contact the hospital immediately for advice if the area becomes sore, painful or swollen or you notice any blistering or shedding.

Effect of VELETRI on blood pressure and heart rate

VELETRI can cause your heart to beat faster or slower. Also your blood pressure can become too low. While you are being treated with VELETRI, your heart rate and blood pressure will be checked. The symptoms of low blood pressure include **dizziness** and **fainting**.

Tell your doctor if you get these symptoms. Your dose may need to be reduced or your infusion stopped.

Children and adolescents

The safety and efficacy of VELETRI in children have not yet been established.

Other medicines and VELETRI

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription.

Some medicines may affect how VELETRI works, or make it more likely that you'll have side effects. VELETRI can also affect how some other medicines work if taken at the same time. These include:

- medicines used to **treat high blood pressure**
- medicines used to **prevent blood clots**
- medicines used to **dissolve blood clots**
- medicines to treat **inflammation or pain** (also called 'NSAIDs')
- digoxin (used to treat **heart disease**).

Tell your doctor or pharmacist if you are taking any of these.

Pregnancy and breastfeeding

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine as your symptoms could worsen during pregnancy.

It is not known whether the ingredients of VELETRI can pass into breast-milk. **You should stop breastfeeding your child during treatment with VELETRI**.

Driving and using machines

Your treatment may have an effect on the ability to drive or use machinery.

Don't drive or use machines unless you're feeling well.

VELETRI contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per vial, that is to say essentially ‘sodium-free’.

3. How to take VELETRI

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

VELETRI comes as a powder in a small glass vial. The powder needs to be dissolved before use.

VELETRI should not be given as a quick injection into your vein. It should always be given as an intravenous infusion.

Your doctor will decide how much VELETRI is right for you. The amount you are given is based on your body weight, and your type of illness. Your dose may be increased or decreased depending on how well you respond to treatment.

VELETRI is given by slow infusion (drip) into a vein.

Pulmonary arterial hypertension
Your first treatment will be given to you in a hospital. This is because your doctor needs to monitor you and find the best dose for you.

You will start with an infusion of VELETRI. The dose will be increased, until your symptoms are relieved, and any side effects are manageable. Once the best dose has been found, a permanent tube (line) will be fitted into one of your veins. You can then be treated using an infusion pump.

Kidney dialysis
You will be given an infusion of VELETRI for the duration of your dialysis.

Using VELETRI at home (only for treatment of Pulmonary Arterial Hypertension)
If you are treating yourself at home, your doctor or nurse will show you how to prepare and use VELETRI. They will also advise you how to stop treatment if necessary. Stopping VELETRI must be done gradually. It is very important that you follow **all** their instructions carefully.

VELETRI comes as a powder in a glass vial. Before use, the powder needs to be dissolved in a liquid. The liquid does not contain a preservative. If you have any of the liquid left over, it must be thrown away.

Looking after the injection line
If you have been fitted with a ‘line’ into a vein, it is **very important** to keep this area clean, otherwise you could get an infection. Your doctor or nurse will show you how to clean your ‘line’ and the area around it. It is very important that you follow all of their instructions carefully. It is also **very important** that you carefully follow all instructions regarding the change of the pump drug delivery reservoir (cassette) and that you always use an extension set with an in-line filter, as instructed by your doctor **to reduce the risk of an infection**.

If you take more VELETRI than you should
Seek urgent medical attention if you think you have used or been given too much VELETRI. Symptoms of overdose may include headache, nausea, vomiting, fast heart rate, warmth or tingling, or feeling like you might pass out (feeling faint/dizziness).

If you forget to take VELETRI
Do not take a double dose to make up for a forgotten dose.

If you stop taking VELETRI

Stopping VELETRI must be done gradually. If the treatment is stopped too quickly you may get serious side effects, including dizziness, feeling weak and breathing difficulties. If you have problems with the infusion pump or an injection line that stops or prevents treatment with VELETRI, **contact your doctor, nurse or hospital** immediately.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Very common side effects
These may affect **more than 1 in 10** people:
- headache
- jaw pain
- pain
- being sick (vomiting)
- feeling sick (nausea)
- diarrhoea
- redness of your face (flushing)

Common side effects
These may affect **up to 1 in 10** people:
- infection of the blood (*septicaemia*)
- heart beating faster
- slow heart beat
- low blood pressure
- bleeding at various sites and bruising more easily than normal, for example from the nose or gums
- stomach discomfort or pain
- chest pain
- joint pain
- feeling anxious, feeling nervous
- rash
- pain at the injection site

Common side effects that may show up in blood tests
- decrease in the number of blood platelets (cells that help the blood to clot)

Uncommon side effects
These may affect **up to 1 in 100** people:
- sweating
- dry mouth

Rare side effects
These may affect **up to 1 in 1 000** people:
- infection at the injection site

Very rare side effects
These may affect **up to 1 in 10 000** people:
- feeling of tightness around the chest
- feeling tired, weak
- feeling agitated
- pale skin
- redness at the injection site

- overactive thyroid gland
- blockage of the injection catheter

Other side effects
It is not known how many people are affected by:
- enlarged or overactive spleen
- build up of fluid in the lungs (pulmonary oedema)
- increase in sugar (glucose) in the blood
- ascites (build-up of fluid in the belly)
- too much pumping of blood from the heart leading to shortness of breath, fatigue, swelling of the legs and abdomen due to fluid build-up, persistent cough

Reporting of side effects

Tell your doctor or nurse immediately, as these may be signs of infection of the blood or low blood pressure or serious bleeding:
- You feel that your heart is beating faster, or you have chest pain or shortness of breath.
- You feel dizzy or feel faint, especially on standing.
- You have fevers or chills.
- You have more frequent or longer periods of bleeding.

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet.

You can also report side effects directly via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store VELETRI

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date, which is stated on the carton after EXP. The expiry date refers to the last day of that month.

This medicinal product (powder for solution for infusion) does not require any special temperature storage conditions. Do not freeze.

The reconstituted solution should be immediately further diluted to the final concentration (see section 7). For storage conditions after reconstitution and dilution of the medicinal product see section 7.

Do not use this medicine if you notice any particles in the reconstituted solution.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What VELETRI contains

VELETRI 0.5 mg, Powder for Solution for Infusion
- The active substance is epoprostenol (as epoprostenol sodium).

Each vial contains 0.531 mg epoprostenol sodium equivalent to 0.5 mg epoprostenol
One mL of reconstituted solution contains 0.1 mg epoprostenol (as epoprostenol sodium).

VELETRI 1.5 mg, Powder for Solution for Infusion

- The active substance is epoprostenol (as epoprostenol sodium).
  Each vial contains 1.593 mg epoprostenol sodium equivalent to 1.5 mg epoprostenol.
  One mL of reconstituted solution contains 0.3 mg epoprostenol (as epoprostenol sodium).

- The other ingredients are Sucrose, Arginine and Sodium Hydroxide (for pH adjustment).

What VELETRI looks like and contents of the pack

White to off-white powder in a clear glass vial with a rubber stopper and an aluminium flip-off cap.
Each pack contains one vial 0.5 mg powder.
Each pack contains one vial 1.5 mg powder.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder:
Janssen-Cilag Limited
50-100 Holmers Farm Way
High Wycombe
Buckinghamshire
HP12 4EG
UK

Manufacturer:
Janssen Pharmaceutica NV
Turnhoutseweg 30
B-2340 Beerse
Belgium

This medicinal product is authorised in the Member States of the EEA under the following names:

Veletri
Caripul®

This leaflet was last revised in April 2021.

The following information is intended for medical or healthcare professionals only:

7. INFORMATION FOR HEALTHCARE PROFESSIONALS

Renal Dialysis

There is 1 pack available for use in the treatment of renal dialysis:

- One vial containing sterile, freeze-dried VELETRI equivalent to 0.5 mg VELETRI supplied alone.

Reconstitution:
Withdraw 5 mL of either Sterile Water for Injection or Sodium Chloride 0.9% Injection diluent into a sterile syringe, inject the contents of the syringe into the vial containing VELETRI and shake gently until the

powder has dissolved. The reconstituted solution should be examined prior to further dilution. Its use is forbidden in the presence of discolouration or particles. Any unused reconstituted solution should be disposed of in accordance with local requirements.

Dilution:
The reconstituted solution should be immediately further diluted to the final concentration. Further dilution should be performed with the same diluent as used for reconstitution of the sterile, lyophilised powder.

Calculation of infusion rate:
Infusion rates may be calculated using the following formula:

$$\text{Infusion rate (mL/min)} = \frac{\text{Dosage (ng/kg/min)} \times \text{bodyweight (kg)}}{\text{Concentration of solution (ng/mL)}}$$

Infusion rate (mL/h) = Infusion rate (mL/min) × 60

Pulmonary Arterial Hypertension

There are 2 packs available for use in the treatment of pulmonary arterial hypertension, as follows:

- One vial containing sterile, freeze-dried VELETRI equivalent to 0.5 mg VELETRI supplied alone.
- One vial containing sterile, freeze-dried VELETRI equivalent to 1.5 mg VELETRI supplied alone.

Reconstitution:
Withdraw 5 mL of either Sterile Water for Injection or Sodium Chloride 0.9% Injection diluent into a sterile syringe, inject the contents of the syringe into the vial containing VELETRI and shake gently until the powder has dissolved. The reconstituted solution should be examined prior to further dilution. Its use is forbidden in the presence of discolouration or particles. Any unused reconstituted solution should be disposed of in accordance with local requirements.

Dilution:
The reconstituted solution should be immediately further diluted to the final concentration. Further dilution should be performed with the same diluent as used for reconstitution of the sterile, lyophilised powder. VELETRI when administered chronically, should be prepared in a drug delivery reservoir appropriate for the infusion pump.

Suitable ambulatory pumps to be used for the administration of VELETRI include:

- CADD-Legacy 1
- CADD-Legacy PLUS
- CADD-Solis VIP (variable infusion profile)

Manufactured by Smiths Medical.

Pump accessories found to be compatible with the administration of VELETRI include:

- CADD disposable Medication Cassette Reservoir 50 mL; 100 mL from Smiths Medical.
- CADD extension set with in-line 0.2 micron filter (CADD extension set with male luer, 0.2- micron air-eliminating filter, clamp, and integral anti-siphon valve with male luer) from Smiths Medical.

Only extension sets with an in-line 0.22 micron filter placed between the infusion pump and the catheter must be used. It is recommended to use filters with a hydrophilic polyethersulfone membrane. The extension set and the in-line filter must be changed at least every 48 hours.

The vial containing 0.5 mg epoprostenol must be used for the preparation of solutions with final concentrations below 15 000 ng/mL.

Table 1 provides examples for preparing frequently used concentrations of VELETRI solutions. Each vial is for single use only.

Table 1: Frequently used concentrations – Examples of Reconstitution and Dilution

Final Concentration (ng/mL)	Directions:
3 000 ng/mL	Dissolve contents of one 0.5 mg vial with 5 mL of either Sterile Water for Injection or Sodium Chloride 0.9% Injection. Withdraw 3 mL of the vial contents and add to a sufficient volume of the identical diluent to make a total of 100 mL.
5 000 ng/mL	Dissolve contents of one 0.5 mg vial with 5 mL of either Sterile Water for Injection, or Sodium Chloride 0.9% Injection. Withdraw entire vial contents and add to a sufficient volume of the identical diluent to make a total of 100 mL.
10 000 ng/mL	Dissolve contents of two 0.5 mg vials, each with 5 mL of either Sterile Water for Injection or Sodium Chloride 0.9% Injection. Withdraw entire vial contents and add to a sufficient volume of the identical diluent to make a total of 100 mL.
15 000 ng/mL*	Dissolve contents of one 1.5 mg vial with 5 mL of either Sterile Water for Injection or Sodium Chloride 0.9% Injection. Withdraw entire vial contents and add to a sufficient volume of the identical diluent to make a total of 100 mL.
30 000 ng/mL*	Dissolve contents of two 1.5 mg vials, each with 5 mL of either Sterile Water for Injection or Sodium Chloride 0.9% Injection. Withdraw entire vial contents and add to a sufficient volume of the identical diluent to make a total of 100 mL.
30 000 ng/mL*	Dissolve contents of one 1.5 mg vial, with 5 mL of either Sterile Water for Injection or Sodium Chloride 0.9% Injection. Withdraw entire vial contents and add to a sufficient volume of the identical diluent to make a total of 50 mL.

* Solutions with higher final concentrations may be necessary for patients who receive long-term administration of VELETRI.

VELETRI diluted to the final concentration in the drug delivery reservoir as directed can be administered immediately at room temperature (25°C) or, if stored, for up to 8 days at 2 to 8°C as per the conditions of use outlined in Table 2.

Table 2: Maximum duration of administration (hours) at room temperature (25°C) of fully diluted solutions stored in the drug delivery reservoir

Final concentration range	Immediate administration	If stored for up to 8 days at 2 to 8°C
≧3 000 ng/mL and <15 000 ng/mL	48 hours	24 hours
≧15 000 ng/mL	48 hours	48 hours

Do not expose the fully diluted solution to direct sunlight.

Special precautions for storage

This medicinal product does not require any special temperature storage conditions. Do not freeze.
The reconstituted solution should be immediately further diluted to the final concentration.
Reconstitution and dilution should be carried out immediately prior to use.
Freshly prepared epoprostenol diluted solutions for the treatment of pulmonary arterial hypertension can be administered immediately at 25°C, or stored in the drug delivery reservoir in order to protect from light for up to 8 days at between 2 to 8°C as per the conditions of use outlined in Table 2.