Package leaflet: Information for the user

Treprostinil 1 mg/ml Solution For Infusion
Treprostinil 2.5 mg/ml Solution For Infusion
Treprostinil 5 mg/ml Solution For Infusion
Treprostinil 10 mg/ml Solution For Infusion

Treprostinil

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.
- 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.

In this leaflet:

1. What Treprostinil is and what it is used for

What Treprostinil is
The active ingredient of Treprostinil Solution For Infusion is treprostinil.
Treprostinil belongs to a group of medicines which work in a similar way to the naturally occurring prostacyclins. Prostacyclins are hormone-like substances which reduce blood pressure by relaxing blood vessels, causing them to widen, which allows the blood to flow more easily. Prostacyclins can also have an influence in preventing blood from clotting.

What Treprostinil is used to treat
Treprostinil is used to treat idiopathic or heritable pulmonary arterial hypertension (PAH) in patients with moderate severity of the symptoms. Pulmonary arterial hypertension is a condition where your blood pressure is too high in the blood vessels between the heart and the lungs, causing shortness of breath, dizziness, tiredness, fainting, palpitations or abnormal heartbeat, dry cough, chest pain and swollen ankles or legs.

Treprostinil is initially administered as a continuous subcutaneous (under the skin) infusion. Some patients may become unable to tolerate this because of local site pain and swelling. Your doctor will decide whether Treprostinil can be administered by continuous intravenous infusion (directly into a vein with the insertion of a central venous tube (catheter) that is connected to an external pump or, depending on your condition, a pump surgical implanted under the skin of your belly (abdomen). Your doctor will determinate what is the best option for you.

How Treprostinil works
Treprostinil lowers blood pressure within the pulmonary artery, by improving blood flow and reducing the amount of work for the heart. Improved blood flow leads to an improved supply of oxygen to the body and reduced strain on the heart, causing it to function more effectively. Treprostinil improves the symptoms associated with PAH and the ability to exercise in patients who are limited in terms of activity.

2. Before you use Treprostinil

Do not use Treprostinil
- if you are **allergic** (hypersensitive) to treprostinil or any of the other ingredients of this medicine listed in section 6
- if you have been diagnosed with a disease called **"pulmonary veno-occlusive disease"**. This is a disease in which the blood vessels that carry blood through your lungs become swollen and clogged resulting in a higher pressure in the blood vessels between the heart and the lungs
- if you have severe **liver disease**
- if you have a **heart problem**, for example:
  - a **myocardial infarction** (heart attack) within the last six months
  - severe **changes in heart rate**
  - severe **coronary heart disease or unstable angina**
  - a **heart defect** has been diagnosed, such as a faulty heart valve that causes the heart to work poorly
  - any disease of the heart which is not being treated or not under close medical observation
- if you are at a specific **high risk of bleeding** – for example, active stomach ulcers, injuries, or other bleeding conditions
- if you have had a **stroke within the last 3 months**, or any other interruption of blood supply to the brain.

Warnings and precautions
Before you start taking Treprostinil, tell your doctor:
- if you suffer from any **liver disease**
- if you have been advised that you are **medically obese** (BMI greater than 30 kg/m^2)
- if you have **Human Immunodeficiency Virus** (HIV) infection
- if you have **high blood pressure** in your liver veins (portal hypertension)
- if you have a **birth defect in your heart** which affects the way your blood flows through it

During your treatment with Treprostinil, tell your doctor:
- if your blood pressure decreases (hypotension)
- if you experience a rapid increase in breathing difficulties or persistent cough (this can be related to congestion in the lungs or asthma or other condition), **consult your doctor immediately**
- if you have excessive bleeding as treprostinil may increase the risk, by preventing your blood from clotting
- if you develop a fever whilst receiving intravenous Treprostinil or the intravenous infusion site becomes red, swollen and / or painful to the touch, as this could be a sign of infection.

Other medicines and Treprostinil
Please tell your doctor if you are taking or have recently taken or might use any other medicines.

Please tell your doctor if you are taking:
- medicines used to treat **high blood pressure** (antihypertensive drugs or other vasodilators)
- drugs used to increase the rate of **urination** (diuretics) including furosemide
- medicines that stop **blood clotting** (anticoagulants) such as warfarin, heparin or nitric oxide based products
- any non-steroidal anti-inflammatory (**NSAID**) drugs (e.g. acetylsalicylic acid, ibuprofen)
- medicines that may increase or decrease the effect of Treprostinil (e.g. gemfibrozil, rifampicin, trimethoprim, deferasirox, phenytoin, carbamazepine, phenobarbital, St John's Wort) as your doctor may need to adjust your dose of Treprostinil.

Pregnancy and breastfeeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine.

Treprostinil is not recommended if you are pregnant, planning to become pregnant, or think that you might be pregnant, unless considered essential by your doctor. The safety of this medicine for use during pregnancy has not been established.

Treprostinil is not recommended for use in breastfeeding, unless considered essential by your doctor. You are advised to stop breastfeeding if Treprostinil is prescribed for you, because it is not known whether this medicine passes into breast milk.

Contraception is strongly recommended during treprostinil treatment.

Driving and using machines
Treprostinil may induce low blood pressure with dizziness or fainting. In such a case do not drive or operate machinery and ask your doctor for advice.

Treprostinil contains sodium
This medicine contains up to 78.4 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to 3.9 % of the recommended maximum daily dietary intake of sodium for an adult.

3. How to use Treprostinil
Always take this medicine exactly as your doctor has told you. Check with your doctor if you are not sure.

Treprostinil is administered as a continuous infusion, either:
- subcutaneously (under the skin) via a small tube (cannula) which is located in your abdomen or thigh;

or,
- intravenously via a tube (catheter) that is usually located in your neck, chest or groin.

For subcutaneous infusion the product should be administered undiluted.
For intravenous infusion the product should be diluted in accordance with the instructions of the prescriber and may only be diluted with sterile water for injection or 0.9% (w/v) of sodium chloride injection.

In both cases, Treprostinil is pushed through the tubing by a portable pump placed out of your body (external).

Before you leave the hospital or clinic, the doctor will tell you how to prepare Treprostinil and at what rate the pump should deliver your Treprostinil.

Flushing of the infusion line whilst connected may cause accidental overdose.

Alternatively, Treprostinil can be administered intravenously via an implantable infusion pump usually surgically inserted under the skin of your belly (abdomen). In this case, the pump and tubing are both fully inside your body (internal), and you will have to attend the hospital periodically (e.g. each 4 weeks) in order to get the internal reservoir refilled.

In any case, information on how to use the pump correctly and what to do if it stops working should also be given to you. The information should also tell you who to contact in an emergency.

Treprostinil is diluted only when administered with a continuous intravenous infusion.

For intravenous infusion with external portable pump: You must only dilute your Treprostinil solution with either Sterile Water for Injection or 0.9% Sodium Chloride Injection (as provided by your doctor).

For intravenous infusion with implantable infusion pump: You must attend the hospital periodically (e.g. each 4 weeks) where the health care provider must dilute your Treprostinil solution with 0.9% Sodium Chloride Injection and refill the internal reservoir.

Adult patients
Treprostinil is available as 1 mg/ml, 2.5 mg/ml, 5 mg/ml or 10 mg/ml solution for infusion. Your doctor will determine the infusion rate and dose appropriate for your condition.

Overweight patients
If you are overweight (weigh 30% or more than your ideal body weight) your doctor will determine the initial and subsequent doses based on your ideal body weight. Please also refer to Section 2, "Warnings and precautions".

Older people
Your doctor will determine the infusion rate and dose appropriate for your condition.

Children and adolescents
Limited data are available for children and adolescents.

Dosage adjustment
The infusion rate can be reduced or increased on an individual basis under **medical supervision only**.

The aim of adjusting the infusion rate is to establish an effective maintenance rate which improves symptoms of PAH while minimizing any undesirable effects.

If your symptoms increase or if you need complete rest, or are confined to your bed or chair, or if any physical activity brings on discomfort and your symptoms occur at rest, do not increase your dose without medical advice. Treprostinil may no longer be sufficient to treat your disease and another treatment may be required.

How can blood stream infections during treatment with intravenous Treprostinil be prevented?
As with any long-term intravenous treatment, there is a risk of getting blood stream infections. Your doctor will train you on how to avoid this.

If you use more Treprostinil than you should
If you accidentally overdose on Treprostinil, you may experience nausea, vomiting, diarrhoea, low blood pressure (dizziness, light-headedness or fainting), skin flushes and/or headaches.

If any of these effects become severe then you should contact your doctor or hospital immediately. Your doctor may reduce or discontinue the infusion until your symptoms have disappeared. Treprostinil will then be reintroduced at a dose level recommended by your doctor.

If you stop using Treprostinil
Always use Treprostinil as directed by your doctor or hospital specialist. Do not stop using Treprostinil unless your doctor has advised you to.

Abrupt withdrawal or sudden reductions in the dose of Treprostinil may cause the pulmonary arterial hypertension to return with the potential for rapid and severe deterioration in your condition.

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

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

Very common side effects (may affect more than 1 in 10 people)
- widening of blood vessels with flushing of the skin
- pain or tenderness around the infusion site
- skin discolouration or bruising around the infusion site
- headaches
- skin rashes
- nausea
- diarrhoea
- jaw pain

Common side effects (may affect up to 1 in 10 people
- dizziness
- vomiting
- light-headedness or fainting due to low blood pressure
- itching or redness of the skin
- swelling of feet, ankles, legs or fluid retention
- bleeding episodes such as nose bleeds, coughing up blood, blood in the urine, bleeding from the gums, blood in the faeces
- joint pain, muscle pain, pain in the legs and/or arms

Other possible side effects (frequency not known cannot be estimated from the available data)
- infection at the infusion site
- abscess at the infusion site
- a decrease of blood clotting cells (platelets) in the blood (thrombocytopenia)
- bleeding at the infusion site
- bone pain
- skin rashes with discolouration or raised bumps
- tissue infection under the skin (cellulitis)
- 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.

Additional side effects associated with the intravenous route of administration
- inflammation of the vein (thrombophlebitis)
- blood stream bacterial infection (bacteraemia)* (refer to Section 3)
- septicaemia (severe blood bacterial infection)

* life-threatening or fatal cases of blood stream bacterial infection have been reported

Reporting of side effects
If you get any side effects talk to your doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme website 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 Treprostinil
Keep out of the sight and reach of children.

This medicinal product does not require any special storage conditions.

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

Do not use Treprostinil if you notice any damage to the vial, discolouration or other signs of deterioration.

A Treprostinil vial must be used or discarded within 30 days after first opening.

During continuous subcutaneous infusion, a single reservoir (syringe) of undiluted Treprostinil must be used within 72 hours.

During continuous intravenous infusion using external portable pumps, a single reservoir (syringe) of diluted Treprostinil must be used within 24 hours.

During continuous intravenous infusion using implantable infusion pumps, Treprostinil introduced in the reservoir of the pump must be used within 39 days maximum (chemical, physical and microbiological in-use stability of Treprostinil solution administered by intravenous infusion has been demonstrated for up to 39 days at 40°C at the diluted concentrations as low as 0.5 mg/ml and as such 10 mg/ml in an implantable pump with titanium drug reservoir). The health care professional at hospital will tell you the duration of the interval before each next refill of the reservoir.

Any remaining diluted solution should be discarded.

For instructions on use please refer to Section 3. "How to use Treprostinil".

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 Treprostinil Solution contains
The active substance is treprostinil 1 mg/ml, 2.5 mg/ml, 5 mg/ml, 10 mg/ml.
The other ingredients in Treprostinil Solution are sodium citrate dehydrate (E331), sodium chloride, metacresol, water for injections and for pH adjustment: sodium hydroxide (E524) and hydrochloric acid (E507).

What Treprostinil Solution looks like and the contents of the pack
Treprostinil Solution is a clear colourless to slightly yellow solution, available in a 20 ml clear glass vial sealed with a rubber stopper and a colour coded flip-off seal:
- Treprostinil 1 mg/ml Solution For Infusion has a rubber yellow cap.
- Treprostinil, 2.5 mg/ml Solution For Infusion has a rubber blue cap.
- Treprostinil, 5 mg/ml Solution For Infusion has a rubber green cap.
- Treprostinil, 10 mg/ml Solution For Infusionhas a rubber red cap.

Each carton contains one vial.

Marketing Authorisation holder and manufacturer:
Dr. Reddy's Laboratories (UK) Ltd,
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Component:	Leaflet
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Date Modified:	21/Nov/23
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Previous DR No:	DR000520
Previous Material Number:	150090046
Commercial	CC1000068766
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DRUGS Code:	DRUGS
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