Treposuvi 1,0/2,5/5,0/10,0 mg/ml 10 ml 1 vial (UK) (TREP116-117-118-119)
Kwizda

PIL, page 1/2

24.08.2022: Neusatz (PG)
06.12.2022: change to Treposuvi (PG)
09.12.2022: one more change to Treposuvi (PG)
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Package leaflet: Information for the user

Treposuvi® 1 mg/ml solution for infusion
Treposuvi® 2.5 mg/ml solution for infusion
Treposuvi® 5 mg/ml solution for infusion
Treposuvi® 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, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:
1. What Treposuvi is and what it is used for
2. What you need to know before you use Treposuvi
3. How to use Treposuvi
4. Possible side effects
5. How to store Treposuvi
6. Contents of the pack and other information

1. What Treposuvi is and what it is used for

What Treposuvi is
The active ingredient of Treposuvi 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 Treposuvi is used for
Treposuvi 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.

Treposuvi 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 Treposuvi 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 surgically implanted under the skin of your belly (abdomen). Your doctor will decide what is the best option for you.

How Treposuvi works
Treposuvi 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. Treposuvi improves the symptoms associated with PAH and the ability to exercise in patients who are limited in terms of activity.

2. What you need to know before you use Treposuvi

Do not use Treposuvi:
- if you are allergic 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 heart attack (myocardial infarction) 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
Talk to your doctor before using Treposuvi:
- 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 HIV (Human Immunodeficiency Virus) 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 Treposuvi, 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 Treposuvi
Tell your doctor if you are using, have recently used 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 Treposuvi.

Pregnancy and breast-feeding
Treposuvi 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.

Contraception is strongly recommended during Treposuvi treatment.

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

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.

Driving and using machines
Treposuvi 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.

Treposuvi contains sodium
Please tell your doctor if you are on a controlled sodium diet. He/She will take into account that one vial of Treposuvi contains the following amounts of sodium:

Treposuvi 1 mg/ml solution for infusion:
This medicine contains 36.8 mg sodium (main component of cooking/table salt) in each 10 ml vial. This is equivalent to 1.8% of the recommended maximum daily dietary intake of sodium for an adult.

Treposuvi 2.5 mg/ml solution for infusion:
This medicine contains 37.3 mg sodium (main component of cooking/table salt) in each 10 ml vial. This is equivalent to 1.9% of the recommended maximum daily dietary intake of sodium for an adult.

Treposuvi 5 mg/ml solution for infusion:
This medicine contains 39.1 mg sodium (main component of cooking/table salt) in each 10 ml vial. This is equivalent to 2.0% of the recommended maximum daily dietary intake of sodium for an adult.

Treposuvi 10 mg/ml solution for infusion:
This medicine contains 37.4 mg sodium (main component of cooking/table salt) in each 10 ml vial. This is equivalent to 1.9% of the recommended maximum daily dietary intake of sodium for an adult.

3. How to use Treposuvi

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

Treposuvi 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.

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

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) or sodium chloride injection.

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

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

Alternatively, Treposuvi 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 or clinic 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.

Treposuvi 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 for Injection (as provided by your doctor).

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

Adult patients
Treposuvi 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".

Elderly patients
Your doctor will determine the infusion rate and dose appropriate for your condition.

Use in 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. This medicine may no longer be sufficient to treat your disease and another treatment may be required.

How can blood stream infections during treatment with intravenous Treposuvi 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 Treposuvi than you should
If you accidentally overdose on this medicine, 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. Treposuvi solution for infusion will then be reintroduced at a dose level recommended by your doctor.

If you stop using Treposuvi
Always use Treposuvi as directed by your doctor or hospital specialist. Do not stop using Treposuvi 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 (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 (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

Not known (frequency 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
- tissue infection under the skin (cellulitis)
- bone pain
- skin rashes with discolouration or raised bumps
- cardiac insufficiency with high volume of blood pumped by the heart per period of time, resulting in shortness of breath, fatigue, swelling of the legs and abdomen, and persistent coughing (high-output-heart failure)

Additional side effects associated with the intravenous route of administration (frequency cannot be estimated from the available data)
- 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 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 Treposuvi

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

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

Do not use this medicine if you notice any damage to the vial, discolouration or other signs of deterioration.
A Treposuvi vial must be used or discarded within 30 days after first opening.

Shelf life during continuous subcutaneous infusion
The chemical, physical and microbial in-use stability of a single container (syringe) of undiluted treprostinil administered via subcutaneous infusion could be established at 37°C for a period of 14 days. Other storage times and conditions after first opening fall to the responsibility of the user.

Shelf life during continuous intravenous infusion
The chemical, physical and microbial in-use stability of a single container (syringe) of diluted treprostinil solution administered via intravenous infusion could be established at 37°C for a period of 24 h in polyvinylchloride, polypropylene and glass (concentration as low as 0.004 mg/ml). To minimise the risk of blood stream infections the maximum period for use of diluted treprostinil should not exceed 24 h. Other storage times and conditions after first opening fall to the responsibility of the user.

During continuous intravenous infusion using implantable infusion pumps, diluted Treposuvi introduced in the reservoir of the pump must be used within 30 days maximum. The health care professional will tell you the duration of the interval until the next refill of the reservoir.

Any remaining diluted solution should be discarded.

For instructions on use please refer to section 3. "How to use Treposuvi".

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 Treposuvi contains
The active substance is treprostinil (1 mg/ml, 2.5 mg/ml, 5 mg/ml, 10 mg/ml).

Each ml contains 1 mg treprostinil, as treprostinil sodium.
Each ml contains 2.5 mg treprostinil, as treprostinil sodium.
Each ml contains 5 mg treprostinil, as treprostinil sodium.
Each ml contains 10 mg treprostinil, as treprostinil sodium.

The other ingredients are:
Sodium citrate, sodium chloride, sodium hydroxide, hydrochloric acid (for pH adjustment), metacresol and water for injections.

What Treposuvi looks like and the contents of the pack
Treposuvi is a clear colourless to slightly yellow solution free from visible particles, available in a 10 ml clear glass vial sealed with a rubber stopper and a colour coded aluminium cap:

- Treposuvi 1 mg/ml solution for infusion has a **yellow** rubber cap.
- Treposuvi 2.5 mg/ml solution for infusion has a **blue** rubber cap.
- Treposuvi 5 mg/ml solution for infusion has a **green** rubber cap.
- Treposuvi 10 mg/ml solution for infusion has a **magenta** rubber cap.

Each carton contains one vial.

Marketing Authorisation Holder and Manufacturer
AOP Orphan Pharmaceuticals GmbH
Leopold-Ungar-Platz 2
1190 Vienna, Austria

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