Package leaflet: Information for the user

Trepulmix 1 mg/ml solution for infusion
Trepulmix 2.5 mg/ml solution for infusion
Trepulmix 5 mg/ml solution for infusion
Trepulmix 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. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Trepulmix is and what it is used for

What Trepulmix is
The active ingredient of Trepulmix 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 Trepulmix is used to treat
Trepulmix is used for the treatment of adult patients with inoperable chronic thromboembolic pulmonary hypertension (CTEPH), or persistent or recurrent CTEPH after surgical treatment (severity classified WHO Functional Class (FC) III or IV), to improve exercise capacity and symptoms of the disease. Chronic thromboembolic pulmonary 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.

How Trepulmix works
Trepulmix 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 increased supply of oxygen to the body and reduced strain on the heart, causing it to function more effectively. Trepulmix improves the symptoms associated with CTEPH and the ability to exercise in patients who are limited in terms of activity.

2. What you need to know before you use Trepulmix

Do not use Trepulmix:
- 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 Trepulmix if you:
- suffer from any liver disease
- suffer from kidney disease
- have been advised that you are medically obese (BMI greater than 30 kg/m^2)
- are on a low sodium diet

During your treatment with Trepulmix, 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

Children and adolescents
Trepulmix must not be used in children and adolescents.

Other medicines and Trepulmix
Tell your doctor if you are taking/using, have recently taken/used or might take/use any other medicines. Please tell your doctor if you are taking:
- medicines used to treat **high blood pressure** (antihypertensive medicines or other vasodilators)
- medicines 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**) medicines (e.g. acetylsalicylic acid, ibuprofen)
- medicines which may enhance or weaken the effects of Trepulmix (e.g. gemfibrozil, rifampicin, trimethoprim, deferasirox, phenytoin, carbamazepine, phenobarbital, St. John's wort.), as your doctor may need to adjust the dosage of Trepulmix.

Pregnancy and breast-feeding
Trepulmix 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 Trepulmix treatment.

Trepulmix is not recommended for use in breast-feeding, unless considered essential by your doctor. You are advised to stop breast-feeding if Trepulmix 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
Trepulmix 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.

Trepulmix contains sodium
Please tell your doctor if you are on a controlled sodium diet. They will take into account:
Trepulmix 1 mg/ml solution for infusion
This medicine contains 36.8 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to 1.8% of the recommended maximum daily dietary intake of sodium for an adult.

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

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

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

3. How to use Trepulmix

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

Trepulmix is administered undiluted as a continuous subcutaneous infusion (under the skin) via a small tube (cannula) which is located in your abdomen or thigh;

Trepulmix is pushed through the tubing by a portable pump.

Before you leave the hospital or clinic, your doctor will tell you how to prepare Trepulmix and at what rate the pump should deliver your treprostinil. 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.
Flushing of the infusion line whilst connected may cause accidental overdose.

Adult patients
Trepulmix 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.

Elderly patients
No special dose adjustments are necessary for these patients.

Patients with liver or kidney disease
Your doctor will determine the infusion rate and dose appropriate for your condition.

Infusion rate
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 CTEPH while minimising 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. Trepulmix may no longer be sufficient to treat your disease and another treatment may be required.

If you use more Trepulmix than you should
If you accidentally overdose Trepulmix, 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 you should contact your doctor or hospital immediately. Your doctor may reduce or discontinue the infusion until your symptoms have disappeared. Trepulmix solution for infusion will then be reintroduced at a dose level recommended by your doctor.

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

Abrupt withdrawal or sudden reductions in the dose of Trepulmix 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 10people)
- widening of blood vessels
- pain around the infusion site
- reaction around the infusion site
- bleeding or bruising around the infusion site
- headaches
- nausea
- diarrhoea
- jaw pain

Common (may affect up to 1 in 10 people)
- dizziness
- light-headedness or fainting due to low blood pressure
- skin rashes
- muscle pain (myalgia)
- joint pain (arthralgia)
- swelling of feet, ankles, legs or fluid retention
- hot flush
- pain in arms and / or legs

Uncommon (may affect up to 1 in 100 people)
- swollen eyelids (eyelid oedema)
- indigestions

- vomiting
- skin itches
- exanthema
- back pain
- decreased appetite
- tiredness

Other possible side effects observed in pulmonary arterial hypertension (PAH) patients:
- bleeding episodes such as: as nose bleeds, coughing up blood, blood in the urine, bleeding from the gums, blood in the faeces

Other possible side effects observed during clinical practice:
- infection at the infusion site
- abscess at the infusion site
- a decrease of blood clotting cells (platelets) in the blood (thrombocytopenia)
- bone pain
- skin rashes with discolouration or raised bumps
- tissue infection under the skin (cellulitis)

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 Trepulmix

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.

This medicinal product does not require any special storage conditions.

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

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

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

Do not throw away any medicines via waste water 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 Trepulmix contains
The active substance is treprostinil.

Trepulmix 1 mg/ml solution for infusion
Each ml of solution contains 1 mg treprostinil (as sodium salt).
Each 10 ml vial of solution contains 10 mg treprostinil (as sodium salt).

Trepulmix 2.5 mg/ml solution for infusion
Each ml of solution contains 2.5 mg treprostinil (as sodium salt)
Each 10 ml vial of solution contains 25 mg treprostinil (as sodium salt).

Trepulmix 5 mg/ml solution for infusion
Each ml of solution contains 5 mg treprostinil (as sodium salt).
Each 10 ml vial of solution contains 50 mg treprostinil (as sodium salt).

Trepulmix 10 mg/ml solution for infusion
Each ml of solution contains 10 mg treprostinil (as sodium salt).
Each 10 ml vial of solution contains 100 mg treprostinil (as sodium salt).

The other ingredients are:
Sodium citrate, sodium chloride, sodium hydroxide, hydrochloric acid, metacresol and water for injections. See section 2, "Trepulmix contains sodium".

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

Trepulmix 1 mg/ml solution for infusion
Trepulmix 1 mg/ml solution for infusion has a yellow rubber cap.

Trepulmix 2.5 mg/ml solution for infusion
Trepulmix 2.5 mg/ml solution for infusion has a blue rubber cap.

Trepulmix 5 mg/ml solution for infusion
Trepulmix 5 mg/ml solution for infusion has a green rubber cap.

Trepulmix 10 mg/ml solution for infusion
Trepulmix 10 mg/ml solution for infusion has a red rubber cap.

Each carton contains one vial.

Not all pack sizes may be marketed.

Marketing Authorisation holder

SciPharm Sàrl
7, Fausermillen
L-6689 Mertert
Luxembourg

Manufacturer

AOP Orphan Pharmaceuticals GmbH
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