Package leaflet: Information for the user

Tracleer 125 mg film-coated tablets
bosentan

Read all of this leaflet carefully before you start taking 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, please ask your doctor or pharmacist.
- 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.

What is in this leaflet

1. What Tracleer is and what it is used for

Tracleer tablets contain bosentan, which blocks a naturally occurring hormone called endothelin-1 (ET-1), which causes blood vessels to narrow. Tracleer therefore causes blood vessels to expand and belongs to the class of medicines called "endothelin receptor antagonists".

Tracleer is used to treat:
- **Pulmonary arterial hypertension** (PAH): PAH is a disease of severe narrowing of the blood vessels in the lungs resulting in high blood pressure in the blood vessels (the pulmonary arteries) that carry blood from the heart to the lungs. This pressure reduces the amount of oxygen that can get into the blood in the lungs, making physical activity more difficult. Tracleer widens the pulmonary arteries, making it easier for the heart to pump blood through them. This lowers the blood pressure and relieves the symptoms.

Tracleer is used to treat patients with class III PAH to improve exercise capacity (the ability to carry out physical activity) and symptoms. The 'class' reflects the seriousness of the disease: 'class III' involves marked limitation of physical activity. Some improvements have also been shown in patients with class II PAH. 'Class II' involves slight limitation of physical activity. The PAH for which Tracleer is indicated can be:
- primary (with no identified cause or familial);
- caused by scleroderma (also called systemic sclerosis, a disease where there is abnormal growth of the connective tissue that supports the skin and other organs);
- caused by congenital (inborn) heart defects with shunts (abnormal passageways) causing abnormal flow of blood through the heart and lungs.

- **Digital ulcers**: (sores on the fingers and toes) in adult patients with a condition called scleroderma. Tracleer reduces the number of new finger and toe ulcers that appear.

2. What you need to know before you take Tracleer

Do not take Tracleer
- **if you are allergic to bosentan** or any of the other ingredients of this medicine (listed in section 6)
- **if you have liver problems** (ask your doctor)
- **if you are pregnant, or could get pregnant** because you are not using reliable contraceptive methods. Please read the information under "Contraceptives" and "Other medicines and Tracleer"
- **if you are taking cyclosporine A** (a medicine used after a transplant or to treat psoriasis)

If any of these apply to you, tell your doctor.

Warnings and precautions
Tests your doctor will do before treatment
- a blood test to check your liver function
- a blood test to check for anaemia (low haemoglobin)
- a pregnancy test if you are a woman of childbearing potential

Some patients taking Tracleer have been found to have abnormal liver function tests and anaemia (low haemoglobin).

Tests your doctor will do during treatment
During treatment with Tracleer, your doctor will arrange for regular blood tests to check for changes in your liver function and haemoglobin level.

For all these tests please refer also to the Patient Alert Card (inside your pack of Tracleer tablets). It is important that you have these regular blood tests as long as you are taking Tracleer. We suggest you write the date of your most recent test and also of your next test (ask your doctor for the date) on the Patient Alert Card, to help you remember when your next test is due.

Blood tests for liver function
These will be done every month for the duration of treatment with Tracleer. After an increase in dose an additional test will be done after 2 weeks.

Blood tests for anaemia
These will be done every month for the first 4 months of treatment, then every 3 months after that, as patients taking Tracleer may get anaemia.

If these results are abnormal, your doctor may decide to reduce your dose or stop treatment with Tracleer and to perform further tests to investigate the cause.

Children and adolescents
Tracleer is not recommended in paediatric patients with systemic sclerosis and ongoing digital ulcer disease. Please see also section 3. How to take Tracleer.

Other medicines and Tracleer
Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. It is especially important to tell your doctor if you are taking:
- cyclosporine A (a medicine used after transplants and to treat psoriasis), which must not be used together with Tracleer.
- sirolimus or tacrolimus, which are medicines used after transplants, as these are not recommended to be used together with Tracleer.

- glibenclamide (a diabetes medicine), rifampicin (a tuberculosis medicine), fluconazole (a medicine against fungal infections), ketoconazole (a medicine used to treat Cushing's syndrome), or nevirapine (an HIV medicine), as these medicines are not recommended to be used together with Tracleer.
- other medicines for the treatment of HIV infection, which may require special monitoring if used together with Tracleer.
- hormonal contraceptives, which are not effective as the sole method of contraception when you take Tracleer. Inside your pack of Tracleer tablets you will find a Patient Alert Card which you should read carefully. Your doctor and/or gynaecologist will establish the contraception which is appropriate for you.
- other medications for the treatment of pulmonary hypertension: sildenafil and tadalafil;
- warfarin (an anticoagulant agent);
- simvastatin (used to treat hypercholesterolaemia).

Driving and using machines
Tracleer has no or negligible influence on the ability to drive and use machines. However, Tracleer can induce hypotension (decrease of your blood pressure) which can make you feel dizzy, affect your vision and affect your ability to drive and use machines. Therefore, if you feel dizzy or that your vision is blurred while taking Tracleer, do not drive or operate any tools or machines.

Women of childbearing age
Do NOT take Tracleer if you are pregnant or planning to become pregnant.

Pregnancy tests
Tracleer may harm unborn babies conceived before starting or during treatment. If you are a woman who could become pregnant, your doctor will ask you to take a pregnancy test before you start taking Tracleer, and regularly while you are taking Tracleer.

Contraceptives
If it is possible that you could become pregnant, use a reliable form of birth control (contraception) while you are taking Tracleer. Your doctor or gynaecologist will advise you about reliable contraceptive methods while taking Tracleer. Because Tracleer may make hormonal contraception (e.g., oral, injection, implant, or skin patches) ineffective, this method on its own is not reliable. Therefore, if you use hormonal contraceptives you must also use a barrier method (e.g., female condom, diaphragm, contraceptive sponge, or your partner must also use a condom). Inside your pack of Tracleer tablets you will find a Patient Alert Card. You should complete this card and take it to your doctor at your next visit so that your doctor or gynaecologist can assess whether you need additional or alternative reliable contraceptive methods. Monthly pregnancy tests are recommended while you are taking Tracleer and are of childbearing age.

Tell your doctor immediately if you become pregnant while you are taking Tracleer, or plan to become pregnant in the near future.

Breast-feeding
Tell your doctor immediately **if you are breast-feeding**. You are advised to stop breast-feeding if Tracleer is prescribed for you, because it is not known whether this medicine passes into breast milk.

Fertility
If you are a man taking Tracleer, it is possible that this medicine may lower your sperm count. It cannot be excluded that this may affect your ability to father a child. Talk to your doctor if you have any questions or concerns about this.

Tracleer contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

3. How to take Tracleer

Treatment with Tracleer should only be started and monitored by a doctor who has experience in the treatment of PAH or systemic sclerosis. Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

Tracleer with food and drink
Tracleer can be taken with or without food.

Recommended dose

Adult
The treatment in adults is usually started for the first 4 weeks with 62.5 mg twice daily (morning and evening), from then your doctor will usually advise you to take a 125 mg tablet twice daily, depending on how you react to Tracleer.

Children and adolescents
The dose recommendation in children is only for PAH. For children aged 1 year and older, treatment with Tracleer is usually started with 2 mg per kg bodyweight twice daily (morning and evening). Your doctor will advise you on your dosing.

Please note that Tracleer is also available as a dispersible 32 mg tablet formulation, which may make correct dosing easier for children and patients with low body weight or difficulties to swallow film-coated tablets.

If you have the impression that the effect of Tracleer is too strong or too weak, talk to your doctor in order to find out whether your dose needs to be changed.

How to take Tracleer
Tablets should be taken (morning and evening), swallowed with water. The tablets can be taken with or without food.

If you take more Tracleer than you should
If you take more tablets than you have been told to take, contact your doctor immediately.

If you forget to take Tracleer
If you forget to take Tracleer, take a dose as soon as you remember, then continue to take your tablets at the usual times. Do not take a double dose to make up for forgotten tablets.

If you stop taking Tracleer
Suddenly stopping your treatment with Tracleer may lead to your symptoms getting worse. Do not stop taking Tracleer unless your doctor tells you to. Your doctor may tell you to reduce the dose over a few days before stopping completely.

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

4. Possible side effects

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

The most serious side effects with Tracleer are
- Abnormal liver function which may affect more than 1 in 10 people
- Anaemia (low blood value) which may affect up to 1 in 10 people. Anaemia may occasionally require blood transfusion

Your liver and blood values will be monitored during treatment with Tracleer (see section 2). It is important that you have these tests as ordered by your doctor.

Signs that your liver may not be working properly include:
- nausea (urge to vomit)
- vomiting
- fever (high temperature)
- pain in your stomach (abdomen)
- jaundice (yellowing of your skin or the whites of your eyes)
- dark-coloured urine
- itching of your skin
- lethargy or fatigue (unusual tiredness or exhaustion)
- flu-like syndrome (joint and muscle pain with fever)

If you notice any of these signs **tell your doctor immediately**.

Other side effects

Very common (may affect **more than one in 10** people):

- Headache
- Oedema (swelling of the legs and ankles or other signs of fluid retention)

Common (may affect **up to one in 10** people):

- Flushed appearance or redness of skin
- Hypersensitivity reactions (including skin inflammation, itching and rash)
- Gastrooesophageal reflux disease (acid reflux)
- Diarrhoea
- Syncope (fainting)
- Palpitations (fast or irregular heart beats)
- Low blood pressure
- Nasal congestion

Uncommon (may affect **up to one in 100** people):

- Thrombocytopenia (low number of blood platelets)
- Neutropenia/leukopenia (low number of white blood cells)
- Elevated liver function tests with hepatitis (inflammation of the liver) including possible exacerbation of underlying hepatitis and/or jaundice (yellowing of the skin or the whites of the eyes)

Rare (may affect **up to one in 1 000** people):

- Anaphylaxis (general allergic reaction), angioedema (swelling, most commonly around the eyes, lips, tongue or throat)
- Cirrhosis (scarring) of the liver, liver failure (serious disturbance of liver function)

Blurred vision have also been reported at an unknown frequency (frequency cannot be estimated from the available data).

Side effects in children and adolescents
The side effects that have been reported in children treated with Tracleer are the same as those in adults.

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

In the **United Kingdom (Northern Ireland)**, 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.

In **Ireland**, you can also report side effects directly via:
HPRA Pharmacovigilance
Website: www.hpra.ie

In **Malta**, report side effects to: ADR Reporting
Website: www.medicinesauthority.gov.mt/adrportal

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

5. How to store Tracleer

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 and on the blister after "EXP".
For white high-density polyethylene bottles, use within 30 days after the first opening.

For PVC/PE/PVDC/aluminium-blisters:
Do not store above 30°C.

For white high-density polyethylene bottles:
This medicinal product does not require any special storage conditions.

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

6. Contents of the pack and other information

What Tracleer contains

- **Tracleer 125 mg film-coated tablets:** The active substance is bosentan as monohydrate. Each tablet contains 125 mg of bosentan (as monohydrate).
- **The other ingredients** in the tablet core are maize starch, pregelatinised starch, sodium starch glycolate (Type A), povidone, glycerol dibehenate and magnesium stearate. **The film-coat** contains hypromellose, glycerol triacetate, talc, titanium dioxide (E171), iron oxide yellow (E172), iron oxide red (E172) and ethylcellulose.

What Tracleer looks like and contents of the pack

Tracleer 125 mg film-coated tablets are orange-white, oval film-coated tablets with "125" on one side.

PVC/PE/PVDC/aluminium-blisters containing **14 film-coated tablets.** Cartons contain 56 or 112 film-coated tablets (Tracleer 125 mg film-coated tablets).

White high-density polyethylene bottles with a silica gel desiccant containing 56 film-coated tablets. Cartons contain 56 film-coated tablets (Tracleer 125 mg film-coated tablets).
Do not swallow the desiccant.

Not all pack sizes may be marketed.

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Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu/.