



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

EMA/551408/2018  
EMA/H/C/000401

## Tracleer (*bosentan*)

An overview of Tracleer and why it is authorised in the EU

### What is Tracleer and what is it used for?

Tracleer is used to treat patients with class III pulmonary arterial hypertension (PAH) to improve exercise capacity (the ability to carry out physical activity) and reduce symptoms. PAH is abnormally high blood pressure in the arteries of the lungs. The 'class' reflects the severity of the disease: 'class III' PAH involves marked limitation of physical activity. The PAH can be:

- primary (with no identified cause or inherited);
- 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.

Some improvement with Tracleer can also occur in patients with class II PAH. 'Class II' involves slight limitation of physical activity.

Tracleer can also be used in adults with systemic sclerosis in whom poor blood circulation caused by the disease has led to the development of digital ulcers (sores on the fingers and toes). Tracleer is given to reduce the number of new digital ulcers.

Tracleer contains the active substance bosentan.

### How is Tracleer used?

Tracleer can only be obtained with a prescription and treatment should only be started and monitored by a doctor who has experience in the treatment of PAH or systemic sclerosis.

It is available as film-coated tablets (62.5 mg; 125 mg) and as dispersible tablets (32 mg).

Tracleer is taken morning and evening. In adults, it should be started at a dose of 62.5 mg twice a day for four weeks and then increased to the usual dose of 125 mg twice a day. In children with PAH aged

**Official address** Domenico Scarlattilaan 6 • 1083 HS Amsterdam • The Netherlands

**Address for visits and deliveries** Refer to [www.ema.europa.eu/how-to-find-us](http://www.ema.europa.eu/how-to-find-us)

**Send us a question** Go to [www.ema.europa.eu/contact](http://www.ema.europa.eu/contact) **Telephone** +31 (0)88 781 6000

An agency of the European Union



1 year and older, the recommended starting and maintenance dose is 2 mg per kilogram body weight twice a day.

Patients should take the film-coated tablets with water. The dispersible tablets are only for use in patients who cannot swallow the film-coated tablets. The dispersible tablets should be mixed with a little water on a spoon before being taken. For more information about using Tracleer, see the package leaflet or contact your doctor or pharmacist.

## **How does Tracleer work?**

The active substance in Tracleer, bosentan, blocks a naturally occurring hormone called endothelin-1 (ET-1), which causes blood vessels to narrow. Tracleer therefore prevents blood vessels from narrowing.

In PAH, severe narrowing of the blood vessels in the lungs increases blood pressure and reduces the amount of blood entering the lungs. By expanding these blood vessels, pressure is reduced and symptoms are improved.

In patients with systemic sclerosis and digital ulcer disease, there is narrowing of the blood vessels of the fingers and toes leading to ulcers. Bosentan improves blood circulation and thereby, prevents the development of new digital ulcers.

## **What benefits of Tracleer have been shown in studies?**

### **Treatment of PAH**

In PAH, Tracleer film-coated tablets added to patient's current therapy was more effective than placebo (a dummy treatment) in improving the distance patients could walk in 6 minutes (a way of measuring exercise capacity) after 16 weeks of treatment.

This is based on two studies in a total of 245 adults with class III or IV disease that was either primary or caused by scleroderma. In the larger study patients were able to walk 44 metres further. Similar results were seen in a study in 54 adults with class III PAH that was associated with congenital heart defects. There were too few patients with class IV disease to support the use of the medicine in this group.

In a study in 185 patients with class II disease the distance the patients could walk over 6 minutes was similar in the Tracleer and placebo groups. However, Tracleer decreased the resistance to blood flow by 23%, indicating a widening of the blood vessels, compared with placebo after 6 months of treatment.

Improvements were also seen in a study of 19 children aged between 3 and 15 years taking the film-coated tablets.

Two additional studies looked at the effects of Tracleer dispersible tablets in children: the first study included 36 children with PAH aged between 2 and 11 years, while the second study included 64 children with PAH aged from 3 months up to 11 years. The PAH seemed to remain stable in almost all of the children during the 12 or 24 weeks of treatment.

### **Treatment of systemic sclerosis with digital ulcers**

Tracleer was more effective than placebo at reducing the development of new digital ulcers based on two studies in a total of 312 adults. In the first study, patients taking Tracleer had an average of 1.4 new digital ulcers after 16 weeks, compared with 2.7 in the patients taking placebo. Similar results

were seen in the second study after 24 weeks. The second study which also looked at the effect of Tracleer on digital ulcer healing in 190 patients did not find any effect.

### **What are the risks associated with Tracleer?**

The most common side effects with Tracleer (which may affect more than 1 in 10 people) are headache, fluid retention, anaemia (low levels of haemoglobin, the protein in red blood cells that carries oxygen around the body) and abnormal results of blood tests to check the liver. For the full list of side effects Tracleer, see the package leaflet.

Tracleer must not be used in patients who have certain liver problems, who are pregnant or could become pregnant and who are not using reliable contraceptive methods or who are taking ciclosporin (a medicine that acts on the immune system). For the full list of restrictions, see the package leaflet.

### **Why has Tracleer been approved?**

The European Medicines Agency decided that Tracleer's benefits are greater than its risks and it can be authorised for use in the EU.

### **What measures are being taken to ensure the safe and effective use of Tracleer?**

The company that makes Tracleer will provide a patient alert card to remind patients of the need for regular blood tests for liver function and to use effective contraception to avoid pregnancy.

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of Tracleer have also been included in the summary of product characteristics and the package leaflet.

As for all medicines, data on the use of Tracleer are continuously monitored. Side effects reported with Tracleer are carefully evaluated and any necessary action taken to protect patients.

### **Other information about Tracleer**

Tracleer received a marketing authorisation valid throughout the EU on 15 May 2002.

Further information on Tracleer can be found on the Agency's website: [ema.europa.eu/Find medicine/Human medicines/European public assessment reports](https://ema.europa.eu/Find/medicine/Human_medicines/European_public_assessment_reports).

This medicine overview was last updated in 10-2019.