EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Tracleer

bosentan

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AUTHORISED
This medicine is authorised for use in the European Union.

Overview

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

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 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.

Tracleer : EPAR - Medicine overview (PDF/142.41 KB)

First published: 05/08/2009
Last updated: 03/12/2019
EMA/551408/2018

Available languages (22)

Tracleer : EPAR - Risk-management-plan summary (PDF/59.31 KB)

First published: 26/08/2019

More detail is available in the summary of product characteristics

This EPAR was last updated on 29/10/2021

Authorisation details

Product details

Name	Tracleer
Agency product number	EMEA/H/C/000401
Active substance	bosentan (as monohydrate)
International non-proprietary name (INN) or common name	bosentan
Therapeutic area (MeSH)	• Scleroderma, Systemic • Hypertension, Pulmonary
Anatomical therapeutic chemical (ATC) code	C02KX01

Publication details

Publication details	
Marketing-authorisation holder	Janssen-Cilag International N.V.
Revision	41
Date of issue of marketing authorisation valid throughout the European Union	14/05/2002
Contact address	Janssen-Cilag International N.V. Turnhoutseweg 30 BE-2340 Beerse Belgium

Product information

28/01/2021 Tracleer - EMEA/H/C/000401 - P46-87

Tracleer : EPAR - Product Information (PDF/481.64 KB)

First published: 05/08/2009
Last updated: 21/07/2021

Available languages (24)

Contents

- Annex I - Summary of product characteristics
- Annex IIA - Manufacturing-authorisation holder responsible for batch release
- Annex IIB - Conditions of the marketing authorisation
- Annex IIIA - Labelling
- Annex IIIB - Package leaflet

Please note that the size of the above document can exceed 50 pages.

You are therefore advised to be selective about which sections or pages you wish to print.

Tracleer : EPAR - All Authorised presentations (PDF/28.86 KB)

First published: 05/08/2009
Last updated: 20/10/2016

Available languages (24)

Tracleer : EPAR - Conditions imposed on member states for safe and effective use - Annex IV (PDF/24.07 KB)

First published: 23/01/2008
Last updated: 23/01/2008

Available languages (21)

Pharmacotherapeutic group

Antihypertensives

Therapeutic indication

Treatment of pulmonary arterial hypertension (PAH) to improve exercise capacity and symptoms in patients with WHO functional class III.Efficacy has been shown in:

- Primary (idiopathic and familial) PAH;
- PAH secondary to scleroderma without significant interstitial pulmonary disease;
- PAH associated with congenital systemic-to-pulmonary shunts and Eisenmenger's physiology.

Some improvements have also been shown in patients with PAH WHO functional class II.

Tracleer is also indicated to reduce the number of new digital ulcers in patients with systemic sclerosis and ongoing digital ulcer disease.

Assessment history

Changes since initial authorisation of medicine

Tracleer : EPAR - Procedural steps taken and scientific information after authorisation (PDF/288.78 KB)

First published: 05/08/2009
Last updated: 21/07/2021

Tracleer-H-C-000401-P46-087 : EPAR - Assessment Report - Variation (PDF/281.03 KB)

Adopted

First published: 29/10/2021
EMA/3311/2021

EMA/3311/2021

Tracleer-H-C-PSUSA-00000425-201611 : EPAR - Scientific conclusions and grounds for the variation to the terms of the marketing authorisation(s) (PDF/66.27 KB)

First published: 04/10/2017
Last updated: 04/10/2017
EMA/CHMP/542107/2017

Tracleer-H-C-PSUSA-00000425-201511 : EPAR - Scientific conclusions and grounds for the variation to the terms of the marketing authorisation(s) (PDF/64.63 KB)

First published: 16/12/2016
Last updated: 16/12/2016
EMA/862750/2016

Tracleer-H-C-401-P46 : EPAR - Assessment Report (PDF/477.37 KB)

Adopted

First published: 05/10/2015
Last updated: 05/10/2015
EMA/554571/2015

Tracleer-H-C-PSUSA-00000425-201411 : EPAR - Scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation (PDF/69.27 KB)

First published: 21/09/2015
Last updated: 21/09/2015
EMA/CHMP/594929/2015

Tracleer-H-C-401-P46-0081 : EPAR - Assessment Report - Variation (PDF/1.73 MB)

Adopted

First published: 15/07/2015
Last updated: 15/07/2015
EMA/CHMP/473644/2015

Tracleer-H-C-401-II-0066 : EPAR - Assessment Report - Variation (PDF/2.08 MB)

Adopted

First published: 13/03/2015
Last updated: 13/03/2015
EMA/168487/2015

Tracleer-H-C-401-X-0039 : EPAR - Assessment Report - Extension (PDF/280.57 KB)

First published: 05/08/2009
Last updated: 05/08/2009

Tracleer-H-C-401-II-0037 : EPAR - Assessment Report - Variation (PDF/318.41 KB)

First published: 29/08/2008
Last updated: 29/08/2008

CHMP post-authorisation summary of positive opinion for Tracleer on 26 June 2008 (PDF/33.5 KB)

Adopted

First published: 26/06/2008
Last updated: 26/06/2008
EMEA/CHMP/210276/2008

Tracleer-H-C-401-II-0029 : EPAR - Scientific Discussion - Variation (PDF/373.23 KB)

Adopted

First published: 01/08/2007
Last updated: 01/08/2007

Tracleer-H-C-401-II-0027 : EPAR - Scientific Discussion - Variation (PDF/218.12 KB)

Adopted

First published: 19/07/2007
Last updated: 19/07/2007

Tracleer : EPAR - Steps taken after authorisation when a cutoff date has been used (PDF/84.86 KB)

First published: 21/10/2005
Last updated: 21/10/2005

Initial marketing-authorisation documents

Tracleer : EPAR - Scientific Discussion (PDF/437.79 KB)

First published: 21/10/2005
Last updated: 21/10/2005

Tracleer : EPAR - Procedural steps taken before authorisation (PDF/85.67 KB)

First published: 21/10/2005
Last updated: 21/10/2005

More information on Tracleer

This product is no longer an orphan medicine. It was originally designated an orphan medicine for the following orphan indications:

- treatment of pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension
- treatment of systemic sclerosis

Related content

- Tracleer: Paediatric investigation plan

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