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EPAR summary for the public

Stayveer

bosentan

This is a summary of the European public assessment report (EPAR) for Stayveer. It explains how the Agency assessed the medicine to recommend its authorisation in the EU and its conditions of use. It is not intended to provide practical advice on how to use Stayveer.

For practical information about using Stayveer, patients should read the package leaflet or contact their doctor or pharmacist.

What is Stayveer and what is it used for?

Stayveer is a medicine that contains the active substance bosentan. It is used to treat patients with class III pulmonary arterial hypertension (PAH) to improve exercise capacity (the ability to carry out physical activity) and symptoms. PAH is abnormally high blood pressure in the arteries of the lungs. The 'class' reflects the seriousness of the disease: 'class III' 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 improvements have also been shown in patients with class II PAH. 'Class II' involves slight limitation of physical activity.

Stayveer 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). Stayveer is intended to reduce the number of new digital ulcers that are formed.

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This medicine is the same as Tracleer, which is already authorised in the European Union (EU). The company that makes Tracleer has agreed that its scientific data can be used for Stayveer ('informed consent').

How is Stayveer used?

Stayveer 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.

Stayveer is available as tablets (62.5 mg and 125 mg), which are swallowed with water. It is taken morning and evening. In adults, the starting dose is 62.5 mg twice a day for four weeks, which is increased to the usual dose of 125 mg twice a day. In children with PAH, the dose to use is calculated based on body weight, and usually starts at 2 mg per kilogram body weight twice a day. See the package leaflet for full details.

The doctor should assess the patient's response to Stayveer and review the need for further treatment after eight weeks in patients with PAH who have not improved, and on a regular basis in patients with systemic sclerosis and ongoing digital ulcer disease. If the doctor decides to stop Stayveer, the dose should be gradually reduced.

Patients who take Stayveer must be given the special reminder card that summarises the safety information about the medicine.

How does Stayveer work?

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

PAH is a debilitating disease where there is severe narrowing of the blood vessels of the lungs. It causes high blood pressure in the vessels taking blood from the right side of 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. By expanding these blood vessels, the blood pressure is reduced and symptoms are improved.

In patients with systemic sclerosis and ongoing digital ulcer disease, bosentan improves blood circulation in the fingers and toes, preventing the development of new digital ulcers.

What benefits of Stayveer have been shown in studies?

In PAH, Stayveer has been studied in four main studies: two in a total of 245 adults with class III or IV disease that was either primary or caused by scleroderma, one in 54 adults with class III PAH that was associated with congenital heart defects, and one in 185 patients with class II disease. The studies compared Stayveer with placebo (a dummy treatment), when they were added to standard treatment. The main measure of effectiveness was how far the patients could walk in six minutes (a way of measuring exercise capacity), but the study in class II disease also looked at the change in the resistance to blood flow in the lungs' blood vessels (a marker of how narrow the blood vessels are).

In class III or IV PAH that was either primary or caused by scleroderma, the two studies showed that patients treated with Stayveer were able to walk further than patients treated with placebo after 16 weeks (44 metres further in the larger study), but there were too few patients with class IV disease to support the use of the medicine in this group. Similar results were seen in the patients with congenital heart defects. In patients with class II disease, Stayveer caused the resistance of the blood vessels to decrease by 23% compared with placebo after six months of treatment, but the distance the patients

could walk over six minutes was similar in the two groups. A study was also carried out in 19 children aged between three and 15 years, where some improvements were seen in measurements relating to the heart and arteries.

In systemic sclerosis with digital ulcers, two studies have compared Stayveer with placebo in a total of 312 adults. The main measure of effectiveness was based on the number of new digital ulcers developing during the studies. One of the studies also looked at the effect of Stayveer on healing in 190 patients, by measuring the time taken for one selected digital ulcer in each patient to heal completely. Stayveer was more effective at reducing the development of new digital ulcers than placebo. In the first study, patients taking Stayveer 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, but Stayveer did not have any effect on digital ulcer healing.

What are the risks associated with Stayveer?

In PAH, the most common side effects with Stayveer (which may affect more than 1 patient in 10) are headache and abnormal results of tests carried out to check the liver. In patients with digital ulcers, the most common side effects (which may affect more than 1 patient in 10) are abnormal liver tests, oedema (swelling) and fluid retention. Because of the risk of liver problems, the doctor will measure the levels of liver enzymes before treatment, and every month during treatment with Stayveer. For the full list of all side effects reported with Stayveer, see the package leaflet.

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

Why is Stayveer approved?

The Agency's Committee for Medicinal Products for Human Use (CHMP) decided that Stayveer's benefits are greater than its risks and recommended that it be approved for use in the EU.

What measures are being taken to ensure the safe and effective use of Stayveer?

A risk management plan has been developed to ensure that Stayveer is used as safely as possible. Based on this plan, safety information has been included in the summary of product characteristics and the package leaflet for Stayveer, including the appropriate precautions to be followed by healthcare professionals and patients.

In addition, the company that makes Stayveer will provide an educational kit for prescribers and an information booklet for patients in each Member State, explaining the safety of Stayveer (especially its effects on the liver and in pregnancy) and its interactions. The company will also carefully control the distribution of the medicine in each Member State, and collect information on its use in patients with systemic sclerosis and ongoing digital ulcers.

Other information about Stayveer

The European Commission granted a marketing authorisation valid throughout the European Union for Stayveer on 24 June 2013.

The full EPAR for Stayveer can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European public assessment reports. For more information about treatment with Stayveer, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

This summary was last updated in 06-2013.