EMA/741775/2015
EMEA/H/C/000839

EPAR summary for the public

Volibris

ambrisentan

This is a summary of the European public assessment report (EPAR) for Volibris. It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the medicine to reach its opinion in favour of granting a marketing authorisation and its recommendations on the conditions of use for Volibris.

What is Volibris?

Volibris is a medicine that contains the active substance ambrisentan. It is available as tablets (5 and 10 mg).

What is Volibris used for?

Volibris is used alone or combined with other medicines to treat adults with pulmonary arterial hypertension (PAH).

PAH is abnormally high blood pressure in the arteries of the lungs. Volibris is used in patients with class II or III disease. The 'class' reflects the seriousness of the disease: 'class II' involves slight limitation of physical activity and 'class III' involves marked limitation of physical activity. Volibris has been shown to be effective in PAH with no identified cause and in PAH caused by connective tissue disease.

Because the number of patients with PAH is low, the disease is considered 'rare', and Volibris was designated an 'orphan medicine' (a medicine used in rare diseases) on 11 April 2005.

The medicine can only be obtained with a prescription.

How is Volibris used?

Treatment with Volibris must be started by a doctor who has experience in the treatment of PAH.

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Treatment with Volibris is started at a dose of 5 mg once a day and may be increased to 10 mg daily depending on response and how well the medicine is tolerated. The increased dose of 10 mg is recommended when the medicine is used with tadalafil (another medicine for PAH). When taken with ciclosporin (a medicine that reduces the activity of the immune system) the dose of Volibris should be 5 mg a day and the patient should be closely monitored by their doctor.

How does Volibris work?

PAH is a debilitating disease where there is severe constriction (narrowing) of the blood vessels of the lungs. It causes high blood pressure in the vessels taking 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. The active substance in Volibris, ambrisentan, blocks the receptors for a hormone called endothelin, which causes blood vessels to constrict. By blocking the effect of endothelin, Volibris allows the vessels to dilate (expand), helping to lower the blood pressure and improving symptoms.

How has Volibris been studied?

Various doses of Volibris (2.5, 5 and 10 mg) have been compared with placebo (a dummy treatment) in two main studies involving a total of 394 patients with PAH, most of whom had class II or III disease that was of unknown cause or caused by connective tissue disease. The main measure of effectiveness was the change in the distance the patients could walk in six minutes after 12 weeks of treatment. This is a way of measuring the change in exercise capacity (the ability to carry out physical activity).

In addition, treatment with a combination of Volibris (10 mg) and tadalafil has been compared with either Volibris or tadalafil alone in another main study involving 605 patients with PAH. The main measure of effectiveness was the risk of clinical failure (the patients' disease getting worse).

What benefit has Volibris shown during the studies?

Results of the two studies comparing Volibris with placebo showed that Volibris was more effective than placebo at improving exercise capacity in patients with class II or III disease. Overall, in the two studies taken together, the patients could walk an average of around 345 m in six minutes at the start of the study. The patients taking 5 mg Volibris once a day could walk an average of 36 m more after 12 weeks of treatment, while the patients taking placebo could walk 9 m less. Patients with class III disease and those with PAH caused by connective tissue disease gained a greater benefit from the 10 mg dose than from the 5 mg dose.

In the study comparing Volibris and tadalafil with either medicine alone, 18% of patients (46 out of 253) given combination treatment experienced clinical failure compared with 31% (77 out of 247) given either Volibris or tadalafil alone. The risk of the disease getting worse within a year was 11% in patients given the combination treatment and 24% in those given a single medicine (Volibris or tadalafil). Over a three-year period the likelihood of the disease getting worse was 32% with the combined treatment and 44% with a single medicine.

What is the risk associated with Volibris?

The most common side effects with Volibris (seen in more than 1 patient in 10) are headache (including sinus headache and migraine), peripheral oedema (swelling, especially of the ankles and

feet) and fluid retention. For the full list of all side effects reported with Volibris, see the package leaflet.

Volibris must not be used in people who are hypersensitive (allergic) to soya, ambrisentan or any of the other ingredients. Because it might be able to cause birth defects, Volibris must not be used in pregnant women or in women who could become pregnant unless they are using reliable contraception. It must not be used in patients who are breastfeeding, who have severe liver problems or who have high levels of liver enzymes in the blood. It must not be used in patients with idiopathic pulmonary fibrosis (long-term disease in which hard fibrous tissue continuously forms in the lungs), with or without secondary pulmonary hypertension (high blood pressure in the lungs).

Why has Volibris been approved?

The CHMP decided that Volibris's benefits are greater than its risks and recommended that it be given marketing authorisation.

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

A risk management plan has been developed to ensure that Volibris 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 Volibris, including the appropriate precautions to be followed by healthcare professionals and patients.

In addition, the company that markets Volibris has agreed with EU Member States on systems to control the distribution of Volibris. The company also distributes information packs to provide healthcare workers, patients, and the male partners of female patients with information on the medicine's side effects and the need to avoid pregnancy.

Other information about Volibris

The European Commission granted a marketing authorisation valid throughout the EU for Volibris on 21 April 2008.

The full EPAR for Volibris 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 Volibris, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

The summary of the opinion of the Committee for Orphan Medicinal Products for Volibris can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/Rare disease designation.

This summary was last updated in 11-2015.