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Volibris *(ambrisentan)*

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

What is Volibris and what is it used for?

Volibris is a medicine that 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.

Volibris contains the active substance ambrisentan.

How is Volibris used?

Volibris can only be obtained with a prescription and treatment must be started by a doctor who has experience in the treatment of PAH.

Volibris is available as tablets (5 and 10 mg). Treatment is started at a dose of 5 mg once a day and the doctor may increase it to 10 mg daily depending on response and any side effects experienced by the patient. 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.

For more information about using Volibris, see the package leaflet or contact your doctor or pharmacist.

How does Volibris work?

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 heart to the lungs and reduces the

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flow of blood to the lungs. As a result, the amount of oxygen that can get into the blood in the lungs is reduced, making physical activity more difficult. The active substance in Volibris, ambrisentan, blocks the receptors for a hormone called endothelin, which causes blood vessels to become narrow. By blocking the effect of endothelin, Volibris allows the vessels to expand, helping to lower the blood pressure and improving symptoms.

What benefits of Volibris have been shown in studies?

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. Results showed that Volibris was more effective than placebo at improving exercise capacity (the ability to carry out physical activity). The main measure of effectiveness was the change in the distance the patients could walk in 6 minutes after 12 weeks of treatment.

Overall, in the two studies taken together, the patients could walk an average of around 345 m in 6 minutes at the start of the study. After 12 weeks of treatment, patients taking 5 mg Volibris once a day could walk an average of 36 m more while patients taking placebo had got worse and 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 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 proportion of patients who died or whose disease got worse. Results showed that 18% of patients (46 out of 253) given combination treatment died or their disease got worse compared with 31% (77 out of 247) given either Volibris or tadalafil alone. The risk of the disease getting worse or the patient dying 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 are the risks 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 side effects 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 is Volibris approved?

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

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

The company that markets Volibris will provide a patient card containing important information on the medicine's side effects and the need to avoid pregnancy during treatment.

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

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

Other information about Volibris

Volibris received a marketing authorisation valid throughout the EU on 21 April 2008.

Further information on Volibris can be found on the Agency's website: ema.europa.eu/medicines/human/EPAR/volibris.

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