EMA/51814/2014
EMEA/H/C/002737

EPAR summary for the public

Adempas

riociguat

This is a summary of the European public assessment report (EPAR) for Adempas. 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 Adempas.

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

What is Adempas and what is it used for?

Adempas is a medicine that contains the active substance riociguat. It is used to increase the ability to carry out physical activity in adults with the following forms of pulmonary hypertension (high blood pressure in the blood vessels of the lungs):

- Chronic thromboembolic pulmonary hypertension (CTEPH, where the blood vessels of the lungs are blocked or narrowed with blood clots). Adempas is used to treat patients with CTEPH who cannot be operated on, or in whom CTEPH remains or returns after surgery.
- Pulmonary arterial hypertension (PAH, where the walls of the blood vessels of the lungs are thickened and the vessels become narrowed). Adempas can be used on its own or in combination with other medicines for PAH called 'endothelin receptor antagonists'.

Adempas is used in patients with functional class II to III CTEPH or PAH. The 'class' reflects the seriousness of the disease: 'class II' involves slight limitation of physical activity while 'class III' involves marked limitation of physical activity.

Because the number of patients with CTEPH or with PAH is low, the diseases are considered 'rare', and Adempas was designated an 'orphan medicine' (a medicine used in rare diseases) on 20 December 2007.

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How is Adempas used?

Adempas 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 CTEPH or PAH.

Adempas is available as tablets (0.5, 1, 1.5, 2 and 2.5 mg). The recommended starting dose is 1 mg three times a day (approximately 6 to 8 hours apart) for two weeks. The dose is then increased every two weeks until the appropriate dose for the individual patient is established. The maximum dose should not exceed 2.5 mg three times a day. Treatment with the established dose should continue unless patients experience signs and symptoms of low blood pressure, in which case the dose should be reduced.

For further information, see the package leaflet.

How does Adempas work?

CTEPH and PAH are debilitating diseases where there is severe narrowing of the blood vessels of the lungs. This causes high blood pressure in the vessels taking blood from the heart to the lungs and reduces the blood flow 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 Adempas, riociguat, stimulates an enzyme called 'soluble guanylate cyclase' in the blood vessels of the lungs, which causes the blood vessels to relax and widen. This helps to lower the blood pressure in the lungs and improve symptoms of CTEPH and PAH.

What benefits of Adempas have been shown in studies?

Adempas has been shown to be effective at improving the distance patients with CTEPH or PAH could walk in six minutes (a way of measuring exercise capacity):

- Adempas was compared with placebo (a dummy treatment) in one main study in 262 patients with CTEPH who could not be operated, or in whom CTEPH remained or returned after surgery. Before treatment, the patients could walk an average of 347 metres in six minutes. After 16 weeks, patients treated with Adempas could walk on average 46 metres further in six minutes than patients taking placebo.
- The medicine was also compared with placebo in another main study in 445 patients with PAH. Before treatment the patients could walk an average of 363 metres in six minutes. After 12 weeks, patients treated with Adempas could walk 36 metres further in six minutes than patients taking placebo.

What are the risks associated with Adempas?

The most common side effects with Adempas (which may affect more than 1 in 10 people) are headache, dizziness, dyspepsia (heartburn), peripheral oedema (swelling, especially of the ankles and feet), nausea (feeling sick), diarrhoea and vomiting. Serious side effects include haemoptysis (coughing up blood) and pulmonary haemorrhage (bleeding in the lungs). For the full list of all side effects reported with Adempas, see the package leaflet.

Adempas must not be used in patients with severely reduced liver function, with systolic blood pressure (blood pressure when the heart is contracting) below 95 mmHg before starting treatment, or during pregnancy. It must also not be used together with medicines called 'PDE 5 inhibitors' (a class of medicines used for PAH or erectile dysfunction) or with nitrates or nitric oxide donors (often used to

treat high blood pressure, chest pain and heart disease, or as recreational drugs). For the full list of restrictions, see the package leaflet.

Why is Adempas approved?

The Agency's Committee for Medicinal Products for Human Use (CHMP) decided that Adempas's benefits are greater than its risks and recommended that it be approved for use in the EU. The CHMP considered that Adempas led to significant improvements in exercise capacity in patients with CTEPH or PAH. It also noted that no other medicines have been authorised for CTEPH. Regarding safety, the Committee considered that side effects of concern, including haemoptysis and pulmonary haemorrhage, have been adequately reflected in the product information and risk management plan.

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

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

Further information can be found in the summary of the risk management plan.

Other information about Adempas

The European Commission granted a marketing authorisation valid throughout the European Union for Adempas on 27 March 2014.

The full EPAR and risk management plan summary for Adempas 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 Adempas, 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 Adempas can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/Rare disease designation.

This summary was last updated in 02-2014.