



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Adempas not for use in patients with pulmonary hypertension caused by idiopathic interstitial pneumonia

EMA recommendation follows early termination of a clinical trial in these patients

The European Medicines Agency (EMA) recommends that Adempas (riociguat) should not be used in patients with 'symptomatic pulmonary hypertension associated with idiopathic interstitial pneumonia' or PH-IIP (high blood pressure in the arteries of the lungs caused by a lung disease called idiopathic interstitial pneumonia). Adempas is not authorised for use in PH-IIP patients. The recommendation follows the early termination of a phase II clinical trial called RISE-IIP which was investigating the effects of Adempas in this patient population. Preliminary results showed an increased number of deaths and serious adverse events, including breathing problems and lung infections, with Adempas compared with placebo (a dummy treatment). The available data do not indicate a clinically significant benefit from Adempas treatment in these patients.

The product information for Adempas will be updated to add a contraindication for PH-IIP to help ensure that Adempas is not used in these patients. The population for which Adempas is currently authorised is different from that included in the RISE-IIP study. The benefits of Adempas continue to outweigh its risks in its authorised uses (see below).

Information for patients

- Adempas has been investigated in a study in patients with PH-IIP. This is a condition where there is high blood pressure in the lungs caused by a lung disease called idiopathic interstitial pneumonia. The study was terminated early because more serious problems or deaths were seen in patients taking Adempas than in those taking placebo (a dummy treatment). Serious problems observed included breathing problems and lung infections.
- Patients in the study who had been receiving Adempas have stopped treatment with this medicine and are being carefully monitored.
- Adempas is not authorised for use in patients with PH-IIP and your doctor will not prescribe Adempas if you have this condition.
- Adempas is still approved to treat other types of high blood pressure in the lungs described below. Studies have shown the benefits of using Adempas to treat these other types of high blood pressure in the lungs and an acceptable level of safety.



- If you have any questions about your treatment, contact your healthcare professional.

Information for healthcare professionals

- A contraindication in PH-IIP patients will be included in the prescribing information for Adempas following early termination of the RISE-IIP clinical trial and based on preliminary data from the trial.
- The terminated clinical trial involved 145 PH-IIP patients treated with either Adempas or placebo. The primary endpoint was change in the 6 minute walking distance test after 26 weeks of treatment.
- At the time of the interim assessment leading to the termination of the trial, 21 deaths had been observed, 17 patients taking Adempas and 4 patients taking placebo. Serious adverse events, which were mostly respiratory disease or lung infections, were also higher among patients taking Adempas.
- Preliminary data indicated that treatment with Adempas did not provide a clinically significant benefit for PH-IIP patients.
- Adempas is not authorised for use in PH-IIP. Adempas continues to have a positive benefit-risk balance for its authorised uses (listed below).
- If any patients with PH-IIP are being treated with Adempas, this treatment should be discontinued and the patient's clinical status carefully monitored.
- A letter will be sent to healthcare professionals informing them of the EMA recommendations.

More about the medicine

Adempas has been authorised in the EU since 27 March 2014. 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 lungs):

- Chronic thromboembolic pulmonary hypertension (CTEPH, where the blood vessels of the lungs are blocked or narrowed with blood clots).
- Pulmonary arterial hypertension (PAH, where the walls of the blood vessels of the lungs are thickened and the vessels become narrowed). For PAH, efficacy has been shown in patients with idiopathic (of unknown cause) or heritable PAH or PAH caused by connective tissue disease.

More about the procedure

Recommendations on Adempas have been issued in the context of a review of a safety signal. A safety signal is information on a new or incompletely documented adverse event that is potentially caused by a medicine and that warrants further investigation.

The review of safety signals was carried out by EMA's Pharmacovigilance Risk Assessment Committee (PRAC), the Committee responsible for the evaluation of safety issues for human medicines. Since in this case the outcome of the signal evaluation was a recommendation for regulatory action concerning the centrally authorised medicine Adempas (i.e. change to the product information to include a new

contraindication), the PRAC recommendation was sent to EMA's Committee for Medicinal Products for Human Use (CHMP), which endorsed it.

The company that markets Adempas is expected to take action according to the recommendations.

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