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PRAC recommends measures to reduce risk of heart problems with Corlentor/Procoralan (ivabradine)

PRAC recommendations to be considered by CHMP for final opinion

The EMA's Pharmacovigilance Risk Assessment Committee (PRAC) has completed a review of Corlentor/Procoralan (ivabradine) and has made recommendations aimed at reducing the risk of heart problems, including heart attack and bradycardia (excessively low heart rate), in patients taking the medicine. Corlentor/Procoralan is used to treat symptoms of angina (chest pain due to problems with the blood flow to the heart) and to treat heart failure.

The PRAC made recommendations about the resting heart rate of patients before starting treatment or when the dose is adjusted, recommendations on when treatment should be stopped and recommendations regarding use with other medicines. Because patients treated with Corlentor/Procoralan are at an increased risk of developing atrial fibrillation (a heart condition that causes an irregular and often abnormally fast heart rate), the PRAC recommended monitoring for this condition in patients treated with Corlentor/Procoralan. In addition, the PRAC recommended that, when used for angina, Corlentor/Procoralan should only be used to alleviate symptoms as the available data do not indicate that the medicine provides benefits on outcomes such as reducing heart attack or cardiovascular death (death due to heart problems).

These recommendations follow a review of the final data from the SIGNIFY study, which evaluated whether treatment with Corlentor/Procoralan in patients with coronary heart disease (heart disease caused by the obstruction of the blood vessels that supply the heart muscle) without heart failure reduces the rate of events such as heart attacks when compared with placebo (a dummy treatment). The study showed that in a subgroup of patients who had symptomatic angina (Canadian Cardiovascular Society class II - IV) there was a small but significant increase in the combined risk of cardiovascular death or non-fatal heart attack with Corlentor/Procoralan compared with placebo (3.4% vs 2.9% yearly incidence rates). The data also indicated a higher risk of bradycardia with Corlentor/Procoralan compared with placebo (17.9% vs. 2.1%).

In its evaluation the PRAC also assessed other available data on the safety and effectiveness of Corlentor/Procoralan which showed that the risk of atrial fibrillation is increased in patients treated with Corlentor/Procoralan compared with controls (4.86% vs 4.08%).

The PRAC noted that patients in the SIGNIFY study were started on a higher than recommended dose of Corlentor/Procoralan and received up to 10 mg twice a day, which is higher than the currently authorised maximum daily dose (7.5 mg twice a day). The PRAC considered that the higher dose used

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in the study did not fully explain the findings. However, the Committee reiterated that the starting dose for angina should not exceed 5 mg twice a day and that the maximum dose should not exceed 7.5 mg twice a day.

The PRAC recommendations will now be forwarded to the Committee for Medicinal Products for Human Use (CHMP), which will adopt the Agency's final opinion and provide clear guidance to patients and healthcare professionals.

More about the medicine

Corlentor and Procoralan are identical medicines that contain the active substance ivabradine. Corlentor/Procoralan is used to treat symptoms of long-term stable angina (chest pain due to problems with the blood flow to the heart) in adults with coronary heart disease (disease of the heart caused by the obstruction of the blood vessels that supply blood to the heart muscle) who have a normal heart rhythm. Corlentor/Procoralan is also used in patients with long-term heart failure (when the heart cannot pump enough blood to the rest of the body).

Corlentor/Procoralan is available as tablets. It works by lowering the heart rate thereby reducing the stress on the heart and slowing the progression of heart failure and reducing or preventing the symptoms of angina.

Corlentor/Procoralan received an EU-wide marketing authorisation on 25 October 2005.

More about the procedure

The review of Procoralan/Corlentor was initiated on 8 May 2014 at the request of the European Commission, under Article 20 of Regulation (EC) No 726/2004.

The review has been carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), the Committee responsible for the evaluation of safety issues for human medicines, which made a set of recommendations. The PRAC recommendations will now be forwarded to the Committee for Medicinal Products for Human Use (CHMP), responsible for questions concerning medicines for human use, which will adopt the Agency's final opinion.

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