EMA/762499/2014
EMEA/H/C/000597

EPAR summary for the public

Procoralan

ivabradine

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

What is Procoralan?

Procoralan is a medicine that contains the active substance ivabradine. It is available as tablets (5 and 7.5 mg. The 5 mg tablets have a score line that enables them to be divided into two halves each containing 2.5 mg ivabradine).

What is Procoralan used for?

Procoralan is used to treat the symptoms of long-term stable angina (pains to the chest, jaw and back, brought on by physical effort) in adults with coronary artery 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. It is used in patients who cannot be treated with beta-blockers (another type of medicine to treat angina) or in combination with beta-blockers in patients whose disease is not controlled with them alone and whose heart rate is at least 70 beats per minute.

Procoralan is also used in patients with long-term heart failure (when the heart cannot pump enough blood to the rest of the body) who have a normal heart rhythm but whose heart rate is at least 75 beats per minute. It is used in combination with standard therapy including beta-blockers, or in patients who cannot be treated with beta-blockers.

The medicine can only be obtained with a prescription.

How is Procoralan used?

Procoralan is taken twice a day with meals, once in the morning and once in the evening.

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The recommended starting dose is 5 mg twice a day, which the doctor may increase to 7.5 mg twice a day or decrease to 2.5 mg twice a day depending on the patient's heart rate. If the heart rate decreases during treatment to between 50 and 60 beats per minute, the dose of 5 mg twice daily should be maintained. The adjustment is made after three to four weeks in long-term stable angina and after two weeks in long-term heart failure. In patients over 75 years old, a lower starting dose of 2.5 mg twice a day can be used. For angina, the starting dose should never exceed 5 mg twice daily in patients under 75 years of age. Treatment must be stopped if the heart rate decreases persistently below 50 beats per minute or if symptoms of bradycardia (slow heart rate) continue. When used for angina, treatment should be stopped if there is no improvement in symptoms after 3 months and the doctor should consider stopping treatment if the improvement in symptoms or the reduction in the heart rate is only limited.

How does Procoralan work?

The symptoms of angina are caused by the heart not receiving enough oxygenated blood. In stable angina, these symptoms appear during physical effort. The active substance in Procoralan, ivabradine, works by blocking the 'I_f currents' in the sinus node, the 'pacemaker' for the heart that controls the heart's contractions and regulates the heart rate. When these currents are blocked, the heart rate is lowered, so that the heart has less work to do and needs less oxygenated blood. Procoralan therefore reduces or prevents the symptoms of angina.

The symptoms of heart failure are caused by the heart not pumping enough blood around the body. By lowering the heart rate, Procoralan reduces the stress on the heart, thereby slowing the progression of heart failure and improving symptoms.

How has Procoralan been studied?

Procoralan has been studied in five main studies involving over 4,000 adults with long-term stable angina. The medicine was compared with placebo (a dummy treatment) in 360 patients, atenolol (a beta-blocker) in 939 patients and amlodipine (another medicine used to treat angina) in 1,195 patients. It was also compared with placebo as an add-on to atenolol in 889 patients and as an add-on to amlodipine in 728 patients. Each study lasted three to four months. The main measure of effectiveness was how long the patients could exercise on a bicycle or a treadmill, measured at the start and the end of each study.

Procoralan has also been compared with placebo in one main study involving 6,558 patients with long-term moderate to severe heart failure. The main measure of effectiveness was the time until death due to disease of the heart or blood vessels, or hospitalisation due to worsening heart failure.

Another study compared Procoralan with placebo in 19,102 patients with coronary heart disease and without clinical heart failure. The main measure of effectiveness was a reduction in the risk of death due to heart problems and non fatal heart attack.

What benefit has Procoralan shown during the studies?

In patients with long-term stable angina, Procoralan was more effective than placebo at improving exercise capacity and was as effective as atenolol and amlodipine. Procoralan was also more effective than placebo when added to atenolol. However, adding Procoralan to amlodipine did not provide an additional benefit.

In patients with long-term heart failure, Procoralan was more effective than placebo at preventing death due to disease of the heart or blood vessels or hospitalisation due to worsening heart failure:

24.5% (793 out of 3,241) of patients treated with Procoralan died or were hospitalised for the first time due to worsening heart failure, compared with 28.7% (937 out of 3,264) of patients treated with placebo.

In the large study in patients with coronary heart disease and without clinical heart failure, a specific subgroup of patients who had symptomatic angina had a small but significant increase in the combined risk of cardiovascular death or non-fatal heart attack with Procoralan compared with placebo (3.4% vs 2.9% yearly incidence rates). However it should be noted that patients in this study were given doses higher than the recommended dose (up to 10 mg twice a day).

What is the risk associated with Procoralan?

The most common side effect with Procoralan (seen in more than 1 patient in 10) is luminous phenomena or 'phosphenes' (a temporary brightness in the field of vision). For the full list of all side effects reported with Procoralan, see the package leaflet.

Procoralan must not be used in patients who have a resting heart rate below 70 beats per minute, very low blood pressure, various types of heart disorder (including cardiogenic shock, rhythm disorders, heart attack, unstable or acute (sudden) heart failure and unstable angina) or severe liver problems. It must not be used in women who are pregnant, breast-feeding or by women who could become pregnant and who are not using appropriate contraceptives. For the full list of restrictions, see the package leaflet.

Caution is needed if Procoralan is taken with some other medicines. See the package leaflet for full details.

Why has Procoralan been approved?

The CHMP concluded that Procoralan was shown to be effective in long-term angina with an acceptable safety profile for it to provide an alternative treatment for patients who cannot take beta-blockers or whose disease is not controlled with them. It also concluded that Procoralan was effective in long-term heart failure with an acceptable safety profile. The Committee decided that Procoralan's benefits are greater than its risks and recommended that it be given marketing authorisation.

For the treatment of angina, Procoralan was originally approved for patients whose heart rate is at least 60 beats per minute. However, the use was later restricted to patients whose heart rate is at least 70 beats per minute.[1]

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

A risk management plan has been developed to ensure that Procoralan is used as safely and effectively as possible. Based on this plan, safety information has been included in the summary of product characteristics and the package leaflet for Procoralan, including the appropriate precautions to be followed by healthcare professionals and patients.

[1] In the context of a procedure under Article 20 of Regulation (EC) No 726/2004. More information can be found here.

Other information about Procoralan:

The European Commission granted a marketing authorisation valid throughout the European Union for Procoralan on 25 October 2005.

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

This summary was last updated in 12-2014.