EMA/17925/2019
EMEA/H/C/000597

Procoralan *(ivabradine)*

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

What is Procoralan and what is it used for?

Procoralan is a heart medicine 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).The medicine is used in patients who have a normal heart rhythm, and whose heart rate is at least 70 beats per minute. It is used in those who cannot be treated with beta blockers (another type of medicine to treat angina) or in combination with a beta blocker in patients whose disease is not controlled by beta blockers alone.

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 and 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.

Procoralan contains the active substance ivabradine.

How is Procoralan used?

Procoralan is available as tablets (5 and 7.5 mg) and it can only be obtained with a prescription.

The recommended starting dose is 5 mg twice a day with meals, which the doctor may increase to 7.5 mg twice a day or decrease to 2.5 mg (half a 5-mg tablet) twice a day depending on the patient's heart rate and symptoms. In patients over 75 years old, a lower starting dose of 2.5 mg twice a day can be used. Treatment must be stopped if the heart rate is persistently below 50 beats per minute or if symptoms of bradycardia (slow heart rate) continue despite dose reduction. When used for angina, treatment should be stopped if symptoms do not improve after 3 months. Also, the doctor should consider stopping treatment if the medicine has only a limited effect on reducing angina symptoms or reducing the heart rate within 3 months.

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

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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.

What benefits of Procoralan have been shown in studies?

Angina

Procoralan was compared with placebo (a dummy treatment) and other treatments in five main studies involving over 4,000 adults with long-term stable angina. The main measure of effectiveness was how long patients could exercise on a bicycle or a treadmill, which was measured at the start and the end of each study. Each study lasted three to four months.

Results showed that the medicine was more effective than placebo in one of the studies in 360 patients. It was as effective as atenolol (a beta blocker) in a study of 939 patients and as effective as amlodipine (another medicine used to treat angina) in a study of 1,195 patients. In a fourth study in 889 patients, Procoralan was more effective than placebo, when both were added to atenolol. However, a fifth study in 728 patients showed that adding Procoralan to amlodipine did not provide an additional benefit.

A sixth study compared Procoralan with placebo in 19,102 patients with coronary artery 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.

In this study, 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).

Heart failure

Procoralan was compared with placebo in one main study involving over 6,500 patients with long-term moderate to severe heart failure. Results showed that 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 due to worsening heart failure, compared with 28.7% (937 out of 3,264) of patients receiving placebo.

What are the risks associated with Procoralan?

The most common side effect with Procoralan (which may affect more than 1 in 10 people) is luminous phenomena or 'phosphenes' (a temporary brightness in the field of vision). Bradycardia (slow heart rate) is common (it may affect up to 1 in 10 people). 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. Procoralan must not be taken with a number of other medicines.

For the full list of restrictions with Procoralan, see the package leaflet.

Why is Procoralan authorised in the EU?

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

For the treatment of angina, Procoralan was originally authorised 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?

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

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

Other information about Procoralan

Procoralan received a marketing authorisation valid throughout the EU on 25 October 2005.

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

This overview was last updated in 11-2018.

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