15 November 2019
EMA/613378/2019
EMEA/H/C/002697/II/0029

Withdrawal of application to change the marketing authorisation for Opsumit (macitentan)

Janssen-Cilag International NV withdrew its application for the use of Opsumit in the treatment of chronic thromboembolic pulmonary hypertension (CTEPH), a condition that causes high blood pressure in the lungs.

The company withdrew the application on 8 November 2019.

What is Opsumit and what is it used for?

Opsumit is a medicine used for the long-term treatment of pulmonary arterial hypertension (PAH), in which abnormally high blood pressure in the lungs leads to symptoms such as breathlessness and fatigue. If left untreated PAH can result in weakening of the heart muscle or heart failure.

Opsumit has been authorised in the EU since December 2013. It contains the active substance macitentan and is available as tablets.

Further information on Opsumit's current uses can be found on the Agency's website: ema.europa.eu/en/medicines/human/EPAR/opsumit

What change had the company applied for?

The company applied to extend the use of Opsumit to treat CTEPH which is similar to PAH but has a different cause (mainly blood clots).

Opsumit was expected to be used for patients with CTEPH that cannot be corrected by surgery and that causes undue symptoms such as breathlessness or chest pain when the patient carries out normal physical activities (WHO functional classes II and III).

How does Opsumit work?

The active substance in Opsumit, macitentan, works by blocking receptors in the blood vessels which are the targets for endothelin, a substance naturally produced in the body. When endothelin attaches to these receptors it triggers a narrowing of the blood vessels walls and increases the blood pressure.

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

© European Medicines Agency, 2019. Reproduction is authorised provided the source is acknowledged.

By blocking these receptors in the lungs, macitentan helps stop this effect, widening the blood vessels in the lungs and thereby bringing down the blood pressure.

Opsumit was expected to work in patients with CTEPH in the same way that it works in patients with PAH.

What did the company present to support its application?

The company presented data from a main study involving 80 patients with CTEPH that could not be corrected with surgery in which the patients were given either Opsumit or placebo (a dummy treatment). The study looked at improvements in pulmonary vascular resistance (PVR) after four months. PVR is a measure of how hard the heart has to work to push blood through the blood vessels in the lungs.

How far into the evaluation was the application when it was withdrawn?

The application was withdrawn after the European Medicines Agency had evaluated the initial information from the company and had prepared questions for the company. After the Agency had assessed the company's responses to the questions, there were still some unresolved issues.

What did the Agency recommend at that time?

Based on the review of the information and the company's responses to the Agency's questions, at the time of the withdrawal, the Agency had some concerns and its provisional opinion was that Opsumit could not have been authorised for the treatment of CTEPH.

The results of the main study were difficult to interpret, and there were several deviations from the study protocol which may have made the results less reliable. Therefore, at the time of the withdrawal, the Agency's opinion was that the company had not provided enough information to support the application for a change to the marketing authorisation of Opsumit.

What were the reasons given by the company for withdrawing the application?

In its letter notifying the Agency of the withdrawal of application, the company stated that it had withdrawn the application following feedback from EMA's human medicines committee (CHMP) about the study and the way it was carried out.

Does this withdrawal affect patients in clinical trials?

The company informed the Agency that it does not anticipate any consequences on ongoing clinical trials with Opsumit. If you are in a clinical trial and need more information about your treatment, speak with your clinical trial doctor.

What is happening with Opsumit for the treatment of PAH?

There are no consequences on the use of Opsumit in its currently authorised use.