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Withdrawal of application for the marketing authorisation of Epixram (levetiracetam)

Neuraxpharm Pharmaceuticals S.L. withdrew its application for a marketing authorisation of Epixram for the treatment of seizures in patients with epilepsy.

The company withdrew the application on 19 September 2024.

What is Epixram and what was it intended to be used for?

Epixram was developed for the treatment of epilepsy. It was to be used on its own in patients aged 16 years and older with newly diagnosed epilepsy, to treat partial onset seizures (starting in a specific part of the brain) with or without generalisation (when the abnormal electrical activity spreads through the brain).

Epixram was also meant to be used as an add-on to other epilepsy medicines in patients aged 12 years and older to treat:

- partial onset seizures with or without generalisation in patients with epilepsy;
- myoclonic seizures (short shock-like jerks of a muscle or group of muscles) in patients with juvenile myoclonic epilepsy;
- primary generalised tonic-clonic seizures (major seizure with loss of consciousness) in patients with idiopathic generalised epilepsy (a type of epilepsy that is thought to have a genetic cause).

Epixram contains the active substance levetiracetam and was to be available as prolonged-release granules to be taken by mouth. Prolonged release means that the active substance is released slowly into the body over a few hours after taking the medicine.

Epixram was developed as a 'hybrid medicine' of Keppra. This means that Epixram contained the same active substance as Keppra, but was presented in a different way. While Keppra is available as tablets, a solution to be taken by mouth and an infusion (drip) into a vein, Epixram was to be provided as prolonged-release granules.

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How does Epixram work?

The active substance in Epixram, levetiracetam, is used for the treatment of epilepsy. Epilepsy is caused by excessive electrical activity in the brain. The exact way in which levetiracetam works is still unclear but it seems to interfere with a protein called synaptic vesicle protein 2A, which is found in the spaces between nerves and is involved in the release of chemical messengers from nerve cells. Levetiracetam stabilises the electrical activity in the brain and prevents the occurrence of seizures in patients with epilepsy.

What did the company present to support its application?

Studies on the benefits and risks of the active substance have already been carried out with the reference medicine, Keppra, and therefore did not all need to be repeated for Epixram. As for every medicine, the company provided studies on the quality of Epixram. The company also carried out studies to investigate whether Epixram is 'bioequivalent' to the reference medicine, Keppra. Two medicines are bioequivalent when they produce the same levels of the active substance in the body and are therefore expected to have the same effect.

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

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

What did the Agency recommend at that time?

Based on the review of the data and the company's response to the Agency's questions, at the time of the withdrawal, the Agency had some concerns and its provisional opinion was that Epixram could not have been authorised for the treatment of seizures in patients with epilepsy.

The Agency determined that the data provided by the company did not show bioequivalence between Epixram and the reference medicine, Keppra. As a result, in line with EMA's guideline for hybrid medicines, the Agency requested that the company provide further data to show that Epixram is equivalent to the reference medicine, and so will have the same effects, along with additional safety information for Epixram. Although the company provided data from a study based on real world data, the Agency considered that the data provided were not sufficient to allow it to conclude on therapeutic equivalence of effect.

Therefore, at the time of the withdrawal, the Agency's opinion was that the company had not provided enough data to support the marketing authorisation of Epixram.

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

In its letter notifying the Agency about withdrawing their application, the company cited a change in their regulatory strategy as the reason for doing so.

Does this withdrawal affect patients in clinical trials?

The company informed the Agency that there was no ongoing clinical trial using Epixram.