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Withdrawal of application for the marketing authorisation of Ekesivy (diclofenamide)

Sun Pharmaceutical Industries Europe B.V. withdrew its application for a marketing authorisation of Ekesivy for the treatment of muscle disorders called periodic paralysis.

The company withdrew the application on 2 October 2019.

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

Ekesivy contains the active substance diclofenamide and was to be available as tablets for the treatment of periodic paralysis, a group of inherited muscle disorders that causes attacks of weakness or inability to move that can last a few hours to a few days.

Ekesivy was developed as a 'hybrid medicine'. This means that it was intended to be similar to a 'reference medicine' containing the same active substance and already authorised in the European Union. The reference medicine is Fenamide, a medicine authorised in Italy for the treatment of glaucoma.

Ekesivy was designated an 'orphan medicine' (a medicine used in rare diseases) on 27 June 2016 for the treatment of periodic paralysis. Further information on the orphan designation can be found on the Agency's website: ema.europa.eu/medicines/human/orphan-designations/eu3161677.

How does Ekesivy work?

Periodic paralysis is caused by abnormalities in the ion channels, tiny pores in the muscle cells that control the passage of charged particles (ions) such as sodium and potassium, which play a key role in the contraction and relaxation of muscles. The way Ekesivy works in periodic paralysis is not fully understood but it is thought to increase the removal of bicarbonate, sodium and potassium through the urine. This increases acidity in the body, which studies show can help normalise ion channels in muscle cells, thus allowing better control of muscle contraction.

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What did the company present to support its application?

The company presented the results from a study in 71 patients with either hypokalaemic periodic paralysis (where a low potassium blood level triggers attacks) or hyperkalaemic periodic paralysis (where a high potassium blood level triggers attacks). Patients received either Ekesivy or placebo (dummy treatment) for 9 weeks. The main measure of effectiveness was the number of attacks per week in the last 8 weeks of treatment.

How far into the evaluation was the application when it was withdrawn?

The application was withdrawn after the European Medicines Agency had evaluated the initial information from the company and had prepared questions for the company. The company had not responded to the questions at the time of the withdrawal.

What did the Agency recommend at that time?

Based on the review of the data, at the time of the withdrawal, the Agency had some concerns and its provisional opinion was that Ekesivy could not have been authorised for the treatment of periodic paralysis.

The Agency had concerns on a number of aspects relating to the quality, effectiveness and safety of the medicine. Amongst these concerns, the Agency noted that the company had not provided information on how data on the reference medicine, Fenamide, could be linked with Ekesivy, and laboratory studies were not provided to support the proposed use of Ekesivy, despite the reference medicine being used in a different condition. The company did not provide data on how the medicine is absorbed, modified and removed from the body. The Agency was concerned that the way the study in patients was carried out and the analysis of results was not sufficiently robust to show that Ekesivy worked well enough and was acceptably safe for its proposed use.

Therefore, at the time of the withdrawal, the Agency's opinion was that, because effectiveness was not proven, the benefits of Ekesivy did not outweigh its risks.

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

In its letter notifying the Agency of the withdrawal of the application, the company stated that it decided to withdraw its application because the Agency's concerns could not be addressed within the available time frame.

Does this withdrawal affect patients in clinical trials?

The company informed the Agency that there are no ongoing clinical trials with Ekesivy.