21 March 2013
EMA/172695/2013
EMEA/H/C/002371

Questions and answers

Withdrawal of the marketing authorisation application for Fanaptum (iloperidone)

On 13 March 2013, Vanda Pharmaceuticals Ltd officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a marketing authorisation for Fanaptum for the treatment of schizophrenia.

What is Fanaptum?

Fanaptum is a medicine that contains the active substance iloperidone. It was to be available as tablets.

What was Fanaptum expected to be used for?

Fanaptum was expected to be used to treat schizophrenia in adults.

Schizophrenia is a mental illness that has a number of symptoms, including disorganised thinking and speech, hallucinations (hearing or seeing things that are not there), suspiciousness and delusions (false beliefs).

How is Fanaptum expected to work?

The active substance in Fanaptum, iloperidone, is an antipsychotic medicine. It is known as an 'atypical' antipsychotic because it is different from the older antipsychotic medicines that have been available since the 1950s. The way it works is unclear, but it is thought to attach to certain receptors on the surface of nerve cells in the brain. This disrupts signals transmitted between brain cells by 'neurotransmitters', the chemicals that allow nerve cells to communicate with each other. Iloperidone is thought to block receptors for the neurotransmitters dopamine and 5-hydroxytryptamine (also called serotonin), which are involved in schizophrenia. By blocking these receptors, iloperidone is expected to normalise the activity of the brain and reduce the symptoms of the disease.

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What did the company present to support its application?

The effects of Fanaptum were first tested in experimental models before being studied in humans.

The company presented the results of four main studies of four or six weeks' duration. The studies, involving 2,081 patients, compared Fanaptum with placebo (a dummy treatment). In all studies, the main measure of effectiveness was the change in the patients' symptoms after four or six weeks, assessed using a standard scale for schizophrenia.

How far into the evaluation was the application when it was withdrawn?

The evaluation had finished and the CHMP had given a negative opinion. The company had requested a re-examination of the negative opinion, but this re-examination had not yet finished when the company withdrew.

What was the recommendation of the CHMP at that time?

Based on the review of the data, at the time of the withdrawal, the CHMP had given a negative opinion recommending that the marketing authorisation be refused for Fanaptum for the treatment of schizophrenia.

At the time of the negative opinion, the CHMP concluded that the short-term effectiveness of Fanaptum in studies was modest when compared with placebo, and that longer-term effectiveness has not been shown sufficiently. The CHMP noted that Fanaptum has a delayed onset of action which it considered to be a disadvantage. In terms of safety, the CHMP was concerned about the medicine's effects on the heart: Fanaptum was shown to make the 'QT interval' (part of the heartbeat) to last for longer than normal. This side effect, called 'QT prolongation', can lead to arrhythmias (irregular heartbeats). The Committee considered that this risk was significant and not manageable by the risk minimisation measures proposed by the company.

Therefore, at the time of the withdrawal, the CHMP was of the opinion that the benefits of Fanaptum 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 application, the company stated that it was withdrawing the application because the CHMP identified missing data which would not be available within the regulatory timeframe.

The withdrawal letter is available here.

What consequences does this withdrawal have for patients in clinical trials?

The company informed the CHMP that there are no consequences for patients currently included in clinical trials with Fanaptum.

If you are in a clinical trial and need more information about your treatment, contact the doctor who is giving it to you.