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Questions and answers

Refusal of the marketing authorisation for Fanaptum (iloperidone)

On 13 December 2012, the Committee for Medicinal Products for Human Use (CHMP) adopted a negative opinion, recommending the refusal of the marketing authorisation for the medicinal product Fanaptum, intended for the treatment of schizophrenia.

The company that applied for authorisation is Vanda Pharmaceuticals Ltd. It may request a re-examination of the opinion within 15 days of receipt of notification of this negative opinion.

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

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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.

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.

What were the CHMP's main concerns that led to the refusal?

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 that point in time, the CHMP was of the opinion that the benefits of Fanaptum did not outweigh its risks and recommended that it be refused marketing authorisation.

What consequences does this refusal 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.