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Questions and answers

Refusal of the marketing authorisation for Fanaptum (iloperidone)

Outcome of re-examination

On 20 July 2017, 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.

The company requested a re-examination of the initial opinion. After considering the grounds for this request, the CHMP re-examined the opinion, and confirmed the refusal of the marketing authorisation on 9 November 2017.

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 does Fanaptum work?

The active substance in Fanaptum, iloperidone, is an antipsychotic medicine. The way it works is unclear, but it is thought to attach to certain receptors (targets) for neurotransmitters on nerve cells in the brain. Neurotransmitters are substances that nerve cells use to communicate with neighbouring cells. Iloperidone is thought to block receptors for the neurotransmitters dopamine and 5-hydroxytryptamine (also called serotonin), which play a role 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 company presented the results of 2 main studies of 4 and 26 weeks' duration. The short-term study, involving 567 patients, compared Fanaptum with the schizophrenia medicine ziprasidone and with placebo (a dummy treatment). In this study, the main measure of effectiveness was the change in the patients' symptoms after 4 weeks, assessed using a standard scale for schizophrenia. The long-term study, involving 193 patients, compared Fanaptum with placebo. It measured the time until the patient's symptoms came back (first relapse).

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

At the time of the initial recommendation, the CHMP considered that the effectiveness of Fanaptum in studies was modest. The CHMP also noted that the medicine starts to have its effects after 2 to 3 weeks of treatment, which is a concern when treating sudden (acute) episodes of schizophrenia.

In terms of safety, the CHMP was concerned about the medicine's effects on the heart: Fanaptum causes QT prolongation, a change in the heart's electrical activity which can cause a life-threatening abnormality of heart rhythm. The Committee considered that this risk was significant despite the measures proposed by the company to minimise it.

Finally, the CHMP was concerned that Fanaptum is broken down in the body by liver enzymes whose activity is reduced in certain patients and by certain other medicines. As a result, some patients may have increased blood concentrations of Fanaptum, which would increase their risk of QT prolongation.

During the re-examination the CHMP looked again at the data submitted by the company and the company's proposal to introduce several new measures to manage the risk of QT prolongation. The measures included restricting use to patients whose treatment with another antipsychotic did not work or was no longer tolerated, and prohibiting use in patients who cannot effectively break down the medicine or are taking certain other medicines.

However, the CHMP was still concerned about the risk of QT prolongation and considered that the measures proposed would not appropriately address this risk in clinical practice. In addition, the Committee was still concerned by the modest effectiveness of Fanaptum and its delayed onset of action.

Therefore, the CHMP concluded that the benefits of Fanaptum did not outweigh its risks and maintained its previous recommendation that the medicine be refused marketing authorisation.

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

The company informed the CHMP that there are no ongoing clinical studies with Fanaptum in the EU at the present time.