European Medicines Agency

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Questions and answers on the withdrawal of the application for a change to the marketing authorisation for Invega

International non-proprietary name (INN): ***paliperidone***

On 15 December 2008, Janssen-Cilag International NV officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a change to the marketing authorisation for Invega, to add the treatment of acute manic episodes associated with bipolar I disorder.

What is Invega?
Invega is a medicine containing the active substance paliperidone. It is available as prolonged-release tablets (tablets that release paliperidone slowly from the tablet over a few hours).
Invega is already used to treat schizophrenia, 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 (mistaken beliefs).

What was Invega expected to be used for?
Invega was also expected to be used in adults with bipolar I disorder, a mental illness in which patients have manic episodes (periods of abnormally high mood), alternating with periods of normal or depressed mood. Invega was expected to be used to treat acute (sudden) manic episodes.

How is Invega expected to work?
The active substance in Invega, paliperidone, 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. Paliperidone is an active breakdown product (metabolite) of risperidone, another antipsychotic medicine that has been used in the treatment of schizophrenia since the 1990s and in the treatment of bipolar I disorder since the early 2000s.
In the brain, paliperidone attaches to several different receptors on the surface of nerve cells. This disrupts signals transmitted between brain cells by 'neurotransmitters', chemicals that allow nerve cells to communicate with each other. Paliperidone acts mainly by blocking the receptors for the neurotransmitters dopamine and 5-hydroxytryptamine (also called serotonin), which are involved in bipolar I disorder. By blocking these receptors, paliperidone is expected to help normalise the activity of the brain and reduce the symptoms of acute manic episodes.

What documentation did the company present to support its application to the CHMP?
The company presented the results of three main studies involving a total of 1,262 adults with bipolar I disorder who were having an acute manic episode.
Two of the studies compared Invega taken alone with placebo (a dummy treatment), one in 469 patients over three weeks and another in 493 patients over 12 weeks. The 12-week study also included a group of patients treated with quetiapine taken alone (another treatment for bipolar I disorder).
The third study compared the effects of Invega and placebo when they were taken together with either lithium or sodium valproate (other treatments for bipolar I disorder). The study involved 300 patients and lasted six weeks.

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In all three studies, the main measure of effectiveness was the change in the severity of acute manic episodes, as measured using a standard symptom scale.

How far into the evaluation was the application when it was withdrawn?
The application was at day 85 when the company withdrew. The CHMP was evaluating the initial documentation provided by the company.
The CHMP normally takes up to 90 days to adopt an opinion after it has received an application for a change to a marketing authorisation. Following the CHMP's opinion, it usually takes around six weeks for the European Commission to update the licence.

What was the recommendation of the CHMP at that time?
The CHMP was evaluating the initial documentation provided by the company and had not yet made any recommendations.

What were the reasons given by the company to withdraw the application?
The letter from the company notifying the EMEA of the withdrawal of the application is available here.

What are the consequences of the withdrawal for patients undergoing clinical trials with Invega?
The company informed the CHMP that there are no consequences for patients currently included in clinical trials with Invega for bipolar I disorder or any other disease. If you are in a clinical trial and need more information about your treatment, contact the doctor who is giving it to you.

What is happening with Invega used for the treatment of schizophrenia?
There are no consequences on the use of Invega in its authorised indication, for which the balance of benefits and risks remains unchanged.