



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Update as of 2 May 2026:

The company for Iloperidone Vanda Pharmaceuticals has withdrawn its previously submitted notice of intent to request a re-examination of EMA's opinion of 26 February 2026.

Refusal of the marketing authorisation for Iloperidone Vanda Pharmaceuticals (iloperidone)

The European Medicines Agency has recommended the refusal of the marketing authorisation for Iloperidone Vanda Pharmaceuticals, a medicine intended for the treatment of schizophrenia and manic or mixed episodes associated with bipolar I disorder.

The Agency issued its opinion on 26 February 2026. The company that applied for authorisation, Vanda Pharmaceuticals Netherlands B.V., may ask for re-examination of the opinion within 15 days of receiving the opinion.

What is Iloperidone Vanda Pharmaceuticals and what was it intended to be used for?

Iloperidone Vanda Pharmaceuticals was developed as a medicine for the treatment of schizophrenia and the acute (short-term) treatment of manic or mixed episodes associated with bipolar I disorder in adults. Schizophrenia is a mental disorder with symptoms that include disorganised thinking and speech, hallucinations (hearing or seeing things that are not there), suspiciousness and delusions (false beliefs). Bipolar disorder is a condition in which patients have manic episodes (periods of abnormally high mood), alternating with periods of normal mood. They may also have episodes of depression.

Iloperidone Vanda Pharmaceuticals contains the active substance iloperidone and was to be available as tablets.

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How does Iloperidone Vanda Pharmaceuticals work?

The active substance in Iloperidone Vanda Pharmaceuticals, iloperidone, is an antipsychotic medicine that attaches 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 blocks receptors for the neurotransmitters dopamine and 5-hydroxytryptamine (also called serotonin), which play a role in schizophrenia and bipolar disorder. By blocking these receptors, iloperidone is expected to reduce the symptoms of these conditions.

What did the company present to support its application?

The company presented the results of five main studies involving over 3,000 patients with schizophrenia. In the studies, which investigated different doses of Iloperidone Vanda Pharmaceuticals and different durations of treatment (4 or 6 weeks for treatment of schizophrenia; 26 to 52 weeks for prevention of relapses (when symptoms come back)), Iloperidone Vanda Pharmaceuticals was compared with the schizophrenia medicines ziprasidone, risperidone, haloperidol or with placebo (a dummy treatment).

The main measure of effectiveness in the studies was the change in patients' symptoms, assessed using a standard scale for schizophrenia. The long-term study (up to 52 weeks) measured the time until the patient's symptoms came back (first relapse).

Another study involved 417 patients with bipolar disorder and compared Iloperidone Vanda Pharmaceuticals with placebo for 4 weeks; the main measure of effectiveness was the change in patients' symptoms, assessed using a standard scale for bipolar disorder.

What were the main reasons for refusing the marketing authorisation?

After assessing the data provided by the company, the Agency was of the opinion that the safety and efficacy of Iloperidone Vanda Pharmaceuticals had not been sufficiently demonstrated.

The Agency concluded that treatment with Iloperidone Vanda Pharmaceuticals is associated with pronounced QT prolongation (a change in the heart's electrical activity which can cause a life-threatening heart rhythm abnormality) which is not outweighed by the benefits of treatment. The Agency considered that feasible and effective measures to manage and address this risk in clinical practice (including how to identify and monitor patients at higher risk of potentially fatal arrhythmias) had not been identified.

In patients with schizophrenia, this risk was not considered to be outweighed by the observed treatment effect, since the results of the short-term studies were not considered statistically robust after additional analyses. In addition, the Agency noted that the medicine starts to have an effect after 1.5 to 3 weeks of treatment, possibly because the dose of Iloperidone Vanda Pharmaceuticals has to be increased slowly, which is a concern as it is intended for immediate and continued treatment of schizophrenia.

In patients with acute manic or mixed episodes associated with bipolar I disorder, the risk of QT prolongation is also not considered to be outweighed by the observed effect in the short-term study, the lack of data comparing the medicine with other treatments or placebo beyond 4 weeks of treatment, as well as the delayed onset of effect.

Therefore, the Agency's opinion was that the benefits of Iloperidone Vanda Pharmaceuticals did not outweigh its risks, and it recommended refusing marketing authorisation.

Does this refusal affect patients in clinical trials or compassionate use programmes?

The company informed the Agency that there are no consequences for patients in clinical trials or in compassionate use programmes with Iloperidone Vanda Pharmaceuticals.

If you are in a clinical trial or compassionate use programme and need more information about your treatment, speak with your clinical trial doctor.