17 December 2009
EMA/830685/2009
EMEA/H/C/1020

Questions and answers on the withdrawal of the marketing authorisation application for Nenad (lisuride)

On 30 November 2009, Axxonis Pharma AG officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a marketing authorisation for Nenad, for the treatment of the signs and symptoms of moderate-to-severe idiopathic restless legs syndrome in adults.

What is Nenad?

Nenad is a transdermal patch (patch that delivers a medicine across the skin) that contains the active substance lisuride.

What was Nenad expected to be used for?

Nenad was expected to be used in adults with moderate-to-severe idiopathic restless legs syndrome. Restless legs syndrome is a disorder where the patient has uncontrollable urges to move the limbs to stop uncomfortable, painful or odd sensations in the body, usually at night. Idiopathic means that the disease has no obvious cause.

How was Nenad expected to work?

The active substance in Nenad, lisuride, is a dopamine agonist. This means that it imitates the action of dopamine, a messenger substance in the parts of the brain that control movement and co ordination. The way lisuride was expected to work in restless legs syndrome is not fully understood. However, the syndrome is thought to be caused by problems in the way dopamine works in the brain, which was expected to be corrected by lisuride.

What documentation did the company present to support its application to the Agency?

The effects of Nenad were first tested in experimental models before being studied in humans. The company presented results of one main study of 309 patients with moderate-to-severe restless legs syndrome. The patients were given Nenad, ropinirole (another medicine for restless legs syndrome) or placebo (a dummy medicine). The main measure of effectiveness was the change in the rating of the

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8416
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union

patients' symptoms after 12 weeks using the International Restless Legs Syndrome rating scale (IRLS) score. The 210 patients who completed the first 12 weeks were also offered the opportunity to continue treatment in an extension study.

The company had also provided results on studies involving patients with Parkinson's disease. However, during the CHMP evaluation, the company withdrew its application for Nenad to be used for this disease.

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 withdrew before the European Commission had issued a decision on this opinion.

What was the recommendation of the CHMP at that time?

Based on the review of the data and the company's response to the CHMP lists of questions, at the time of the withdrawal, the CHMP had given a negative opinion, recommending that the marketing authorisation for Nenad be refused.

The CHMP noted that, while the short-term effectiveness of Nenad for the treatment of restless legs syndrome had been shown, there was not enough evidence to demonstrate its long-term effectiveness. Since restless legs syndrome is often a lifelong disease, long-term data were considered essential. The Committee was also concerned that a large proportion of patients in the study stopped treatment with Nenad because of skin irritation, making the patch unsuitable for long-term use. There were also problems with the patches not sticking well enough to the skin.

Therefore, at that point in time, the CHMP was of the opinion that the benefits of Nenad in the treatment of restless legs syndrome did not outweigh its risks.

What were the reasons given by the company for withdrawing the application?

The letter from the company notifying the CHMP of the withdrawal of the application is available here.

What are the consequences of the withdrawal for patients in clinical trials or compassionate use programmes using Nenad?

The company informed the CHMP that there are no consequences for patients using Nenad in clinical trials or compassionate use programmes.