European Medicines Agency

London, 19 November 2009
Doc. Ref.: EMEA/CHMP/726734/2009

Questions and answers on the recommendation for the refusal of the marketing authorisation for Nenad

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

On 19 November 2009, the Committee for Medicinal Products for Human Use (CHMP) adopted a negative opinion, recommending the refusal of the marketing authorisation for the medicinal product Nenad, intended for the treatment of the signs and symptoms of moderate-to-severe idiopathic restless legs syndrome in adults.
The company that applied for authorisation is Axxonis Pharma AG. It may request a re-examination of the opinion within 15 days of receipt of notification of this negative opinion.

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 is 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 CHMP?
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 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, the company withdrew its application for Nenad to be used for this disease.

7 Westferry Circus, Canary Wharf, London, E14 4HB, UK
Tel. (44-20) 74 18 84 00 Fax (44-20) 74 18 86 68
E-mail: mail@emea.europa.eu http://www.emea.europa.eu

What were the major concerns that led the CHMP to recommend the refusal of the marketing authorisation?
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. Hence, the CHMP recommended that Nenad be refused marketing authorisation.

What are the consequences of the refusal 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.