EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

23 May 2014
EMA/311892/2014
EMEA/H/C/002546

Questions and answers

Refusal of the marketing authorisation for Nerventra (laquinimod)

Outcome of re-examination

On 23 January 2014, the Committee for Medicinal Products for Human Use (CHMP) adopted a negative opinion, recommending the refusal of the marketing authorisation for the medicinal product Nerventra, intended for the treatment of multiple sclerosis. The company that applied for authorisation is Teva Pharma GmbH.

The applicant requested a re-examination of the opinion. After considering the grounds for this request, the CHMP re-examined the initial opinion, and confirmed the refusal of the marketing authorisation on 22 May 2014.

What is Nerventra?

Nerventra is a medicine that contains the active substance laquinimod. It was to be available as capsules.

What was Nerventra expected to be used for?

Nerventra was expected to be used to treat multiple sclerosis (MS), a disease in which the immune system malfunctions, causing inflammation that destroys the protective sheath around the nerves in the brain and spinal cord.

Nerventra was to be used in the type of MS known as relapsing-remitting MS, when the patient has flare-ups of symptoms (relapses) followed by periods of recovery (remissions).

How is Nerventra expected to work?

The exact way Nerventra works is not known, but it is believed to have a modulator effect on the immune system (the body's defences). By modulating the immune system it is expected to help

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8668
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union

control the inflammation and the damage to nerves, thus helping to reduce symptoms and the worsening of disability in patients with MS.

What did the company present to support its application?

The effects of Nerventra were first tested in experimental models before being studied in humans.

The company also provided results of two main studies in patients with relapsing-remitting MS. One of the studies involving 1,106 patients compared Nerventra with placebo (a dummy treatment), while the second study in 1,331 patients compared Nerventra with placebo and another medicine used to treat MS, interferon-beta 1a. Both studies lasted two years and the main measure of effectiveness was based on the reduction in the number of relapses per patient per year (what is known as the 'annualised relapse rate').

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

At the time of the initial recommendation, the CHMP had concerns about results from animal studies showing a higher occurrence of cancers after long-term exposure to the medicine and noted that a similar long-term cancer risk could not be excluded in humans, especially when considering that the way the medicine works in the body is unclear.

There was also a possible risk (again from animal studies) of effects on the unborn baby when the medicine is taken by pregnant women. The CHMP noted that the risk could not be excluded with current data and that animal studies suggest that some of the harmful effects may be delayed and only seen later on in the child's life. In addition, the Committee was not convinced about the effectiveness of the company's proposed measures to prevent pregnancies in women who would take the medicine.

During the re-examination, the CHMP considered advice from an expert group in neurology. The expert group advised that the risks seen in animal studies could have been acceptable if a clear benefit was seen in clinical studies, although a strict pregnancy prevention scheme would have been required. The CHMP noted that the effect of the medicine in preventing relapses was modest, and though its effect in slowing the worsening of disability was encouraging it still needed to be confirmed. Therefore the Committee concluded that the benefits of Nerventra at the dose studied were not sufficient to outweigh the potential risks in patients with relapsing remitting MS and maintained its recommendation that the medicine be refused marketing authorisation.

What consequences does this refusal have for patients in clinical trials or compassionate use programmes?

The company informed the CHMP that there are a number of ongoing and planned clinical trials with Nerventra in patients with multiple sclerosis. The CHMP opinion has no consequences on these trials. If you are taking part in a clinical trial and need more information about your treatment, contact the doctor who is giving it to you.