European Medicines Agency

London, 23 July 2009
Doc. Ref.: EMEA/464033/2009
EMEA/H/C/546/II/24

Questions and answers on recommendation for the refusal of a change to the marketing authorisation for Lyrica
pregabalin

On 23 April 2009, the Committee for Medicinal Products for Human Use (CHMP) adopted a negative opinion, recommending the refusal of a change to the marketing authorisation for the medicinal product Lyrica. The change concerned an extension of indication to add the treatment of fibromyalgia. The company that applied for authorisation is Pfizer Limited.
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 23 July 2009.

What is Lyrica?
Lyrica is a medicine that contains the active substance pregabalin. It is available as capsules.
Lyrica has been authorised since July 2004. It is used to treat adults with the following conditions:
- neuropathic pain (pain due to nerve damage);
- epilepsy in patients who have partial seizures (epileptic fits starting in one specific part of the brain) that cannot be controlled with their current treatment;
- generalised anxiety disorder (long-term anxiety or nervousness about everyday matters).

What was Lyrica expected to be used for?
Lyrica was also expected to be used to treat adults with fibromyalgia, a disease causing long-lasting, widespread pain and painful responses to touch. Fibromyalgia can also cause other symptoms such as tenderness, stiffness, tiredness, anxiety and changes in how the patient sleeps, feels and thinks. The cause of fibromyalgia is not known. Lyrica was expected to be used in patients with moderate to severe pain.

How is Lyrica expected to work?
In fibromyalgia, Lyrica is expected to work in the same way as it does in its existing indications. The active substance in Lyrica, pregabalin, is similar in structure to the body's own 'neurotransmitter' gamma-amino butyric acid (GABA), but has very different biological effects. Neurotransmitters are chemicals that allow nerve cells to communicate with each other. The exact way that pregabalin works is not fully understood, but it is thought to affect the way that calcium enters nerve cells. This reduces the activity of some of the nerve cells in the brain and spinal cord, reducing the release of other neurotransmitters. This is expected to reduce the symptoms of fibromyalgia, such as pain.

What documentation did the company present to support its application to the CHMP?
The company presented the results of five main studies involving over 3,000 adults with fibromyalgia. Most of the patients included in the studies came from outside the European Union (EU).
Four of the studies compared the short-term effects of Lyrica at doses between 150 and 600 mg per day with those of placebo (a dummy treatment) in a total of 2,757 patients. The main measure of effectiveness was the change in pain levels over eight to 14 weeks of treatment.
The fifth study compared the long-term effects of Lyrica with those of placebo in 566 patients who had responded to an initial six weeks of treatment with Lyrica. In this study, the main measure of effectiveness was how long it took until the patient's pain came back. The study lasted for six months.

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 change to the marketing authorisation?
The CHMP was concerned that the benefits of Lyrica in fibromyalgia had not been shown in either the short or the long term. There were no consistent or relevant reductions in pain or other symptoms in the short-term studies, and the maintenance of Lyrica's effect was not shown in the longer study. The Committee was also concerned that the safety and effectiveness of Lyrica had not been shown in patients from the EU.
At that point in time, the CHMP was of the opinion that the benefits of Lyrica in the treatment of fibromyalgia did not outweigh its risks. Hence, the CHMP recommended that the change to the marketing authorisation be refused. The CHMP refusal was confirmed after re-examination.

What are the consequences of the refusal for patients in clinical trials with Lyrica?
The company informed the CHMP that there are currently no ongoing clinical trials with Lyrica in Europe for fibromyalgia.

What is happening for Lyrica for the treatment of neuropathic pain, epilepsy and generalised anxiety disorder?
There are no consequences on the use of Lyrica in the authorised indications, for which the balance of benefits and risks remains unchanged.

The full European Public Assessment Report (EPAR) for Lyrica is available here.