20 April 2018
EMA/207380/2018
EMEA/H/C/004398

Refusal of the marketing authorisation for Alsitek (masitinib)

On 18 April 2018, the Committee for Medicinal Products for Human Use (CHMP) adopted a negative opinion, recommending the refusal of the marketing authorisation for the medicinal product Alsitek, intended for the treatment of amyotrophic lateral sclerosis (ALS).

The company that applied for authorisation is AB Science. It may request a re-examination of the opinion within 15 days of receipt of notification of this negative opinion.

What is Alsitek?

Alsitek is a medicine that contains the active substance masitinib. It was to be available as tablets.

What was Alsitek expected to be used for?

Alsitek was expected to be used to treat amyotrophic lateral sclerosis (ALS). ALS is a progressive disease of the nervous system, where nerve cells in the brain and spinal cord that control voluntary movement gradually deteriorate, causing loss of muscle function and paralysis. Alsitek was to be used in combination with riluzole, another medicine for ALS.

Alsitek was designated an 'orphan medicine' (a medicine to be used in rare diseases) on 29 August 2016 for the treatment of ALS. Further information on the orphan designation can be found here.

How does Alsitek work?

Alsitek is thought to work by reducing the activity of microglia, the main immune (defence) cells of the brain, and mast cells, a type of white blood cell. Microglia and mast cells may play a role in the inflammation and damage to nerves in patients with ALS. By reducing their activity, the medicine is expected to reduce inflammation and damage to nerves, thereby slowing down the worsening of the patient's symptoms.

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What did the company present to support its application?

The applicant presented the results of one main study involving 394 patients with ALS, where Alsitek was compared with placebo (a dummy treatment), both taken together with riluzole. The main measure of effectiveness was the change in the patients' symptoms after 48 weeks of treatment, assessed using a standard scale for ALS.

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

The CHMP concluded that the main study in patients with ALS did not show that Alsitek is effective at slowing down progression of the disease. Although a positive effect on symptoms was seen in the group of patients whose disease worsened at a normal rate compared with those whose disease worsened rapidly, the CHMP considered that this way of classifying patients was arbitrary and did not reflect clinical practice. In addition, there was no reason why the medicine would work in one group of patients and not in others.

Furthermore, an inspection at two of the study sites showed deficiencies in the way the study was conducted, which cast doubt on the integrity of the data.

Finally, the Committee was concerned about the way data from patients who withdrew from treatment were handled, which could have biased the results in favour of Alsitek.

Therefore, the CHMP was of the opinion that the study did not provide reliable evidence on the benefits of Alsitek and recommended that it 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 no consequences for patients in clinical trials or compassionate use programmes.

If you are in a clinical trial or compassionate use programme and need more information about your treatment, contact the doctor who is giving it to you.