20 January 2011
EMA/CHMP/51402/2011
EMEA/H/C/product number

Questions and answers

Refusal of the marketing authorisation for Movectro (cladribine)

Outcome of re-examination

On 23 September 2010, the Committee for Medicinal Products for Human Use (CHMP) adopted a negative opinion, recommending the refusal of the marketing authorisation for the medicinal product Movectro, intended for the treatment of relapsing-remitting multiple sclerosis. The company that applied for authorisation is Merck Serono Europe Limited.

The company 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 20 January 2011.

What is Movectro?

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

What was Movectro expected to be used for?

Movectro was expected to be used to treat the type of multiple sclerosis (MS) known as 'relapsing-remitting' MS.

It was originally expected to be used in patients with high disease activity or in patients who did not tolerate beta-interferon or glatiramer acetate (other medicines used in MS). For the re-examination, the proposed use was restricted to patients with high disease activity or patients with persistent disease activity despite treatment with other medicines.

MS is a disease of the nerves, in which inflammation destroys the protective sheath surrounding the nerve cells, leading to a range of neurological symptoms such as numbness, impaired coordination and balance, weakness, vision and speech impairment. MS is described as 'relapsing-remitting' when the patient has attacks (relapses) in between periods with no symptoms (remissions).

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How is Movectro expected to work?

The active substance in Movectro, cladribine, has been used in anti-cancer medicines since the mid-1990s. Cladribine has a similar structure to purine, one of the substances that make up DNA. In MS, it is expected to work within the lymphocytes (a type of white blood cell) which are involved in the inflammation seen in MS. Cladribine takes the place of purine and interferes with the normal production of new DNA in these cells, preventing them from multiplying, leading to cell death. This is expected to help reduce the inflammation, thereby improving the symptoms of the disease.

What did the company present to support its application?

The effects of Movectro were first tested in experimental models before being studied in humans. The company presented the results of one main study that compared Movectro with placebo (a dummy treatment) in 1,326 patients with relapsing-remitting MS. The main measure of effectiveness was the number of relapses the patients had during the twenty four months of treatment. The study also looked at how long it took for the patient's disabilities to get worse.

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

In September 2010 the CHMP had concerns about the medicine's safety. An increased number of patients with cancer were observed in clinical trials with Movectro compared to the control group. The Committee also noted that the benefits and the most appropriate dosage for treatment had not been fully established in patients who were expected to use the medicine. Therefore, at that point in time, the CHMP was of the opinion that the benefits of Movectro did not outweigh its risks and recommended that it be refused marketing authorisation.

In January 2011, the CHMP's main concerns were not resolved during the re-examination procedure. In particular it was still concerned about Movectro's long term safety, even if the medicine were to be used in the restricted group of patients. Therefore the Committee confirmed its initial negative opinion.

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

The company informed the CHMP that it intends to continue clinical trials with Movectro. Patients involved in such trials should contact their doctor if they have any questions. The company also stated that in all trials with Movectro, an independent data safety monitoring board monitors the safety and efficacy data on a regular basis and has the right and the duty to propose study discontinuation for reasons related to a lack of anticipated benefit or unacceptable safety risk.