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Questions and answers

Refusal of the marketing authorisation for Folotyn (pralatrexate)

On 19 January 2012, the Committee for Medicinal Products for Human Use (CHMP) adopted a negative opinion, recommending the refusal of the marketing authorisation for the medicinal product Folotyn, intended for the treatment of peripheral T-cell lymphoma.

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

What is Folotyn?

Folotyn is a medicine that contains the active substance pralatrexate. It was to be available as a solution for infusion (drip into a vein).

What was Folotyn expected to be used for?

Folotyn was expected to be used to treat adults with peripheral T-cell lymphoma, which is a cancer of the lymphatic system (a network of vessels that transport fluid from tissues through the lymph nodes and into the bloodstream).

Folotyn was designated an 'orphan medicine' (a medicine to be used in rare diseases) on 13 April 2007 for the treatment of peripheral T-cell lymphoma.

How is Folotyn expected to work?

Pralatrexate is an 'antimetabolite' medicine. In the body, it is expected to take the place of folic acid and attach to an enzyme called dihydrofolate reductase (DHFR). DHFR is necessary for the production of new DNA and proteins, which are required for cells to divide and multiply. By attaching to DHFR, pralatrexate is expected to block the enzyme's activity, inhibiting the division of the cancer cells and eventually killing them.

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What did the company present to support its application?

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

The company presented the results of one main study involving a total of 115 adults with peripheral T-cell lymphoma which kept coming back or did not respond to previous treatments. Patients were given Folotyn together with vitamin B12 and folic acid supplements (to compensate for the deficiency in these vitamins that may occur during Folotyn treatment). The main measure of effectiveness was based on the proportion of patients who responded to treatment. Response to treatment ranged from having improvements in symptoms to having no sign of cancer. In this study, Folotyn was not compared with any other treatment.

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

The CHMP was concerned that the main study was designed in a way that did not allow the Committee to assess the benefit of the medicine, particularly since Folotyn was not compared with any other treatment or placebo (a dummy treatment) in another group of patients. Moreover, there was no clear improvement seen in the condition of the patients, as the study looked at the patients' response to treatment but did not further allow the Committee to assess the effect on overall survival (how long the patients lived) or progression free survival (how long the patients lived without their disease getting worse).

At this point in time, the CHMP was of the opinion that there was insufficient evidence to establish the benefits of Folotyn in the treatment of peripheral T-cell lymphoma. Therefore the Committee concluded that the medicine's benefits did not outweigh its risks, and recommended that Folotyn 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 on patients currently included in clinical trials or compassionate use programmes with Folotyn. 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.

The summary of the opinion of the Committee for Orphan Medicinal Products for Folotyn can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/Rare disease designations.