



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Questions and answers

Refusal of the marketing authorisation for Folutyn (pralatrexate)

Outcome of re-examination

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 Folutyn, intended for the treatment of peripheral T-cell lymphoma. The company that applied for the authorisation is Allos Therapeutics 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 19 April 2012.

What is Folutyn?

Folutyn 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 Folutyn expected to be used for?

Folutyn was expected to be used to treat adults with peripheral T-cell lymphoma, which is a cancer of a type of white blood cell called T-cells.

Folutyn 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 Folutyn 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, which is 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.

What did the company present to support its application?

The effects of Folutyn 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 Folutyn together with vitamin B12 and folic acid supplements (to compensate for the deficiency in these vitamins that may occur during Folutyn 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 the disease to having no sign of cancer. In this study, Folutyn was not compared with any other treatment.

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

In January 2012, 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 Folutyn 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). The CHMP was of the opinion that there was insufficient evidence to establish the benefits of Folutyn in the treatment of peripheral T-cell lymphoma. Therefore, at that point in time, the CHMP was of the opinion that the benefits of Folutyn did not outweigh its risks and recommended that it be refused marketing authorisation.

During the re-examination in April 2012, the CHMP's concerns were not resolved. In particular, the Committee considered that the data submitted by the applicant were insufficient to establish the benefits of Folutyn in the treatment of peripheral T-cell lymphoma. The CHMP therefore 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 there are no consequences on patients currently included in clinical trials or compassionate use programmes with Folutyn. 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 Folutyn can be found on the Agency's website: ema.europa.eu/Find_medicine/Human_medicines/Rare_disease_designation.