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Questions and answers

Refusal of the marketing authorisation for Delamanid (delamanid)

On 25 July 2013, the Committee for Medicinal Products for Human Use (CHMP) adopted a negative opinion, recommending the refusal of the marketing authorisation for the medicinal product Delamanid, intended for the treatment of multi-drug resistant tuberculosis.

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

What is Delamanid?

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

What was Delamanid expected to be used for?

Delamanid was expected to be used to treat tuberculosis, a lung infection caused by the bacterium *Mycobacterium tuberculosis* (*M. tuberculosis*). Delamanid was expected to be used in patients with tuberculosis that is multi-drug resistant (resistant to at least isoniazid and rifampicin, two standard anti-tuberculosis medicines) and was to be used together with other medicines.

How is Delamanid expected to work?

The active substance in Delamanid, delamanid, is an antibiotic active against *M. tuberculosis*. Although the precise mode of action is unclear, Delamanid is known to interfere with the production of essential components of the cell walls of *M. tuberculosis* called methoxy-mycolic and keto-mycolic acid.

What did the company present to support its application?

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



The company presented results of one main study involving 481 patients with tuberculosis resistant to standard treatments. Patients in the study were given Delamanid or placebo (a dummy treatment) for two months, as an addition to their other treatments, and the main measure of effectiveness was the proportion of patients who no longer had the bacteria in their sputum.

After the main study had finished patients had the option to receive treatment with Delamanid for six months in an extension study. In addition, a majority of patients who entered the main study were also followed up in a registry study for up to 24 months after entering the main study.

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

The CHMP's main concern was that the benefits of Delamanid in the treatment of multi-drug resistant tuberculosis had not been sufficiently shown. The CHMP considered that the duration of treatment in the main study (two months) was too short to establish the effectiveness of delamanid in treating tuberculosis when added to other anti-tuberculosis medicines. As Delamanid was to be used for at least six months the data from two months' treatment could not be used to predict the effectiveness of delamanid when given for six months. In addition, the results of the extension and follow-up studies could not be used to support the longer term use of Delamanid as the studies included only those patients who had agreed to take part and who might therefore not be representative of the patients as a whole. Finally, the CHMP was of the view that it was not possible from the data submitted to determine the most appropriate dosing for Delamanid.

Therefore, at that point in time, the CHMP was of the opinion that the benefits of Delamanid did not outweigh its risks and recommended that it be refused marketing authorisation.

What consequences does this refusal have for patients in clinical trials?

The company informed the CHMP that there are no consequences for patients currently included in clinical trials with Delamanid.

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