



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Questions and answers

Withdrawal of the marketing authorisation application for Elmisol (levamisole)

On 29 May 2017, ACE Pharmaceuticals BV officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a marketing authorisation for Elmisol, for the treatment of nephrotic syndrome.

What is Elmisol?

Elmisol is a medicine containing the active substance levamisole hydrochloride. It was to be available as tablets (5, 10, 25 and 50 mg).

What was Elmisol expected to be used for?

Elmisol was to be used in children from 2 years of age to treat nephrotic syndrome. Nephrotic syndrome is a kidney disease that is marked by presence of large amounts of protein in the urine and results in fluid build-up in the body, with swelling (oedema), high blood pressure and weight gain. Elmisol was to be used in patients in whom symptoms kept coming back after responding to initial treatment with corticosteroid medicines (steroid sensitive nephrotic syndrome).

Elmisol was designated an 'orphan medicine' (a medicine to be used in rare diseases) on 28 October 2005 for nephrotic syndrome. Further information on the orphan designation can be found [here](#).

How does Elmisol work?

Levamisole has been used for many years to treat a variety of conditions, including worm infections and cancers. It is not completely understood how levamisole works in nephrotic syndrome, but it is known to affect the immune system (the body's natural defences). In patients with nephrotic syndrome, the immune system is believed to attack the kidney in error, resulting in leakage of proteins out of the kidney into urine.



Suppressing the immune system with corticosteroid medicines can bring the disease under control, but these medicines can have marked side effects and affect growth in young patients. Levamisole is thought to modify the action of the immune system, helping to control the disease and so reducing the amount of corticosteroids the patient needs.

What did the company present to support its application?

The company provided the results of studies on the quality, safety and effectiveness of the medicine, including information from the literature. The main study compared levamisole with placebo (a dummy treatment) in children with nephrotic syndrome that had been brought under control with corticosteroids. The study looked at the ability of the medicine to prevent the disease coming back.

How far into the evaluation was the application when it was withdrawn?

The application was withdrawn after the CHMP had evaluated the initial documentation provided by the company and formulated a list of questions. The company had not yet responded to the questions at the time of the withdrawal.

What was the recommendation of the CHMP at that time?

Based on the review of the data, at the time of the withdrawal, the CHMP had some concerns and was of the provisional opinion that Elmisol could not have been approved for the treatment of nephrotic syndrome. The Committee was concerned about some elements of the way the main study was carried out and whether these were in accordance with the requirements of good clinical practice (GCP). Other concerns included the possibility of dosing errors because the different strengths of tablet might get confused, the way the stability of the active substance in the tablets had been tested, and inadequate information on the medicine's actions, distribution in the body and risks of interactions with other medicines.

Therefore, at the time of the withdrawal, the CHMP was of the opinion that the benefits of Elmisol in the proposed indication did not outweigh its risks.

What were the reasons given by the company for withdrawing the application?

In its letter notifying the Agency of the withdrawal of the application, the company stated that it was withdrawing its application because there were concerns about the main study which would prevent its use to support the application.

The withdrawal letter is available [here](#).

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

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

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