



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Questions and answers

Withdrawal of the application for a change to the marketing authorisation for Translarna (ataluren)

On 6 March 2017, PTC Therapeutics International Limited officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for Translarna to be used to treat cystic fibrosis.

What is Translarna?

Translarna is a medicine used to treat patients aged 5 years and older with Duchenne muscular dystrophy who are able to walk. Duchenne muscular dystrophy is a genetic disease that gradually causes weakness and loss of muscle function. Translarna is used in the small group of patients whose disease is caused by a specific genetic defect (called a 'nonsense mutation') in the dystrophin gene.

Translarna has been authorised in the EU since July 2014. It contains the active substance ataluren and is available as granules (125, 250 and 1,000 mg) to be taken by mouth after mixing them with a liquid or semi-solid food.

What was Translarna expected to be used for?

Translarna was also expected to be used to treat cystic fibrosis caused by a nonsense mutation in the CFTR gene. Cystic fibrosis is a genetic disease that causes the build-up of thick secretions in the lungs and digestive system. Patients with this condition experience severe problems with breathing and digestion as well as recurring lung infections.

Translarna was designated an 'orphan medicine' (a medicine to be used in rare diseases) for cystic fibrosis on 27 May 2005. Further information on the orphan designation can be found [here](#).



How does Translarna work?

Cystic fibrosis is caused by a number of different mutations (changes) in the CFTR gene. These mutations all affect the proper working of the CFTR protein, which forms channels involved in the production of mucus in the lungs and digestive juices.

Translarna was to be used in patients whose cystic fibrosis is due to the presence of nonsense mutations in the CFTR gene. Nonsense mutations prematurely stop the production of a normal CFTR protein, leading to a shortened protein that does not function properly. Translarna was expected to work in these patients by enabling the protein-making apparatus in cells to move past the mutation, allowing the cells to produce a functional CFTR protein.

What did the company present to support its application?

The company presented the results of a main study involving 238 patients aged 6 years and above with cystic fibrosis caused by a nonsense mutation. The study compared Translarna with placebo (a dummy treatment). The main measure of effectiveness was the improvement in how well the lungs worked after 48 weeks of treatment, using a measurement called FEV₁. The study also looked at the number of flare-ups (episodes of worsened lung function associated with infection) that occurred.

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

The application was withdrawn after the CHMP had evaluated the documentation provided by the company and formulated lists of questions. After the CHMP had assessed the company's responses to the questions, there were still some unresolved issues.

What was the recommendation of the CHMP at that time?

Based on the review of the data and the company's response to the CHMP lists of questions, at the time of the withdrawal, the CHMP had concerns and was of the provisional opinion that Translarna could not have been approved for the treatment of cystic fibrosis caused by a nonsense mutation.

The main study failed to show that Translarna was more effective than placebo at improving lung function or reducing flare-ups in the overall study population. The company wanted to restrict use of Translarna to patients not using the inhaled antibiotic tobramycin to treat infections, since analysis of the data suggested that this antibiotic might reduce the effectiveness of Translarna. The CHMP was however concerned that the modest benefit seen in patients not using tobramycin might be a chance finding, and further data from an ongoing study would be needed to confirm this effect.

The CHMP was also concerned about harmful effects on the kidneys seen in patients treated with Translarna. These side effects appeared to be due to the fact that Translarna may worsen the effects on the kidney of certain antibiotics given by injection (aminoglycosides and vancomycin), which are important in treating infections in patients with cystic fibrosis. The Committee had requested additional information to demonstrate that these side effects could be reduced by temporarily stopping treatment with Translarna when these antibiotics are given.

Therefore, at the time of the withdrawal, the CHMP was of the opinion that the benefits of Translarna in the treatment of cystic fibrosis 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 application, the company stated that it was withdrawing the application because results of the ongoing confirmatory study, which became available in March 2017, failed to show that Translarna has beneficial effects on lung function and flare-ups in patients with cystic fibrosis caused by a nonsense mutation.

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

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

The company informed the CHMP that clinical trials with Translarna in cystic fibrosis are being terminated.

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

What is happening with Translarna for the treatment Duchenne muscular dystrophy?

There are no consequences on the use of Translarna in its authorised indication.

The full European Public Assessment Report for Translarna can be found on the Agency's website: ema.europa.eu/Find_medicine/Human_medicines/European_public_assessment_reports.