21 February 2014
EMA/36356/2014/rev.1
EMEA/H/C/002720

Update of 21 February 2014:

The applicant for Translarna has requested a re-examination of the CHMP's January 2014 opinion. Upon receipt of the grounds of the request, the CHMP will re-examine its opinion and issue a final recommendation.

Questions and answers

Refusal of the marketing authorisation for Translarna (ataluren)

On 23 January 2014, the Committee for Medicinal Products for Human Use (CHMP) adopted a negative opinion, recommending the refusal of the marketing authorisation for the medicinal product Translarna, intended for the treatment of Duchenne muscular dystrophy.

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

What is Translarna?

Translarna is a medicine that contains the active substance ataluren. It was to be available as granules for making a suspension to be taken by mouth.

What was Translarna expected to be used for?

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

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Translarna was designated an 'orphan medicine' (a medicine to be used in rare diseases) on 27 May 2007 for the treatment of Duchenne muscular dystrophy. For more information, see here.

How is Translarna expected to work?

Patients with Duchenne muscular dystrophy lack normal dystrophin, a protein found in muscles. Because this protein helps to protect muscles from injury as muscles contract and relax, in patients with Duchenne muscular dystrophy the muscles become damaged and eventually stop working.

Duchenne muscular dystrophy can be caused by a number of genetic abnormalities. Translarna was expected to be used in patients whose disease is due to the presence of certain defects (called nonsense mutations) in the dystrophin gene which prematurely stop the production of a normal dystrophin protein, leading to a shortened dystrophin protein that does not function properly. Translarna is thought to work in these patients by enabling the protein-making apparatus in cells to skip over the defect, allowing the cells to produce a functional dystrophin protein.

What did the company present to support its application?

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

The company presented the results of one main study in 174 patients with Duchenne muscular dystrophy, where Translarna was compared with placebo (a dummy treatment). The main measure of effectiveness was the change in the distance the patient could walk in six minutes after 48 weeks of treatment.

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

The CHMP noted that the main study failed to show that patients taking Translarna could walk in six minutes a greater distance than patients taking placebo. Although the company performed additional analyses of the data, the CHMP considered that these were insufficient to provide enough evidence of effectiveness. When other measures of effectiveness were considered, including those directly linked to patients' daily activities, these provided only limited supportive evidence of the beneficial effects of Translarna. Finally, insufficient data had been provided to determine how the medicine works in the body and how its effects change with the dose.

Therefore, at that point in time, the CHMP was of the opinion that the benefits of Translarna did not outweigh its risks and recommended that it 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 for patients currently in clinical trials with ataluren: patients will continue to receive ataluren in the ongoing clinical trials and patient enrollment in the confirmatory trial will continue as planned.

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.