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Translarna (*ataluren*)

An overview of Translarna and why it is authorised in the EU

What is Translarna and what is it used for?

Translarna is a medicine that is used to treat patients aged 2 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.

Duchenne muscular dystrophy is rare, and Translarna was designated an 'orphan medicine' (a medicine used in rare diseases) on 27 May 2005. Further information on the orphan designation can be found here: ema.europa.eu/Find medicine/Human medicines/Rare disease designation

How is Translarna used?

Translarna can only be obtained with a prescription and treatment should be started by a specialist doctor experienced in the management of Duchenne/Becker muscular dystrophy.

Before starting treatment with Translarna, patients will have a genetic test to confirm that their disease is due to a nonsense mutation and that they are therefore suitable for treatment with Translarna.

Translarna is available as granules (125, 250 and 1,000 mg) to be taken by mouth after mixing them with liquid or semi-solid food (such as yogurt). Translarna is taken three times a day, and the recommended dose is 10 mg/kg (10 mg per kilogram body weight) in the morning, 10 mg/kg at midday and 20 mg/kg in the evening (making a total daily dose of 40 mg/kg).

For more information about using Translarna, see the package leaflet or contact a doctor or pharmacist.

How does Translarna 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.

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Duchenne muscular dystrophy can be caused by a number of genetic abnormalities. Translarna is for use 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 works in these patients by enabling the protein-making apparatus in cells to move past the defect, allowing the cells to produce a functional dystrophin protein.

What benefits of Translarna have been shown in studies?

In one main study, involving 174 patients aged 5 to 20 years with Duchenne muscular dystrophy who were able to walk, two doses of Translarna (40 mg/kg daily and 80 mg/kg daily) were 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.

Although an initial analysis of the results of all the data from the study did not show a significant difference in the distances patients in the Translarna and placebo groups could walk, further analyses indicated that walking ability worsened to a lesser extent with 40 mg/kg daily Translarna than with placebo: after 48 weeks of treatment patients receiving 40 mg/kg daily Translarna could walk on average 32 metres more than those given placebo. The effect was more pronounced in a subgroup of patients whose ability to walk was worsening, where patients taking 40 mg/kg daily Translarna could walk on average 50 metres more than those taking placebo. The beneficial effect of the lower dose was also supported by improvements in other measures of effectiveness, including those directly linked to patients' daily activities. No improvement was seen with the higher dose (80 mg/kg daily).

A further study in 230 patients aged 7 to 14 years with worsening walking ability was completed after initial approval, but its results were considered inconclusive. However, data indicated that Translarna had a positive effect on different measures such as time to run or walk 10 metres, time to climb up and down 4 steps and time to loss of walking ability. In both studies, the beneficial effects of Translarna seemed more evident in patients with moderate decline of their disease.

A small study in children aged 2 to 5 years with Duchenne muscular dystrophy found that the usual dose of Translarna 40 mg/kg daily was sufficient. Translarna seemed effective on an assessment of physical activity in 12 patients when compared with past records of 11 patients of similar age who had not been treated with Translarna.

What are the risks associated with Translarna?

The most common side effects with Translarna (which may affect more than 5 in 100 people) are vomiting, diarrhoea, nausea (feeling sick), headache, stomach ache and flatulence.

Translarna must not be used at the same time as aminoglycoside antibiotics given by injection or infusion (drip) into a vein.

For the full list of side effects and restrictions of Translarna, see the package leaflet.

Why is Translarna authorised in the EU?

The European Medicines Agency decided that Translarna's benefits are greater than its risks and it can be authorised for use in the EU.

Despite the need for further data, the Agency considered that the evidence suggests that Translarna slows the progression of the disease and that its safety profile is not of major concern. The Agency

acknowledged that patients with Duchenne muscular dystrophy have an unmet need for treatment of this serious condition.

Translarna has been given 'conditional authorisation'. This means that there is more evidence to come about the medicine, which the company is required to provide. Every year, the Agency will review any new information that becomes available and this overview will be updated as necessary.

What information is still awaited for Translarna?

Since Translarna has been given conditional authorisation, the company that markets it will provide results of a new study comparing Translarna with placebo in order to confirm its effectiveness and safety.

What measures are being taken to ensure the safe and effective use of Translarna?

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of Translarna have been included in the summary of product characteristics and the package leaflet.

As for all medicines, data on the use of Translarna are continuously monitored. Side effects reported with Translarna are carefully evaluated and any necessary action taken to protect patients.

Other information about Translarna

Translarna received a conditional marketing authorisation valid throughout the EU on 31 July 2014.

Further information on Translarna can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European public assessment reports.

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