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Public summary of opinion on orphan designation

Cyclo-L-glycyl-L-2-allylproline for the treatment of Phelan-McDermid syndrome

On 6 January 2021, orphan designation EU/3/20/2394 was granted by the European Commission to Dlrc Pharma Services Limited, Ireland, for cyclo-L-glycyl-L-2-allylproline (also known as NNZ-2591) for the treatment of Phelan-McDermid syndrome.

What is Phelan-McDermid syndrome?

Phelan-McDermid syndrome is a disorder that mainly affects the brain. It is caused by a change in the gene needed to make a protein called SHANK3 that is essential for normal brain development. Children with this condition often have delayed development, intellectual disability, severe speech defects, autistic symptoms, and problems with movement. Other symptoms include seizures (fits) and gastrointestinal problems.

Phelan-McDermid syndrome is a long-term debilitating condition due to intellectual disability, speech defects, seizures, and gastrointestinal problems.

What is the estimated number of patients affected by the condition?

At the time of designation, Phelan-McDermid syndrome affected approximately 0.8 in 10,000 people in the European Union (EU). This was equivalent to a total of around 42,000 people*, and is below the ceiling for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and the knowledge of the Committee for Orphan Medicinal Products (COMP).

What treatments are available?

At the time of designation, no medicines were authorised in the EU for the treatment of Phelan-McDermid syndrome. Treatments were aimed at reducing symptoms of the disease such as physical and speech therapy, medicines for epilepsy and gastrointestinal problems.

*For the purpose of the designation, the number of patients affected by the condition is estimated and assessed on the basis of data from the European Union, Iceland, Liechtenstein, Norway and the United Kingdom. This represents a population of 519,200,000 (Eurostat 2020).

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How is this medicine expected to work?

In patients with Phelan-McDermid syndrome, lack of SHANK3 means the brain cannot produce proteins needed to form synapses, the communication connections between nerve cells. The medicine is similar to a part of IGF-1, a substance in the brain that is essential for synapse formation and brain development. The medicine controls IGF-1 levels and also prevents inflammation in the brain. This is expected to help the brain form new synapses and keep them working, thereby reducing some symptoms of the condition.

What is the stage of development of this medicine?

The effects of the medicine have been evaluated in experimental models.

At the time of submission of the application for orphan designation, no clinical trials with the medicine in patients with Phelan-McDermid syndrome had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for the treatment of Phelan-McDermid syndrome. Orphan designation of the medicine had been granted in the United States for this condition.

In accordance with Regulation (EC) No 141/2000, the COMP adopted a positive opinion on 3 December 2020, recommending the granting of this designation.

Opinions on orphan medicinal product designations are based on the following three criteria:

- the seriousness of the condition;
- the existence of alternative methods of diagnosis, prevention or treatment;
- either the rarity of the condition (affecting not more than 5 in 10,000 people in the EU) or insufficient returns on investment.

Designated orphan medicinal products are products that are still under investigation and are considered for orphan designation on the basis of potential activity. An orphan designation is not a marketing authorisation. As a consequence, demonstration of quality, safety and efficacy is necessary before a product can be granted a marketing authorisation.

For more information

Contact details of the current sponsor for this orphan designation can be found on EMA website.

For contact details of patients' organisations whose activities are targeted at rare diseases see:

- Orphanet, a database containing information on rare diseases, which includes a directory of patients' organisations registered in Europe;
- European Organisation for Rare Diseases (EURORDIS), a non-governmental alliance of patient organisations and individuals active in the field of rare diseases.