



EUROPEAN MEDICINES AGENCY
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Public summary of opinion on orphan designation

L-pyroglutamyl-L-asparaginyl-L-prolyl-D-tyrosyl-D-tryptophan amide for the treatment of amyotrophic lateral sclerosis

On 13 November 2020, orphan designation EU/3/20/2358 was granted by the European Commission to Neuropath Therapeutics Limited, Ireland, for L-pyroglutamyl-L-asparaginyl-L-prolyl-D-tyrosyl-D-tryptophan amide (also known as JAK4D) for the treatment of amyotrophic lateral sclerosis.

What is amyotrophic lateral sclerosis?

Amyotrophic lateral sclerosis (ALS) is a progressive disease of the nervous system, where nerve cells in the brain and spinal cord that control voluntary movement gradually deteriorate, causing loss of muscle function and paralysis. The symptoms of ALS depend on which muscles weaken first, and include loss of balance, loss of control of hand and arm movement, and difficulty speaking, swallowing and breathing. ALS usually starts in mid-life and men are more likely to develop the disease than women.

ALS is a debilitating and life-threatening disease because of the gradual loss of function and its paralysing effect on muscles used for breathing, which usually leads to death from respiratory failure.

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

At the time of designation, amyotrophic lateral sclerosis affected approximately 1 in 10,000 people in the European Union (EU). This was equivalent to a total of around 52,000 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, riluzole was authorised in the EU to treat ALS. Patients also received supportive treatment to relieve the symptoms of the disease, such as physiotherapy and breathing support.

*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).



The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with amyotrophic lateral sclerosis because studies in experimental models have found that the medicine slows down the reduction in muscle function. This assumption will need to be confirmed at the time of marketing authorisation, in order to maintain the orphan status.

How is this medicine expected to work?

The medicine activates receptors (targets) for thyrotropin-releasing hormone in brain cells. The exact way the medicine works in the treatment of ALS is not clear, yet one way it is thought to act is through protecting vulnerable nerve cells from injury caused by excessive glutamate and free radicals. This is expected to slow down the worsening ability to control muscles in patients with ALS.

What is the stage of development of this medicine?

At the time of submission of the application for orphan designation, the evaluation of the effects of the medicine in experimental models was ongoing.

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

At the time of submission, the medicine was not authorised anywhere in the EU for the treatment of ALS or designated as an orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000, the COMP adopted a positive opinion on 8 October 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.