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Public summary of opinion on orphan designation

H-Leu-Pro-Pro-Leu-Pro-Tyr-Pro-OH for the treatment of amyotrophic lateral sclerosis

On 16 December 2019, orphan designation EU/3/19/2231 was granted by the European Commission to AdRes EU B.V., Netherlands, for H-Leu-Pro-Pro-Leu-Pro-Tyr-Pro-OH (also known as IPL344) 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 exact causes are unknown but are believed to include genetic and environmental factors. 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?

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.

*Disclaimer: 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 (EU 28), Norway, Iceland and Liechtenstein. This represents a population of 518,400,000 (Eurostat 2019).

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The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with ALS, because early data showed that the disease progressed more slowly in patients treated with the medicine than in those given standard treatments.

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?

In patients with ALS, certain activities within cells which make up the 'PI3K-Akt signalling pathway' (a mechanism within cells which is important in regulating their growth and survival) are disrupted, increasing the likelihood of the cells being damaged.

This medicine is a short string of amino acids (the building blocks of proteins) that helps increase these activities, thereby protecting cells from damage. This action is expected to reduce the death of nerve cells and thus slow down the progression of the disease.

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, clinical trials with the medicine in patients with ALS were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for the treatment of ALS. 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 7 November 2019, 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

Sponsor's contact details:

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.

Translations of the active ingredient and indication in all official EU languages[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	H-Leu-Pro-Pro-Leu-Pro-Tyr-Pro-OH	Treatment of amyotrophic lateral sclerosis
Bulgarian	H-Leu-Pro-Pro-Leu-Pro-Tyr-Pro-OH	Лечение на амиотрофична латерална склероза
Croatian	H-Leu-Pro-Pro-Leu-Pro-Tir-Pro-OH	Liječenje amiotrofične lateralne skleroze
Czech	H-Leu-Pro-Pro-Leu-Pro-Tyr-Pro-OH	Léčba amyotrofické laterální sklerózy (ALS)
Danish	H-Leu-Pro-Pro-Leu-Pro-Tyr-Pro-OH	Behandling af amyotrofisk lateralsklerose
Dutch	H-Leu-Pro-Pro-Leu-Pro-Tyr-Pro-OH	Behandeling van amyotrofe lateraalsclerose
Estonian	H-Leu-Pro-Pro-Leu-Pro-Tyr-Pro-OH	Amüotroofilise lateraalskleroosi ravi
Finnish	H-Leu-Pro-Pro-Leu-Pro-Tyr-Pro-OH	Amyotrofisen lateraaliskleroosin hoito
French	H-Leu-Pro-Pro-Leu-Pro-Tyr-Pro-OH	Traitement de la sclérose latérale amyotrophique
German	H-Leu-Pro-Pro-Leu-Pro-Tyr-Pro-OH	Behandlung der amyotrophen Lateralsklerose
Greek	H-Leu-Pro-Pro-Leu-Pro-Tyr-Pro-OH	Θεραπεία πλάγιας μυοατροφικής σκλήρυνσης
Hungarian	H-Leu-Pro-Pro-Leu-Pro-Tyr-Pro-OH	Amyotrophiás lateral sclerosis kezelése
Italian	H-Leu-Pro-Pro-Leu-Pro-Tir-Pro-OH	Trattamento della sclerosi laterale amiotrofica
Latvian	H-Lei-Pro-Pro-Lei-Pro-Tir-Pro-OH	Amiotrofiskās laterālās sklerozes ārstēšana
Lithuanian	H-Leu-Pro-Pro-Leu-Pro-Tyr-Pro-OH	Šoninės amiotrofinės sklerozės gydymas
Maltese	H-Leu-Pro-Pro-Leu-Pro-Tyr-Pro-OH	Kura tas-sklerosi laterali amjotrofika
Polish	H-Leu-Pro-Pro-Leu-Pro-Tyr-Pro-OH	Leczenie stwardnienia bocznego zanikowego
Portuguese	H-Leu-Pro-Pro-Leu-Pro-Tir-Pro-OH	Tratamento da esclerose lateral amiotrófica
Romanian	H-Leu-Pro-Pro-Leu-Pro-Tyr-Pro-OH	Tratamentul sclerozei laterale amiotrofice
Slovak	H-Leu-Pro-Pro-Leu-Pro-Tyr-Pro-OH	Liečba amyotrofickej laterálnej sklerózy
Slovenian	H-Lev-Pro-Pro-Lev-Pro-Tir-Pro-OH	Zdravljenje amiotrofične lateralne skleroze
Spanish	H-Leu-Pro-Pro-Leu-Pro-Tir-Pro-OH	Tratamiento de la esclerosis lateral amiotrófica
Swedish	H-Leu-Pro-Pro-Leu-Pro-Tyr-Pro-OH	Behandling av amyotrofisk lateralskleros
Norwegian	H-Leu-Pro-Pro-Leu-Pro-Tyr-Pro-OH	Behandling av amyotrofisk lateralsklerose
Icelandic	H-Leu-Pro-Pro-Leu-Pro-Tyr-Pro-OH	Meðferð við blandaðri hreyfitaugahrörnun

[1] At the time of designation