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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

6-ethynyl-1-(pentan-3-yl)-1H-imidazo[4,5-b]pyrazin-2(3H)-one for the treatment of amyotrophic lateral sclerosis

First publication	4 April 2012
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Disclaimer

Please note that revisions to the Public Summary of Opinion are purely administrative updates. Therefore, the scientific content of the document reflects the outcome of the Committee for Orphan Medicinal Products (COMP) at the time of designation and is not updated after first publication.

On 5 March 2012, orphan designation (EU/3/12/970) was granted by the European Commission to ICON Clinical Research UK Limited, United Kingdom, for 6-ethynyl-1-(pentan-3-yl)-1H-imidazo[4,5-b]pyrazin-2(3H)-one for the treatment of amyotrophic lateral sclerosis.

The sponsorship was transferred to Pharma Gateway AB, Sweden, in February 2015.

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. This causes loss of muscle function and paralysis. The exact causes are unknown but are believed to include genetic and environmental factors. The symptoms of ALS vary depending on which muscles weaken first, and include loss of balance, loss of control of hand and arm movement, 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 long-term 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 due to respiratory failure.

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

At the time of designation, ALS affected less than 1 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 51,000 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, medicines authorised in the EU to treat ALS included riluzole. Patients also received supportive treatment to temporarily relieve the symptoms of the disease, such as physiotherapy and speech therapy.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with ALS because it works in a different way to the existing treatment and early studies in experimental models show that it might improve the muscle function of patients with this condition. 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 is expected to improve muscle function, which is damaged in ALS patients, by increasing the contraction of the muscle. Muscle contraction occurs when a nerve sends a signal to the muscles causing an influx of calcium into muscle cells. The role of calcium is to activate a protein called troponin which is needed for muscle contraction to start.

The medicine is expected to bind to troponin and make it more sensitive to calcium. This means that the muscle can contract with increased muscle strength after nerve stimulation. This is expected to improve the symptoms of ALS.

What is the stage of development of this medicine?

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

At the time of submission of the application for orphan designation, clinical trials with this medicine in patients with ALS were ongoing.

At the time of submission, this medicine was not authorised anywhere in the EU for the treatment of ALS. Orphan designation had been granted in the United States of America for the treatment of ALS.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 11 January 2012 recommending the granting of this designation.

[*]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 27), Norway, Iceland and Liechtenstein.
At the time of designation, this represented a population of 509,000,000 (Eurostat 2012).

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:

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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	6-ethynyl-1-(pentan-3-yl)-1H-imidazo[4,5-b]pyrazin-2(3H)-one	Treatment of amyotrophic lateral sclerosis
Bulgarian	6-етинил-1-(пентан-3-ил)-1H-имидазо[4,5-b]пиразин-2(3H)- он	Лечение на амиотрофична латерална склероза
Croatian	6-etinil-1-(pentan-3-il)-1H-imidazo[4,5-b]pirazin-2(3H)-on	Liječenje amiotrofične lateralne skleroze
Czech	6-ethynyl-1-(pentan-3-yl)-1H-imidazo[4,5-b]pyrazin-2(3H)-on	Léčba amyotrofické laterální sklerózy
Danish	6-ethynyl-1-(pentan-3-yl)-1H-imidazo[4,5-b]pyrazin-2(3H)-on	Behandling af amyotrofisk lateralsklerose
Dutch	6-ethynyl-1-(pentaan-3-yl)-1H-imidazo[4,5-b]pyrazine-2(3H)-on	Behandeling van amyotrofe lateraalsclerose
Estonian	6-etünüül-1-(pentaan-3-üül)-1H-imidaso[4,5-b]pürasiin-2(3H)-on	Amüotroofilise lateraalskleroosi ravi
Finnish	6-etynyyli-1-(pentan-3-yyli)-1H-imidatso[4,5-b]pyratsin-2(3H)-oni	Amyotrofisen lateraaliskleroosin hoito
French	6-éthynyl-1-(pentan-3-yl)-1H-imidazo[4,5-b]pyrazine-2(3H)-one	Traitement de la sclérose latérale amyotrophique
German	6-Ethinyl-1-(pentan-3-yl)-1H-imidazo[4,5-b]pyrazin-2(3H)-on	Behandlung der amyotrophen Lateralsklerose
Greek	6-αιθινυλο-1-(πεντανό-3-υλο)-1H-ιμιδαζό[4,5-b]πυραζίνη-2(3H)- όνη	Θεραπεία πλάγιας μυοατροφικής σκλήρυνσης
Hungarian	6-etinil-1-(pentán-3-il)-1H-imidazo[4,5-b]pirazin-2(3H)-on	Amyotrophiás lateral sclerosis kezelése
Italian	6-etinil-1-(pentan-3-il)-1H-imidazo[4,5-b]pirazina-2(3H)-one	Trattamento della sclerosi laterale amiotrofica
Latvian	6-etinil-1-(pentān-3-il)-1H-imidazo[4,5-b]pirazīn-2(3H)-ons	Amiotrofiskās laterālās sklerozes ārstēšana
Lithuanian	6-etinil-1-(pentan-3-il)-1H-imidazo[4,5-b]pirazin-2(3H)-onas	Šoninės amiotrofinės sklerozės gydymas
Maltese	6-ethynyl-1-(pentan-3-yl)-1H-imidazo[4,5-b]pyrazin-2(3H)-one	Kura tas-sklerosi laterali amjotrofika
Polish	6-etynylo-1-(pentan-3-yl)-1H-imidazo[4,5 b]pyrazyno-2(3H)-on	Leczenie stwardnienia bocznego zanikowego
Portuguese	6-etinil-1-(pentan-3-il)-1H-imidazo[4,5-b]pirazin-2(3H)-octanona	Tratamento da esclerose lateral amiotrófica
Romanian	6-etinil-1-(pentan-3-il)-1H-imidazo[4,5-b]pirazin-2(3H)-onă	Tratamentul sclerozei laterale amiotrofice
Slovak	6-etinyl-1-(pentán-3-yl)-1H-imidazo[4,5-b]pyrazín-2(3H)-ón	Liečba amyotrofickej laterálnej sklerózy

[1] At the time of transfer of sponsorship

Language	Active ingredient	Indication
Slovenian	6-etinil-1-(pentan-3-il)-1H-imidazo[4,5-b]pirazin-2(3H)-on	Zdravljenje amiotrofične lateralne skleroze
Spanish	6-etinil-1-(pentano-3-il)-1H-imidazo[4,5-b]pirazin-2(3H)-ona	Tratamiento de la esclerosis lateral amiotrófica
Swedish	6-etynyl-1-(pentan-3-yl)-1H-imidazo[4,5-b]pyrazin-2(3H)-on	Behandling av amyotrofisk lateralskleros
Norwegian	6-etynyl-1-(pentan-3-yl)-1H-imidazo[4,5-b]pyrazin-2(3H)-on	Лечение на амиотрофична латерална склероза
Icelandic	6-eþýnýl-1-(pentan-3-ýl)-1H-ímídasól[4,5-b]pýrasín-2(3H)- ón	Léčba amyotrofické laterální sklerózy