2 April 2013
EMA/COMP/105652/2013
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Cyclo[L-alanyl-L-seryl-L-isoleucyl-L-prolyl-L-prolyl-L-glutaminyl-L-lysyl-L-tyrosyl-D-prolyl-L-prolyl-(2S)-2-aminodecanoyl-L-alpha-glutamyl-L-threonyl] acetate salt for the treatment of congenital alpha-1 antitrypsin deficiency

On 20 March 2013, orphan designation (EU/3/13/1114) was granted by the European Commission to Polyphor UK, United Kingdom, for cyclo[L-alanyl-L-seryl-L-isoleucyl-L-prolyl-L-prolyl-L-glutaminyl-L-lysyl-L-tyrosyl-D-prolyl-L-prolyl-(2S)-2-aminodecanoyl-L-alpha-glutamyl-L-threonyl] acetate salt for the treatment of congenital alpha-1 antitrypsin deficiency.

What is congenital alpha 1-antitrypsin deficiency?

Congenital alpha-1 antitrypsin deficiency is an inherited disease that is characterised by a deficiency of a protein called 'alpha-1 proteinase inhibitor' or 'alpha-1 antitrypsin' (AAT). One of the functions of AAT is to protect the lungs from attack by an enzyme called neutrophil elastase. Neutrophil elastase is produced by white blood cells in response to infection or irritants to digest damaged tissue in the lungs. In patients lacking AAT, neutrophil elastase activity in the lungs is excessive, causing destruction of tissue, and resulting in a lung disease called emphysema, in which the patient experiences symptoms such as shortness of breath, coughing and wheezing.

Congenital AAT deficiency is a debilitating disease that is long lasting and can be life threatening due to the worsening of lung function and lung infections that occur.

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

At the time of designation, congenital AAT deficiency affected approximately 2.6 in 10,000 people in the European Union (EU). This was equivalent to a total of around 132,000 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).

[*]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. This represents a population of 509,000,000 (Eurostat 2013).

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What treatments are available?

At the time of orphan drug designation, intravenous AAT was authorised in the EU for treating emphysema caused by congenital AAT deficiency.

The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with congenital AAT deficiency based on its mechanism of action, which may complement the action of intravenous AAT and could be used in combination with current treatment. In addition the product will be developed as an inhalation therapy which may not require weekly visits to clinic, as opposed to the currently used intravenous therapy. These assumptions 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?

This medicine comprises 13 amino acids in a form that can be breathed directly into the lungs. In the lungs, the medicine blocks the action of neutrophil elastase by attaching to the sites through which elastase exerts its activity. By reducing elastase activity, the medicine is expected to reduce or slow down the destruction of the lung tissue, thereby improving the symptoms of the disease.

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 medicinal product in experimental models was ongoing.

At the time of submission, no clinical trials with the medicinal product in patients with congenital AAT deficiency had been started.

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

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 6 February 2013 recommending the granting of this designation.

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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	Cyclo[L-alanyl-L-seryl-L-isoleucyl-L-prolyl-L-prolyl-L-glutaminyl-L-lysyl-L-tyrosyl-D-prolyl-L-prolyl-(2S)-2-aminodecanoyl-L-alpha-glutamyl-L-threonyl] acetate salt	Treatment of congenital alpha-1 antitrypsin deficiency
Bulgarian	Цикло[L-аланил-L–серил-L-изолевцил-L-пролил-L- пролил-L-глутаминил-L-лизил-L-тирозил-D- пролил-L-пролил-(2S)-2-аминодеканоил-L-алфа-глутамил-L-треонил] ацетат	Лечение на вроден алфа-1 антитрипсинов дефицит
Czech	Cyclo[L-alanyl-L-seryl-L-isoleucyl-L-prolyl-L-prolyl-L-glutaminyl-L-lysyl-L-tyrosyl-D-prolyl-L-prolyl-(2S)-2-aminodecanoyl-L-alpha-glutamyl-L-threonyl] acetate salt	Léčba vrozeném deficitu alfa-1 antitrypsinu
Danish	Cyclo[L-alanyl-L-seryl-L-isoleucyl-L-prolyl-L-prolyl-L-glutaminyl-L-lysyl-L-tyrosyl-D-prolyl-L-prolyl-(2S)-2-aminodecanoyl-L-alfa-glutamyl-L-threonyl] acetat salt	Behandling af medfødt alfa-1 antitrypsinmangel
Dutch	Cyclo[L-alanyl-L-seryl-L-isoleucyl-L-prolyl-L-prolyl-L-glutaminyl-L-lysyl-L-tyrosyl-D-prolyl-L-prolyl-(2S)-2-aminodecanoyl-L-alpha-glutamyl-L-threonyl] acetaatzout	Behandeling van aangeboren alfa-1 antitrypsine deficiëntie
Estonian	Tsüklo[L-alanüül-L-serüül-L-isoleutsüül-L-prolüül-L-prolüül-L-glutaminüül-L-lüsüül-L-türosüül-D-prolüül-L-prolüül-(2S)-2-aminodekanoüül-L-alfa-glutamüül-L-treonüül] atsetaatsool	Kaasasündinud alfa-1 antitrüpsiini puudulikkuse ravi
Finnish	Syklo[L-alanyyli-L-seryyli-L-isoleusyyli-L-prolyyli-L-prolyyli-L-glutaminyyli-L-lysyyli-L-tyrosyyli-D-prolyyli-L-prolyyli-(2S)-2-aminodekanoyli-L-alfa-glutamyyli-L-treonyyli] asetaattisuola	Synnynnäisen alfa-1 antitrypsiinin puutteen hoito
French	Cyclo[L-alanyl-L-seryl-L-isoleucyl-L-prolyl-L-prolyl-L-glutaminyl-L-lysyl-L-tyrosyl-D-prolyl-L-prolyl-(2S)-2-aminodécanoyl-L-alpha-glutamyl-L-thréonyl], sel d'acétate	Traitement du déficit congénital en alpha-1 antitrypsine
German	Cyclo[L-alanyl-L-seryl-L-isoleucyl-L-prolyl-L-prolyl-L-glutaminyl-L-lysyl-L-tyrosyl-D-prolyl-L-prolyl-(2S)-2-aminodecanoyl-L-alpha-glutamyl-L-threonyl] acetat salz	Behandlung von erblichem Alpha-1 Antitrypsinmangel
Greek	Κύκλο [L-αλανυλο-L-σερυλο-L-ισολευκυλο-L-προλυλο-L-προλυλο-L-γλουταμινυλο-L-λυσυλο-L-τυρόσυλο-D-προλυλο-L-προλυλο-(2S)-2-αμινοδεκανοϋλο-L-α-γλουταμυλο-L-θρεονυλο] οξικό άλας	Θεραπεία της συγγενούς ανεπάρκειας άλφα-1 αντιθρυψίνης

[1] At the time of designation

Language	Active ingredient	Indication
Hungarian	Ciklo[L-alanil-L-szeril-l-izoleucil-L-prolil-L-prolil-L-glutaminil-L-lizil-L-tirozil-D-prolil-L-prolil-(2S)-2-aminodekanoil-L-alfa-glutamil- treonil] acetát	Kongenitális alfa-1 antitripszin hiány kezelése
Italian	Ciclo[L-alanil-L-seril-L-isoleucil-L-prolil-L-prolil-L-glutaminil-L-lisil-L-tyrosil-D-prolil-L-prolil-(2S)-2-aminodecanoil-L-alfa-glutamil-L-threonil] sale acetato	Trattamento del deficit congenito di alfa-1 antitripsina
Latvian	Ciclo[L-alanil-L-seril-L-izoleicil-L-prolil-L-prolil-L-glutaminil-L-lizil-L-tirozil-D-prolil-L-prolil-(2S)-2-aminodekanoil-L-alfa-glutamil-L-treonil] acetāta sāls	Iedzimta alfa -1 antitripsīna deficīta ārstēšana
Lithuanian	Ciklo[L-alanil-L-seril-L-izoleucil-L-prolil-L-prolil-L-glutaminil-L-lizil-L-tirozil-D-prolil-L-prolil-(2S)-2-aminodekanoil-L-alfa-glutamil-L-treonil] acetato druska	Įgimtas alfa -1 antitripsino deficito gydymas
Maltese	Melħ ta' cyclo[L-alanyl-L-seryl-L-isoleucyl-L-prolyl-L-prolyl-L-glutaminyl-L-lysyl-L-tyrosyl-D-prolyl-L-prolyl-(2S)-2-aminodecanoyl-L-alpha-glutamyl-L-threonyl] acetate	Kura tan-nuqqas konġenitu ta' l-alpha-1 antitrypsin
Polish	Cyklo[L-alanylo-L-serylo-L-izoleucylo-L-prolino-L-prolino-L-glutamylo-L-lizylo-L-tyrozynylo-D-prolino-L-prolino-(2S)-2-aminodekanoilo-L-alfa-glutamylo-L-treonylu] octan	Leczenie wrodzonego niedoboru alfa-1 antytrypsyny
Portuguese	Ciclo[L-alanil-L-seril-L-isoleucil-L-prolil-L-prolil-L-glutaminil-L-lisil-L-tirosil-D-prolil-L-prolil-(2S)-2-aminodecanoil-L-alpha-glutamil-L-threonil] acetate salt	Tratamento da deficiência congénita em antitripsina alfa-1
Romanian	Ciclo[L-alanil-L-seril-L-isoleucil-L-prolil-L-prolil-L-glutaminil-L-lisil-L-tirosil-D-prolil-L-prolil-(2S)-2-aminodecanoil-L-alpha-glutamil-L-threonil] acetat	Tratamentul deficitului congenital de alfa-1 antitripsină
Slovak	Cyklo[L-alanyl-L-seryl-L-izoleucyl-L-prolyl-L-prolyl-L-glutaminyl-L-lyzyl-L-tyrozyl-D-prolyl-L-prolyl-(2S)-2-aminodekanoyl-L-alfa-glutamyl-L-treonyl] acetátová soľ	Liečbadeficitu alfa-1 antitrypsínu
Slovenian	Ciclo[L-alanil-L-seril-L-izoleucil-L-prolil-L-prolil-L-glutaminil-L-lizil-L-tirosil-D-prolil-L-prolil-(2S)-2-aminodecanoil-L-alpha-glutamil-L-threonil] acetat	Zdravljenje kongenitalnega pomanjkanja alfa-1 antitripsina
Spanish	Acetato de sal de ciclo[L-alanil-L-seril-L-isoleucil-L-proliil-L-prolil-L-glutaminil-L-lisil-L-tirosil-D-prolil-L-prolil-(2S)-2-aminodecanoil-L-alfa-glutamil-L-treonil]	Tratamiento del déficit congénito de alfa-1 antitripsina
Swedish	Cyklo[L-alanyl-L-seryl-L-isoleucyl-L-prolyl-L-prolyl-L-glutaminyl-L-lysyl-L-tyrosyl-D-prolyl-L-prolyl-(2S)-2-aminodecanoyl-L-alfa-glutamyl-L-threonyl] acetate salt	Behandling av kongenital alpha-1 antitrypsin brist

Language	Active ingredient	Indication
Norwegian	Syklo[L-alanyl-L-seryl-L-isoleucyl-L-prolyl-L-prolyl-L-glutaminyl-L-lysyl-L-tyrosyl-D-prolyl-L-prolyl-(2S)-2-aminodekanoyl-L-alfa-glutamyl-L-treonyl] acetatsalt	Behandling av alfa-1 antitrypsinmangel
Icelandic	Cýcló[L-alanýl-L-serýl-L-ísóleucýl-L-prólýl-L-prólýl-L-glútamínyý-L-lýsýl-L-týrósýl-D-prólýl-L-prólýl-(2S)-2-amínódecanóýl-L-alfa-glútamýl-L-threónýl] acetat salt	Meðferð á meðfæddum alfa-1 andtrýpsínskorti