10 December 2018
EMA/650328/2018

Public summary of opinion on orphan designation

Autologous CD34+ haematopoietic stem and progenitor cells genetically modified with the lentiviral vector IDUA LV, encoding for the alpha-L-iduronidase cDNA for the treatment of mucopolysaccharidosis type I

On 26 October 2018, orphan designation (EU/3/18/2073) was granted by the European Commission to Fondazione Telethon, Italy, for autologous CD34+ haematopoietic stem and progenitor cells genetically modified with the lentiviral vector IDUA LV, encoding for the alpha-L-iduronidase cDNA for the treatment of mucopolysaccharidosis type I.

What is mucopolysaccharidosis type I?

Mucopolysaccharidosis type I is an inherited disease caused by the lack of an enzyme called alpha-L-iduronidase. This enzyme is needed to break down substances in the body called glycosaminoglycans (GAGs). Since patients with mucopolysaccharidosis type I cannot break down GAGs properly, GAGs build up in various organs in the body and damage them. This can cause a range of symptoms including impaired vision, developmental delay, mental disability, joint stiffness and skeletal problems, breathing difficulties, enlarged liver and heart disease. The condition varies in severity, with the mildest form known as Scheie syndrome and the most severe as Hurler syndrome.

Mucopolysaccharidosis type I is a long-term debilitating and life-threatening disease that leads to multiple disabilities and can result in premature death.

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

At the time of designation, mucopolysaccharidosis type I affected approximately 0.01 in 10,000 people in the European Union (EU). This was equivalent to a total of around 500 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 28), Norway, Iceland and Liechtenstein. This represents a population of 517,400,000 (Eurostat 2018).

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

What treatments are available?

At the time of designation, the medicine Aldurazyme (laronidase) was authorised in the EU to treat some of the symptoms of mucopolysaccharidosis type I by replacing the missing enzyme (enzyme replacement therapy). Some patients were treated with haematopoietic stem cell transplantation, a procedure where the patient's bone marrow is replaced by stem cells from a donor; the stem cells are able to develop into normal blood cells that can produce the missing enzyme.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with mucopolysaccharidosis type I because laboratory studies indicate that it may improve effects on the nervous system, which is not possible with current medicines. 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 consists of blood stem cells taken from the patient and treated with a modified virus containing the gene for the missing alpha-L-iduronidase enzyme. The virus carries the gene into the stem cells, enabling them to make blood cells that can produce the enzyme.

When the stem cells are given back to the patient they are expected to begin forming blood cells, including white blood cells called microglia that are found in the brain and spinal cord. These cells will produce the missing enzyme and so can break down GAGs, thereby helping to relieve symptoms of the disease.

The modified virus used to produce this medicine has been designed so that it cannot spread or cause disease in humans.

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 this medicine in patients with mucopolysaccharidosis type I had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for mucopolysaccharidosis type I 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 13 September 2018 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, on the medicine's rare disease designations page.

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	Autologous CD34+ haematopoietic stem and progenitor cells genetically modified with the lentiviral vector IDUA LV, encoding for the alpha-L-iduronidase cDNA	Treatment of mucopolysaccharidosis type I
Bulgarian	Автоложни CD34+ хематопоетични стволови и прогениторни клетки, генетично модифицирани с лентивирусен вектор IDUA LV, кодиращ кДНК на алфа-L-идуронидаза	Лечение на мукополизахаридоза тип I
Croatian	Autologni CD34+ hematopoetske matične stanice i progenitorske stanice genetički modificirane s lentivirusnim vektorom IDUA LV, koji kodira za cDNA alfa-L-iduronidaze	Liječenje mukopolisaharidoze tipa I
Czech	Autologní CD34+ hematopoetická kmenová a progenitorová buňka geneticky modifikovaná lentivirálním vektorem IDUA LV, kódujícím cDNA alfa-L-iduronidázy	Léčba mukopolysacharidozy typu I
Danish	Autolog CD34+ hæmatopoietisk stam-og progenitorcelle genetisk modificeret med lentivirale vektor IDUA LV kodende for alpha-L-iduronidase cDNA	Behandling af mucopolysaccharidose type I
Dutch	Autologe CD34+ hematopoëtische stam en progenitorcel genetisch gemodificeerd met de lentivirale vector IDUA LV, coderend voor het cDNA voor alfa-L-iduronidase	Behandeling van mucopolysacharidose type I
Estonian	Autoloogsed CD34+ hematopoeetilised tüvi- ja eellasrakud mida on geneetiliselt muundatud alfa-L-iduronidaasi cDNA-d kodeeriva lentiviiruslvektori IDUA LV-ga	I-tüüpi mukopolüsahharidoosi ravi
Finnish	Autologinen CD34+ hematopoieettinen kanta-ja progenitorisolu, joka on geneettisesti muokattu lentivirusvektorilla IDUA LV, joka koodaa alfa-L-iduronidaasin cDNA: ta	Tyypin I mukopolysakkaridoosin hoito
French	Cellule hématopoïétique autologue CD34+ et cellule progénitrice génétiquement modifiée avec le vecteur lentiviral IDUA LV, codant pour l'ADNc de l'alpha-L-iduronidase	Traitement de la mucopolysaccharidose de type I
German	Autologe CD34+ hämatopoetische Stamm- und Progenitorzellen, genetisch modifiziert mit dem lentiviralen Vektor IDUA LV, kodierend für die alpha-L-Iduronidase cDNA	Behandlung der Mukopolysaccharidose Typ I

[1] At the time of designation

Language	Active ingredient	Indication
Greek	Αυτόλογα CD34+ αιματοποιητικά βλαστικά και προγονικά κύτταρα γενετικώς τροποποιημένα με τονλεντοϊκό φορέα IDUA LV, που κωδικοποιεί το cDNA της α-L-ιδουρονιδάσης	Θεραπεία βλεννοπολυσακχαρίδωσης, τύπου I
Hungarian	Alfa-L-iduronidáz cDNS-t kódoló, IDUA LV lentivirális vektorral genetikailag módosított autológ CD34+ hematopoietikus ős- és progenitor sejtek	1-es típusú mucopolisaccharidosis kezelése
Italian	Cellule staminali ematopoietiche e cellule progenitrici autologhe CD34+ geneticamente modificate con il vettore lentivirale IDUA LV, codificante per il cDNA dell'alfa-L-iduronidasi	Trattamento della mucopolisaccaridosi di tipo I
Latvian	Autologas CD34+ hematopoētiskās cilmes un celma šūnas, kas ģenētiski modificētas ar lentivirālo vektoru IDUA LV, kas kodē alfa-L-iduronidāzes cDNS	I tipa mukopolisaharidozes ārstēšana
Lithuanian	Autologinė CD34+ hematopoetinės kamieninės ir ląstelės pirmtakės , genetiškai modifikuotos lentivirusiniu vektoriumi IDUA LV, koduojančiu alfa-L-iduronidazės cDNR	Mukopolisacharidozės(I tipo) gydymas
Maltese	Ċellula emogopojetika u progenitor cell awtologa CD34+ ġenetikament modifikata bl-IDUA LV tal-lentiviral, li jikkodifika għall-cDNA alpha-L-iduronidase	Kura tal-mukopolisakkaridożi tat-tip I
Polish	Autologiczny CD34+ hematopoetyczny rdzeń macierzysty i komórki progenitorowe genetycznie zmodyfikowane za pomocą lentiwirusowego wektora IDUA LV, kodującego cDNA alfa-L-iduronidazy	Leczenie mukopolisacharydozy typu I
Portuguese	Células estaminais hematopoiéticas autólogas CD34+ e células progenitoras geneticamente modificadas com o vetor lentiviral IDUA LV que codifica o ADNc da alfa-L-iduronidase	Tratamento da mucopolissacaridose, tipo I
Romanian	Celule stem hematopoietice și celule progenitoare autologe CD34+ modificate genetic cu vectorul lentiviral IDUA LV, care codifică cADN alfa-L-iduronidaza	Tratamentul mucopolizaharidozei de tip I
Slovak	Autológna CD34+ hematopoetická stentná a progenitorová bunka geneticky modifikovaná lentivírusovým vektorom IDUA LV, kódujúcim cDNA alfa-L-iduronidázy	Liečba mukopolysacharidózy typu I
Slovenian	Avtologne CD34+ hematopoetske matične progenitorske celice, gensko spremenjene z lentivirusnim vektorjem IDUA LV, kodiranim za cDNA alfa-L-iduronidaz	Zdravljenje mukopolisaharidoze vrste I
Spanish	Celulas hematopoyético y progenitora Autólogos CD34+ de tallo genéticamente modificado con el vector lentiviral IDUA LV, que codifica el ADNc de alfa-L-iduronidasa	Tratamiento de la mucopolisacaridosis tipo I

Language	Active ingredient	Indication
Swedish	Autologa CD34+ hematopoietiska stam- och progenitorceller genetiskt modifierade med den lentivirala vektorn IDUA LV som kodar för alfa-L-iduronidas cDNA	Behandling av mukopolysackaridos typ I
Norwegian	Autologe CD34+ hematopoietiske stam-og forløperceller genetisk modifisert med den lentivirale vektoren IDUA LV som koder for alfa-L-iduronidase cDNA	Behandling av mukopolysakkaridose type I
Icelandic	Samgena CD34+ blóðmyndandi stofn- og forverafrumur erfðabreyttar með IDUA LV lentiveiru genaferju, sem kóðar fyrir alfa-L-iduronidasa cDNA	Meðferð við slímsykrukvilla gerð I