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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Recombinant human insulin receptor monoclonal antibody-fused-α-L-iduronidase for the treatment of mucopolysaccharidosis type I

On 15 October 2014, orphan designation (EU/3/14/1349) was granted by the European Commission to Voisin Consulting S.A.R.L., France, for recombinant human insulin receptor monoclonal antibody-fused-α-L-iduronidase for the treatment of mucopolysaccharidosis type I.

What is mucopolysaccharidosis type I?

Mucopolysaccharidosis type I is an inherited disease that is caused by the lack of an enzyme called α-L-iduronidase. This enzyme is needed to break down substances in the body called glycosaminoglycans (GAGs). Since patients with mucopolysaccharidosis type I cannot break these substances down, the GAGs gradually build up in most of the organs in the body and damage them. This causes a wide range of symptoms, which may include skeletal deformities, difficulty breathing, problems with the heart, spleen and liver, clouding of the eyes, hearing loss and mental retardation. Without treatment, these symptoms become more severe over time.

Mucopolysaccharidosis type I is a seriously debilitating disease which may be life threatening because it may lead to heart and breathing complication.

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

At the time of designation, mucopolysaccharidosis type I affected approximately 0.03 in 10,000 people in the European Union (EU). This was equivalent to a total of around 1,500 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).

What treatments are available?

At the time of designation, the medicine Aldurazyme (laronidase) was authorised in the EU for the treatment of mucopolysaccharidosis type I. This is an 'enzyme replacement therapy' which works by

*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 511,100,000 (Eurostat 2014).

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providing patients with the enzyme they are lacking. Some patients underwent transplantation to receive haematopoietic (blood) stem cells that are able to produce the missing enzyme.

The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with mucopolysaccharidosis type I because preclinical studies have shown that the medicine may reduce accumulation of GAGs in organs and reduce damage to the brain. 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?

This medicine is expected to work by replacing α-L-iduronidase, the enzyme that is lacking in mucopolysaccharidosis type I. It is made of α-L-iduronidase linked to a 'monoclonal antibody', a type of protein that has been designed to recognise and attach to insulin receptors found on cells throughout the body. Insulin receptors are also located in the blood-brain barrier that separates the bloodstreams from the brain. Once attached to insulin receptors, the medicine is expected to be carried inside the cells in the body and also across the blood-brain barrier into the brain tissue, where the α-L-iduronidase will replace the missing enzyme. The replacement enzyme is expected to help break down GAGs and stop them accumulating in the various tissues, including the brain, thereby relieving the symptoms of the disease.

The medicine is made by a method known as 'recombinant DNA technology': it is made by cells into which a gene (DNA) has been introduced that makes them able to produce the medicine.

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 the 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. Orphan designation of the medicine had been granted in the United States for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 4 September 2014 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

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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	Recombinant human insulin receptor monoclonal antibody-fused-α-L-iduronidase	Treatment of mucopolysaccharidosis type I
Bulgarian	Рекомбинантно моноклонално антитяло съединено с α-L-идуронидаза срещу човешкия инсулинов рецептор.	Лечение на мукополизахаридоза тип I
Croatian	α-L-iduronidaza vezana na rekombinantno monoklonsko protutijelo protiv ljudskog inzulinskog receptora	Liječenje mukopolisaharidoze tipa I
Czech	Rekombinantní lidská monoklonální protilátka fuzovaná s a-Lidurinázou k insulinovému receptoru	Léčba mukopolysacharidózy typ I
Danish	Rekombinant human insulin receptor monoklonalt antistof fusioneret med α-L-iduronidase	Behandling af mucopolysaccharidose type I
Dutch	Recombinant humaan insulinereceptor monoclonaal antilichaam-gefuseerd-α-L-iduronidase	Behandeling van mucopolysaccharidose type I
Estonian	Rekombinantne inimese insuliini retseptori monoklonaalne antikeha liidetud α-L-iduronidaasiga	I.tüüpi mukopolüsahharidoosi ravi
Finnish	Rekombinanttitekniikalla tehty ihmisen monoklonaalinen insuliinireseptori vasta-aine yhdistettynä α-L-iduronidaasiin	Tyypin I mukopolysakkaridoosin
French	Anticorps monoclonal, fusionné à α-L-iduronidase, anti-récepteur de l'insuline humaine recombinante	Traitement des mucopolysaccharidoses de type I
German	Rekombinantes Fusionsprotein aus α-L-Iduronidase und einem monoklonalen Antikörper gegen menschlichen Insulinrezeptor	Behandlung der Mukopolysaccharidose Typ I
Greek	Ανασυνδυασμένη πρωτεΐνη σύντηξης που αποτελείται από αντι-ανθρώπινο μονοκλωνικό αντίσωμα υποδοχέα ινσουλίνης και α-L-ιδουρονιδάση	Θεραπεία της βλενοπολυσακχαρίδωσης τύπου I
Hungarian	α-L-iduronidázhoz fuzionált rekombináns humán inzulinreceptor-ellenes monoklonális antitest	1-es típusú mukopoliszaharidózis kezelése
Italian	Proteina di fusione recombinante consistente in un anticorpo monoclonale contro il recettorer dell'l'insulina umana fuso con α-L-iduronidasi	Trattamento della mucopolisaccaridosi tipo I

[1] At the time of designation

Language	Active ingredient	Indication
Latvian	Rekombinanta cilvēka insulīna receptora monoklonāla antiviela, kas savienota ar α-L-iduronidāzi	I tipa mukopolisaharidozes ārstēšana
Lithuanian	Rekombinantinis žmogaus insulin receptoriaus monokloninis antikūnas susietas su α-L-iduronidaze	Mukopolisacharidozės I tipo gydymas
Maltese	Antikorp monoklonali uman rikombinanti għar-riċettur tal-insulina mgħaqud mal-α-L-iduronate	Kura tal-mukopolisakkaridoži tat-tip I
Polish	Rekombinowane przeciwciało monklonalne przeciw receptorowi insuliny ludzkiej połączone z α-L-iduronidazą	Leczenie mukopolisacharydozy typu I
Portuguese	Anticorpo monoclonal recombinante anti receptor humano da insulina fusionado com α-L-iduronidase	Tratamento da mucopolissacaridose tipo I
Romanian	α-L-iduronidază recombinantă umană fuzionată cu un anticorp monoclonal anti receptor insulinic	Tratamentul mucopolizaharidozei tipeI
Slovak	Rekombinantný fúzny proteín zložený z monoklonálnej protilátky proti ľudskému receptoru pre inzulín a α-L-iduronidázy	Liečba mukopolysacharidózy typu I
Slovenian	Rekombinantno monoklonsko protitelo za insulinski receptor, združeno z α-L-iduronidazo	Zdravljenje mukopolisaharidoze tipa I
Spanish	Anticuerpo monoclonal recombinante anti receptor humano de la insulina fusionado con α-L-iduronidase	Tratamiento de la mucopolisacaridosis tipo I
Swedish	Rekombinant fusionsprotein bestående av en monoklonal antikropp mot human insulinreceptor och α-L-iduronidas.	Behandling av mukopolysackaridos typ I
Norwegian	Rekombinant humant monoklonalt antistoff mot insulin-reseptor fusert til α-L-iduronidase	Behandling av mukopolysakkaridose type I
Icelandic	Raðbrigða manna insúlín viðtaka einstofna mótefna-tengt-α-L-ídúrónidasi	Meðferð á múkópólýsakkharidósis gerð I