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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Recombinant human insulin receptor monoclonal antibody-fused iduronate 2-sulfatase for the treatment of mucopolysaccharidosis type II (Hunter's syndrome)

On 13 November 2013, orphan designation (EU/3/13/1198) was granted by the European Commission to Voisin Consulting S.A.R.L., France, for recombinant human insulin receptor monoclonal antibody-fused iduronate 2-sulfatase for the treatment of mucopolysaccharidosis type II (Hunter's syndrome).

What is mucopolysaccharidosis type II (Hunter's syndrome)?

Mucopolysaccharidosis type II (also known as Hunter's syndrome) is an inherited disease that is caused by the lack of an enzyme called iduronate-2-sulfatase. This enzyme is needed to break down substances in the body called glycosaminoglycans (GAGs). Since patients with Hunter syndrome 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, particularly difficulty breathing, difficulty walking and behavioural problems. Without treatment, these symptoms become more severe over time.

Mucopolysaccharidosis type II primarily affects male patients. It is a seriously debilitating and life-threatening disease that leads to mental disability and death during youth.

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

At the time of designation, mucopolysaccharidosis type II affected not more than 1 in 10,000 people in the European Union (EU). This was equivalent to a total of not more 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).

*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 512,200,000 (Eurostat 2013).

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8416
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union

What treatments are available?

At the time of designation, the medicine Elaprase (idursulfase) was authorised in the EU for the treatment of mucopolysaccharidosis type II. This is an enzyme replacement therapy which works by 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 the medicine 'recombinant human insulin receptor monoclonal antibody-fused iduronate 2-sulfatase' might be of significant benefit for patients with mucopolysaccharidosis type II because early studies in experimental models show that it might improve the neurological (affecting the brain) symptoms of the disease. 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 iduronate-2-sulfatase, the enzyme that is lacking in mucopolysaccharidosis type II. It is made of iduronate-2-sulfatase linked to a 'monoclonal antibody', a type of protein that has been designed to recognise and attach to a specific structure (called an antigen) that is found in the body. The monoclonal antibody in this medicine is expected to attach to the insulin receptors which can be found in various tissues in the body. Insulin receptors are also located in the blood-brain barrier that separates the bloodstreams from the brain. Once attached to the 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 iduronate-2-sulfatase will replace the missing enzyme. The replacement enzyme is expected to help break down GAGs and stop them accumulating in the various tissues, thereby relieving the symptoms of the disease, including those affecting the brain.

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?

At the time of submission of the application for orphan designation, the evaluation of the effects of the medicine in experimental models was ongoing.

At the time of submission of the application for orphan designation, no clinical trials with the medicine in patients with mucopolysaccharidosis type II had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for mucopolysaccharidosis type II. 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 9 October 2013 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:

Voisin Consulting S.A.R.L.
3, rue des Longs Prés
92100 Boulogne Billancourt
France
Tel. +33 141 3183 00
Fax +33 146 2053 38
E-mail: orphan@voisinconsulting.com

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 iduronate 2-sulfatase	Treatment of mucopolysaccharidosis type II (Hunter's syndrome)
Bulgarian	Рекомбинантна идуронат-2-сулфатаза свързана с моноклонално антитяло към инсулиновия рецептор	Лечение на мукополизахаридоза тип 2 (Синдром на Hunter)
Czech	Rekombinantní monoklonální protilátka proti lidskému insulinovému receptoru fuzovaná s iduronátem-2 sulfatázou	Léčba mukopolysacharidózy typ II(Hunter syndrom)
Croatian	Iduronat-2-sulfataza vezana na rekombinantno monoklonsko protutijelo protiv ljudskog inzulinskog receptora	Liječenje mukopolisaharidoze tipa II (Hunterov sindrom)
Danish	Rekombinant humant insulin receptor monoklonalt antistof-knyttet iduronat 2-sulfatase	Behandling af mucopolysaccharidose type II (Hunterrs syndrom)
Dutch	Recombinant humaan insuline receptor monoclonaal antilichaam-gefuseerd aan iduronaat 2-sulfatase	Behandeling van mucopolysaccharidose type II (Hunter's syndroom)
Estonian	Rekombinantne inimese insuliiniretseptori vastane monoklonaalne antikeha, mis on seotud iduronaat 2-sulfataasiga.	2.tüüpi mukopolüsahharidoosi (Hunteri sündroom) ravi
Finnish	Iduronaatti-2-sulfataasi yhdistettynä rekombinanttitekniikalla tehtyyn monoklonaaliseen ihmisen insuliinireseptorin vasta-aineeseen	Tyypin II mukopolysakkaridoosin (Hunterin oireyhtymän) hoito
French	Anticorps monoclonal recombinant humain au récepteur à l'insuline – fusionné à l'iduronate-2-sulfatase	Traitement des mucopolysaccharidoses de type II (syndrome de Hunter)
German	Rekombinantes Fusionsprotein bestehend aus einem Antikörper gegen den menschlichen Insulinrezeptor und der Iduronate-2-Sulfatase	Behandlung der Mukopolysaccharidose Typ II (Hunter-Syndrom)
Greek	Ανασυνδυασμένο μονοκλωνικό αντίσωμα έναντι της ανθρώπινης ινσουλίνης ενωμένο με ιδουρονική-2-σουλφατάση	Θεραπεία της βλενοπολυσακχαρίδωσης τύπου II (σύνδρομο Hunter)
Hungarian	Iduronát 2-szulfatázzal fúzionált rekombináns, humán inzulin-receptort kötő monoklonális ellenanyag	2-es típusú mucopolisaccharidosis (Hunter szindróma) kezelése
Italian	Anticorpo Monoclonale ricombinante per il recettore dell'insulina umana fuso con iduronato 2 solfatasi	Trattamento della mucopolisaccaridosi tipo II (Sindrome di Hunter)

[1] At the time of designation

Language	Active ingredient	Indication
Latvian	Rekombinēts cilvēka insulīna receptoru monoklonāls antigēns – jaukta iduronāta 2-sulfatāze	II. tipa mukopilisaharidozes (Hantera sindroma) ārstēšana
Lithuanian	Rekombinantinis žmogaus insulin receptoriaus monokloninis antikūnas, sulietas su iduronato 2 sulfataze	Mukopolisacharidozės II tipo (*Hunter* sindromo) gydymas
Maltese	Antikorp monoklonali uman rikombinanti għar- riċettur tal-insulina mgħaqud mal-iduronate 2-sulfatase	Kura tal-mukopolisakkaridoži tat-tip II (sindrome ta' Hunter)
Polish	Rekombinowana ludzka 2-sulfataza (w postaci iduronianu) połączona fuzyjnie z przeciwciałem monoklonalnym przeciw ludzkiemu receptorowi insulinowemu	Leczenie mukopolisacharydozy typu II (zespołu Hunter'a)
Portuguese	Anticorpo monoclonal recombinante fusionado com iduronato 2-sulfatase anti receptor humano da insulina	Tratamento da mucopolissacaridose tipo II (syndrome de Hunter)
Romanian	Anticorp uman recombinant anti receptor insulinic, fuzionat cu iduronat 2-sulfataza	Tratamentul mucopolizaharidozei tipeII (Sindrom Hunter)
Slovak	Rekombinantná monoklonálna protilátka proti ľudskému inzulínovému receptoru fúzovaná s iduronát 2-sulfatázou	Liečba mukopolysacharidózy typu II (Hunterov syndróm)
Slovenian	Rekombinantno monoklonsko protitelo proti receptorju za humani insulin, vezano na iduronatno 2 sulfatazo	Zdravljenje mukopolisaharidoze tipa II (Hunterjev sindrom)
Spanish	Anticuerpo monoclonal recombinante humano del receptor de insulina fusionado a iduronate 2 sulfatase	Tratamiento de la mucopolisacaridosis tipo II (sindrome de Hunter)
Swedish	Rekombinant fusionsprotein bestående av en monklonal antikropp riktad mot human insulinreceptor och iduronat 2-sulfatas	Behandling av mukopolysackaridos typ II (Hunters syndrom)
Norwegian	Rekombinant human insulinreseptor monoklonalt antistoff koblet til iduronat 2-sulfatase	Behandling av mukopolysakkaridose type II (Hunters syndrom)
Icelandic	Raðbrigða manna insúlín viðtaka einstofna mótefni-tengt ídúrónat 2-súlfatasa	Meðferð á múkópólýsakkharidósis gerð II (Hunters heilkenni)