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Public summary of opinion on orphan designation

Humanised IGg1 monoclonal antibody targeting human transferrin receptor conjugated to human iduronate-2-sulfatase for the treatment of mucopolysaccharidosis type II (Hunter's syndrome)

On 26 February 2019, orphan designation (EU/3/19/2140) was granted by the European Commission to Artemida Pharma Europe Limited, Ireland, for humanised IGg1 monoclonal antibody targeting human transferrin receptor conjugated to human iduronate-2-sulfatase (also known as JR-141) 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 mucopolysaccharidosis type II 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, mental disability 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 approximately 0.02 in 10,000 people in the European Union (EU). This was equivalent to a total of around 1,000 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 518,400,000 (Eurostat 2019).

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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 replacing the enzyme that patients are lacking. 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 II, with early studies suggesting that this medicine may reduce GAGs build-up in different tissues and organs, including the brain, while the authorised medicine does not reach 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 works by replacing the enzyme that is missing or defective in patients with mucopolysaccharidosis type II, iduronate-2-sulfatase. The medicine comprises of two parts: the missing enzyme and a monoclonal antibody (a type of protein) which allows the medicine to reach the brain. The monoclonal antibody is designed to attach to a target on the blood-brain barrier, which separates the blood from the brain tissue. By replacing the missing enzyme, the medicine is expected to improve the symptoms of the disease, including symptoms affecting the brain.

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, clinical trials with the medicine in patients with mucopolysaccharidosis type II were ongoing in Japan and Brazil.

At the time of submission, the medicine was not authorised anywhere in the EU for treatment of 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 24 January 2019 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 the EMA website.

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	Humanised IGg1 monoclonal antibody targeting human transferrin receptor conjugated to human iduronate-2-sulfatase	Treatment of mucopolysaccharidosis II (Hunter's syndrome)
Bulgarian	Хуманизирано IgG-1 моноклонално антитяло, насочено към рецептора на човешки трансферин, свързано с човешкия ензим идуронат-2-сулфатаза	Лечение на мукополизахаридоза тип 2 (синдром на Хънтър)
Croatian	Humanizirano IgG-1 monoklonsko antitijelo koje cilja receptor ljudskog transferina konjugirano na ljudsku iduronat-2-sulfatazu	Liječenje mukopolisaharidoze tipa II (Hunterov sindrom)
Czech	Humanizovaná monoklonální protilátka IgG-1 cílená na lidský transferinový receptor konjugovaná s lidskou iduronát-2-sulfatázou	Léčba mukopolysacharidózy typu II (Hunterův syndrom)
Danish	Humaniseret IgG-1 monoklonalt antistof målrettet mod human transferrin-receptor konjugeret til human iduronat-2-sulfatase	Behandling af mucopolysaccharidose type II (Hunters syndrom).
Dutch	Gehumaniseerd IgG-1 monoklonaal antilichaam dat zich richt op de humane transferrine receptor geconjugeerd met humane iduronaat 2-sulfatase	Behandeling van mucopolysaccharidose type II (syndroom van Hunter)
Estonian	Inimese iduronaat-2-sulfataasiga konjugeeritud inimese transferriiniretseptori vastane humaniseeritud lgG-1 monoklonaalne antikeha.	II tüüpi mükopolüsahharidoosi (Hunteri sündroom) ravi
Finnish	Ihmisen transferriinireseptoriin kohdistuva, humanisoitu monoklonaalinen IgG-1-vasta-aine, joka on konjugoitu ihmisen iduronaatti-2-sulfataasiin	Tyypin II mukopolysakkaridoosin (Hunterin oireyhtymän) hoito
French	Anticorps monoclonal IgG-1 humanisé dirigé contre le récepteur de la transferrine humaine conjugué à l'iduronate-2-sulfatase humaine	Traitement de la mucopolysaccharidose de type II (syndrome de Hunter)
German	Humanisierter monoklonaler IgG-1-Antikörper gegen den humanen Transferrin-Rezeptor gerichtetet, konjugiert an humane Iduronat-2-Sulfatase	Behandlung von Mukopolysaccharidose Typ II (Morbus Hunter)

[1] At the time of designation

Greek	Ανθρωποποιημένο μονοκλωνικό αντίσωμα IgG-1 που στοχεύει τον υποδοχέα ανθρώπινης τρανσφερίνης συζευγμένο στην ανθρώπινη ιδουρονάτη-2-σουλφατάση	Θεραπεία της βλεννοπολυσακχαρίδωσης τύπου ΙΙ (σύνδρομο Hunter).
Hungarian	humán iduronát-2-szulfatázhoz konjugált humán transzferrin receptor ellenes humanizált IgG-1 monoklonális antitest,	2-es típusú mukopoliszacharidózis (Hunter szindróma) kezelése
Italian	Anticorpo IgG-1 monoclonale umanizzato mirato al recettore della transferrina umana coniugato con iduronato-2-solfatasi umano	Trattamento della mucopolisaccaridosi tipo II (syndrome di Hunter)
Latvian	Humanizēta IgG-1 monoklonālā antiviela, kas vērsta pret cilvēka transferīna receptoru un konjugēta ar cilvēka iduronāta-2-sulfatāzi	II tipa mukopolisaharidozes (Hantera sindroma) ārstēšana
Lithuanian	Humanizuotas IgG-1 monokloninis antikūnas, nukreiptas į žmogaus transferino receptorių sujungtą su žmogaus iduronato 2-sulfataze	II tipo mukopolisaharidozės (Hunter sindromo) gydymas
Maltese	Antikorp monoklonali IGg1 umanizzat li jimmira riċettur ta' transferrin uman konjugat ma' iduronat-2-sulfataži uman	Kura ta' mucopolysaccharidosis II (sindrome ta' Hunter)
Polish	Humanizowane przeciwciało monoklonalne klasy IgG-1 skierowane przeciwko ludzkiemu receptorowi transferyny sprzężone z ludzką 2-sulfatazą iduronianu	Leczenie mukopolisacharydozy typu II (zespołu Huntera)
Portuguese	Anticorpo monoclonal IgG-1 humanizado direcionada para o recetor da transferrina humano conjugado com a iduronato-2-sulfatase humana	Tratamento da mucopolissacaridose II (síndrome de Hunter)
Romanian	Anticorp monoclonal umanizat anti IgG-1 care țintește receptorul transferinei umane conjugat cu iduronat-2-sulfataza umană	Tratamentul da mucopolizaharidozei de tip II (síndromul Hunter)
Slovak	Humanizovaná monoklonálna protilátka typu IgG-1 zameraná na ľudský transferínový receptor konjugovaný na ľudskú iduronát-2-sulfatázu	Liečba mukopolysacharidózy II (Hunterov syndróm)
Slovenian	Humanizirano monoklonsko protitelo IgG-1, usmerjeno proti človeškemu transferinskemu receptorju, konjugirano na človeško iduronat-2-sulfatazo	Zdravljenje mukopolisaharidoze tipa II (Hunterjev sindrom)
Spanish	Anticuerpo monoclonal IgG-1 humanizado dirigido al receptor humano de transferrina conjugado con iduronato-2-sulfatasa humano	Tratamiento de la mucopolisacaridosis tipo II (síndrome de Hunter)

Swedish	Humaniserad monoklonal IgG-1-antikropp mot human transferrinreceptor konjugerad med humant iduronat-2-sulfatas	Behandling av mukopolysackaridos typ II (Hunters syndrom)
Norwegian	Humanisert IgG-1 monoklonalt antistoff mot human transferrinreseptor konjugert med human iduronat-2-sulfatase	Behandling av mukopolysakkaridose type II (Hunters sykdom)
Icelandic	Mannaðlagað IgG-1 einstofna mótefni tengt ídúrónat-2-súlfatasa fyrir transferrínviðtaka í mönnum	Meðferð við slímsykrukvilla tegund II (Hunter heilkenni)