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Public summary of opinion on orphan designation

Adeno-associated viral vector serotype 2/6 encoding zinc-finger nucleases and the human iduronate 2-sulfatase gene for the treatment of mucopolysaccharidosis type II (Hunter's syndrome)

On 17 January 2018, orphan designation (EU/3/17/1956) was granted by the European Commission to Quintiles Ireland Limited, Ireland, for adeno-associated viral vector serotype 2/6 encoding zinc-finger nucleases and the human iduronate 2-sulfatase gene (also called SB-913) 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 515,700,000 (Eurostat 2017).

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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 type II because laboratory studies indicate that it may slow down the worsening of the patient's mental functions. 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 made of a virus containing the gene for the iduronate-2-sulfatase enzyme, which is lacking in patients with mucopolysaccharidosis type II. When given to the patient, the virus is expected to carry the gene into the liver cells, enabling these cells to start producing the enzyme. The enzyme is then expected to enter the blood and be taken up by cells in various other organs, including the brain. As a result, the cells will be able to break down the GAGs, thereby helping to relieve symptoms of the disease.

The type of virus used in this medicine ('adeno-associated virus') does not 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 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 7 December 2017 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	Adeno-associated viral vector serotype 2/6 encoding zinc-finger nucleases and the human iduronate 2-sulfatase gene	Treatment of mucopolysaccharidosis type II (Hunter's syndrome)
Bulgarian	Адено-асоцииран вирусен вектор серотип 2/6, кодиращ цинкови пръстови нуклеази и човешки iduronate 2-сулфатазен ген	Лечение на мукополизахаридоза тип 2 (синдром на Hunter)
Croatian	Adeno-povezani virusni vektor serotipa 2/6 koji kodira nukleaze prstiju cinka i gen za ljudsku idurona 2-sulfataze	Liječenje mukopolisaharidoze tipa II (Hunterov sindrom)
Czech	Adeno-asociovaný virový vektorový sérotyp 2/6 kódující nukleázy prstu zinku a lidský iduronát 2-sulfatasu gen	Léčba mukopolysacharidózy typ II(Hunter syndrom)
Danish	Adeno-associeret viral vektor serotype 2/6, der koder for zinkfinger-nukleaser og det humane iduronat-2-sulfatase-gen	Behandling af mucopolysaccharidose type II (Hunterrs syndrom)
Dutch	Adeno-geassocieerde virale vector serotype 2/6 die coderen voor zinkvinger nucleasen en het humane iduronaat 2-sulfatase gen	Behandeling van mucopolysaccharidose type II (Hunter's syndroom)
Estonian	Adenoviirusega assotsieerunud viirusvektori serotüüp 2/6, mis kodeerib tsink-sõrm nukleaase ja inimese iduronaadi 2-sulfataasi geeni	2.tüüpi mukopolüsahharidoosi (Hunteri sündroom) ravi
Finnish	Adenoassosiotu serotyypin 2/6 virusvektori, joka koodittaa sinkkisorminukleaaseja ja ihmisen iduronaatti-2-sulfataasigeeni	Tyypin II mukopolysakkaridoosin (Hunterin oireyhtymän) hoito
French	Vecteur viral adéno-associé serotype 2/6 codant des nucléases à doigts de zinc et le gène de l'iduronate de 2-sulfatase humaine	Traitement des mucopolysaccharidoses de type II (syndrome de Hunter)
German	Adeno-assoziierte viraler Vektor-Serotyp 2/6, der für Zinkfingernukleasen und das menschliche Iduronat-2-Sulfatase Gen	Behandlung der Mukopolysaccharidose Typ II (Hunter-Syndrom)
Greek	Αδενοσυνδεδεμένος ιικός φορέας οροτύπου 2/6 που κωδικοποιεί νουκλεάσες δακτύλου ψευδαργύρου και το ανθρώπινο γονίδιο ινδουρονική 2-σουλφατάση	Θεραπεία της βλενοπολυσακχαρίδωσης τύπου II (σύνδρομο Hunter)
Hungarian	Adeno-asszociált virális vektor 2/6-os szerotípus, amely cink ujj-nukleázokat kódol, és a humán iduronát-2-szulfatáz gént	2-es típusú mucopolisaccharidosis (Hunter szindróma) kezelése
Italian	Vettore virale adeno-associato di sierotipo 2/6 codificante nucleasi a dita di zinco ed il gene umano del iduronato 2-solfatasi	Trattamento della mucopolisaccaridosi tipo II (Sindrome di Hunter)

[1] At the time of designation

Language	Active ingredient	Indication
Latvian	Adeno saistītā vīrusa serotipa 2/6vektors, kas kodē cinka pirkstu nukleāzes un cilvēka iduronāta 2-sulfatāzes gēnu	II. tipa mukopilisaharidozes (Hantera sindroma) ārstēšana
Lithuanian	Adenoasocijuoto viruso vektoriaus serotipas 2/6, koduojantis cinko pirštelių nukleazės ir žmogaus iduronato 2-sulfatazės geną	Mukopolisacharidozės II tipo (*Hunter* sindromo) gydymas
Maltese	Vettur tal-virus assoċjat ma' adeno serotip 2/6 li jikkodifika n-nukleaži tas-swaba taż-żingu u l-ġene iduronatiku 2-sulfatase	Kura tal-mukopolisakkaridoži tat-tip II (sindrome ta' Hunter)
Polish	Wektor wirusowy związany z adenowirusami serotypu 2/6 kodujący nukleazy z motywem palca cynkowego i gen 2-sulfatazę ludzkiego iduronianu	Leczenie mukopolisacharydozy typu II (zespołu Hunter'a)
Portuguese	Vírus viral adeno-associado serotipo 2/6 que codifica nucleases de dedo de zinco e o gene da iduronato 2-sulfatase humano	Tratamento da mucopolissacaridose tipo II (syndrome de Hunter)
Romanian	Vector viral adeno-asociat de serotip 2/6 care codifică nucleazele "deget de zinc" și gena 2-sulfatază umană iduronat	Tratamentul mucopolizaharidozei tipeII (Sindrom Hunter)
Slovak	Adeno-asociovaný vírusový vektor sérotypu 2/6 kódujúci nukleázy prstového zinku a gén ľudskej iduronát 2-sulfatázu	Liečba mukopolysacharidózy typu II (Hunterov syndróm)
Slovenian	Adeno-povezan virusni vektor serotipa 2/6, ki kodira nukleazo cinkovih prstov in humani iduronatni 2-sulfatazni gen	Zdravljenje mukopolisaharidoze tipa II (Hunterjev sindrom)
Spanish	El vector viral adeno-asociado serotipo 2/6 que codifica las nucleasas de dedo de zinc y el gen iduronato humano 2-sulfatasa	Tratamiento de la mucopolisacaridosis tipo II (sindrome de Hunter)
Swedish	Adeno-associerad viral vektor serotyp 2/6 som kodar för zinkfinger-nukleaser och den humana iduronat-2-sulfatasgenen	Behandling av mukopolysackaridos typ II (Hunters syndrom)
Norwegian	Adenoassosiert virusvektor serotype 2/6 som koder for sinkfingernukleaser og det humane iduronat-2-sulfatase -genet	Behandling av mukopolysakkaridose type II (Hunters syndrom)
Icelandic	Adenó- tengd veiruferja af sermisgerð 2/6 sem kóðar fyrir sinkfingurnúkleasa og manna iduronate 2-súlfatasa geni	Meðferð á múkópólýsakkharidósis gerð II (Hunters heilkenni)