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Public summary of opinion on orphan designation

Recombinant adeno-associated viral vector serotype 9 containing human iduronate-2-sulfatase gene for the treatment of mucopolysaccharidosis type II (Hunter's syndrome)

On 12 October 2017, orphan designation (EU/3/17/1943) was granted by the European Commission to Regenxbio EU Limited, Ireland, for recombinant adeno-associated viral vector serotype 9 containing human iduronate-2-sulfatase gene (also known as RGX-121) 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 less than 1 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 52,000 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 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 might be of significant benefit for patients with mucopolysaccharidosis type II because laboratory studies showed that behavioural problems and problems with thinking, learning and memory, which are currently not treatable by the authorised enzyme replacement therapy product, improved with a single treatment of the medicine. 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 injected into the patient's brain, the virus is expected to carry the gene into the brain cells, enabling the cells to start producing the enzyme. As a result, the cells will be able to break down the GAGs in the brain, thereby helping to relieve problems of behaviour, thinking, learning and memory.

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 EU and 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 5 October 2017 recommending the granting of this designation.

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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	Recombinant adeno-associated viral vector serotype 9 containing human iduronate-2-sulfatase gene	Treatment of mucopolysaccharidosis type II (Hunter's syndrome)
Bulgarian	Рекомбинантен аденосвързан вирусен вектор, серотип 9, носещ човешкия ген за идуронат-2-сулфатаза	Лечение на мукополизахаридоза тип 2 (синдром на Hunter)
Croatian	Rekombinantni adeno-povezani virusni vektor serotipa 9 koji sadrži ljudski gen za iduronat-2-sulfatazu	Liječenje mukopolisaharidoze tipa II (Hunterov sindrom)
Czech	Rekombinantní adeno-asociovaný virový vektore sérotypu 9 obsahující gen humánní iduronát-2-sulfatázy	Léčba mukopolysacharidózy typ II(Hunter syndrom)
Danish	Rekombinant adeno-associeret viral vektor serotype 9 indeholdende human iduronate-2-sulfatase-genet	Behandling af mucopolysaccharidose type II (Hunterrs syndrom)
Dutch	Recombinant adeno-geassocieerde virale vector serotype 9 welke humaan iduronaat-2-sulfatase gen bevat	Behandeling van mucopolysaccharidose type II (Hunter's syndroom)
Estonian	Inimese iduronaat-2-sulfataasi geeni sisaldav rekombinantne adenoviirusega assotsieerunud viirusvektori serotüüp 9	2.tüüpi mukopolüsahharidoosi (Hunteri sündroom) ravi
Finnish	Rekombinantti adenoassosioitu virusvektori, serotyyppi 9, joka sisältää ihmisen iduronaatti-2-sulfataasin geenin	Tyypin II mukopolysakkaridoosin (Hunterin oireyhtymän) hoito
French	Vecteur viral recombinant adéno-associé de sérotype 9 portant le gene de l'iduronate-2-sulfatase humaine	Traitement des mucopolysaccharidoses de type II (syndrome de Hunter)
German	Rekombinanter adeno-assoziierter viraler Vektor des Serotyps 9, der das humane Iduronat-2-Sulfatase Genenthält	Behandlung der Mukopolysaccharidose Typ II (Hunter-Syndrom)
Greek	Ανασυνδυασμένος αδενοσυσχετιζόμενος ιικός φορέας οροτύπου 9, ο οποίος περιέχει το ανθρώπινο γονίδιο της ιδουρονικής-2-σουλφατάσης	Θεραπεία της βλενοπολυσακχαρίδωσης τύπου II (σύνδρομο Hunter)
Hungarian	Humán iduronát-2-szulfatáz gént hordozó, 9-es szerotípusú rekombináns adeno-asszociált virus vektor	2-es típusú mucopolisaccharidosis (Hunter szindróma) kezelése
Italian	Vettore virale adeno-associato ricombinante di sierotipo 9 contenente il gene dell' iduronato-2-solfatasi umana	Trattamento della mucopolisaccaridosi tipo II (Sindrome di Hunter)

[1] At the time of designation

Language	Active ingredient	Indication
Latvian	Rekombinants adenoasociētā vīrusa vektora 9. serotips, kas satur cilvēka iduronāta-2-sulfatāzes gēnu	II tipa mukopolisaharidozes (Hantera sindroma) ārstēšana
Lithuanian	Rekombinantinis adeno-asocijuoto viruso vektoriaus 9 serotipas, pernešantis žmogaus iduronato-2-sulfatazės geną	Mukopolisacharidozės II tipo (*Hunter* sindromo) gydymas
Maltese	Vettur virali assoċjat ma' adeno rikombinanti ta' serotip 9 li fih ġene iduronat-2-sulfataži tal-bniedem	Kura tal-mukopolisakkaridoži tat-tip II (sindrome ta' Hunter)
Polish	Rekombinowany związany z adenowirusami wirusowy wektor serotypu 9, zawierający gen ludzkiej 2-sulfatazy iduronianu	Leczenie mukopolisacharydozy typu II (zespołu Hunter'a)
Portuguese	Vetor viral recombinante adeno-associado do serótipo 9 contendo o gene da enzima de iduronato–2 sulfatase humana	Tratamento da mucopolissacaridose tipo II (syndrome de Hunter)
Romanian	Vector viral recombinant adeno-asociat de serotip 9 care conține gena iduronat-2-sulfatazei umane	Tratamentul mucopolizaharidozei tipeII (Sindrom Hunter)
Slovak	Rekombinantný adeno-asociovaný vírusový vektor sérotypu 9 obsahujúci gén ľudskej iduronát-2-sulfatázy	Liečba mukopolysacharidózy typu II (Hunterov syndróm)
Slovenian	Rekombinantni adeno-asociacijski vektor serotipa 9, ki vsebuje humani iduronat-2-sulfatazo	Zdravljenje mukopolisaharidoze tipa II (Hunterjev sindrom)
Spanish	Vector viral adenoasociado recombinante de serotipo 9 que contiene el gen de la iduronato–2-sulfatasa humana	Tratamiento de la mucopolisacaridosis tipo II (sindrome de Hunter)
Swedish	Rekombinant adenovirus-vektor serotyp 9 innehållande genen för humant iduronat-2-sulfatas	Behandling av mukopolysackaridos typ II (Hunters syndrom)
Norwegian	Rekombinant adenoassosiert virusvektor serotype 9 som inneholder genet for human iduronat-2-sulfatase	Behandling av mukopolysakkaridose type II (Hunters syndrom)
Icelandic	Raðbrigða adenó tengd genaferja af sermisgerð 9 sem inniheldur ídúrónat-2-súlfatasa gen	Meðferð á múkópólýsakkharidósis gerð II (Hunters heilkenni)