16 August 2018
EMA/373289/2018

Public summary of opinion on orphan designation

Recombinant adeno-associated viral vector serotype 9 containing human iduronidase gene for the treatment of mucopolysaccharidosis type I

On 27 June 2018, orphan designation (EU/3/18/2039) was granted by the European Commission to REGENXBIO EU Limited, Ireland, for recombinant adeno-associated viral vector serotype 9 containing human iduronidase gene (also known as RGX-111) for the treatment of mucopolysaccharidosis type I.

What is mucopolysaccharidosis type I?

Mucopolysaccharidosis type I is an inherited disease caused by the lack of an enzyme called alpha-L-iduronidase. This enzyme is needed to break down substances in the body called glycosaminoglycans (GAGs). Since patients with mucopolysaccharidosis type I cannot break down GAGs properly, GAGs build up in various organs in the body and damage them. This can cause a range of symptoms including impaired vision, developmental delay, mental disability, joint stiffness and skeletal problems, breathing difficulties, enlarged liver and heart disease. The condition varies in severity, with the mildest form known as Scheie syndrome and the most severe as Hurler syndrome.

Mucopolysaccharidosis type I is a long-term debilitating and life-threatening disease that leads to multiple disabilities and can result in premature death.

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 to treat some of the physical (non-mental) symptoms of mucopolysaccharidosis type I by replacing the missing enzyme (enzyme replacement therapy). Some patients were treated with haematopoietic stem cell

*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 517,400,000 (Eurostat 2018).

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

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 I because laboratory studies indicate that it may improve the mental symptoms of the condition. 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 alpha-L-iduronidase enzyme, which is lacking in patients with mucopolysaccharidosis type I. When injected into the patient's spine, the virus is expected to carry the gene into nerve cells in the spine and brain, enabling them to start producing the enzyme. As a result, the cells will be able to break down GAGs and so help to relieve symptoms of the disease. The virus may also enter the blood to some extent and be taken up by cells in other organs in the body. It is expected that a single injection will have long-term beneficial effect.

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, clinical trials with the medicine in patients with mucopolysaccharidosis type I were ongoing.

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 mucopolysaccharidosis type I.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 24 May 2018 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	Activeingredient	Indication
English	Recombinant adeno-associated viral vector serotype 9 containing human iduronidase gene	Treatment of mucopolysaccharidosis type I
Bulgarian	Рекомбинантен аденосвързан вирусен вектор, серотип 9, съдържащ човешкия ген за идуронидаза	Лечение на мукополизахаридоза тип I
Croatian	Rekombinantni adeno-povezani virusni vektor serotipa 9 koji sadrži gensku kazetu za ekspresiju ljudske iduronidaza	Liječenje mukopolisaharidoze tipa I
Czech	Rekombinantní adeno-asociovaný virální vektor sérotypu 9 nesoucí lidský gen iduronidázu	Léčba mukopolysacharidozy typu I
Danish	Rekombinant adeno-associeret viral vektor serotype 9 indeholdende human iduronidase - genkassette	Behandling af mucopolysaccharidose type I
Dutch	Recombinant adeno-geassocieerde virale vector serotype 9 welke humaan iduronidase gen bevat	Behandeling van mucopolysacharidose type I
Estonian	Inimese iduronidaasi geeni sisaldav rekombinantne adeno-assotsieerunud viirusvektori serotüüp 9	I-tüüpi mukopolüsahharidoosi ravi
Finnish	Rekombinantti adenoassosioitu virus vektori, serotyyppi 9, joka sisältää ihmisen iduronidaasiin geenikasetin	Tyypin I mukopolysakkaridoosin hoito
French	Vecteur viral recombinant adéno-associé de sérotype 9 portant la cassette d'expression de l'iduronidase humaine	Traitement de la mucopolysaccharidose de type I
German	Rekombinanter adeno-assoziierter viraler Vektor des Serotyps 9, der das humane Iduronidase – Gen enthält	Behandlung der Mukopolysaccharidose Typ I
Greek	Ανασυνδυασμένος αδενο-σχετιζόμενος ιικός φορέας οροτύπου 9, ο οποίος περιέχει το γονίδιο για ανθρώπινη ιδουρονιδάση	Θεραπεία βλεννοπολυσακχαρίδωσης, τύπου I
Hungarian	Humán iduronidáz gént tartalmazó 9-es szerotípusú rekombináns adeno-asszociált virális vektor	I-es típusú mucopolisaccharidosis kezelése
Italian	Vettore virale ricombinante adeno-associato di sierotipo 9 contenente il gene dell' iduronidasi umana	Trattamento della mucopolisaccaridosi di tipo I
Latvian	Rekombinanta adenoasociētā virālā vektora 9. serotips, kas satur cilvēka iduronidāzes gēnu	I tipa mukopolisaharidozes ārstēšana
Lithuanian	Rekombinantis adeno asocijuoto viruso vektoriaus 9 serotipas, turintis žmogaus iduronidazės geną	Mukopolisacharidozės(I tipo) gydymas
Maltese	Vettur virali assoċjat ma' adeno rikombinanti ta' serotip 9 li fih ġene iduronidas tal-bniedem	Kura tal-mukopolisakkaridożi tat-tip I

[1] At the time of designation

Language	Activeingredient	Indication
Polish	Rekombinowany wektor wirusowy AAV serotypu 9, zawierający kasetę ekspresyjną ludzkiej iduronidazy	Leczenie mukopolisacharydozy typu I
Portuguese	Vetor viral recombinante adeno-associado do serótipo 9 contendo a cassete de expressão da enzima de iduronidase humana	Tratamento da mucopolissacaridose, tipo I
Romanian	Vector viral recombinant adeno-asociat de serotip 9 care conține gena iduronidazei umane	Tratamentul mucopolizaharidozei de tip I
Slovak	Rekombinantný adenoasociovaný virálny vektor sérotypu 9 obsahujúci exprimujúcu kazetu ľudskej iduronidázy	Liečba mukopolysacharidózy typu I
Slovenian	Rekombinantni adeno-asociacijski virusni vektor serotipa 9, ki vsebuje gen za humano iduronidazo	Zdravljenje mukopolisaharidoze vrste I
Spanish	Vector viral adenoasociado recombinante adenoasociado del serotipo 9 que contiene casete de expresión el gen de la iduronidase humana	Tratamiento de la mucopolisacaridosis tipo I
Swedish	Rekombinant adenovirus-vektor serotyp 9 innehållande expressionskassett för human iduronidaz	Behandling av mukopolysackaridos typ I
Norwegian	Rekombinant adenoassosiert virusvektor serotype 9 som inneholder genet for human iduronidase	Behandling av mukopolysakkaridose type I
Icelandic	Raðbrigða adenótengd veiruferja af sermisgerð 9 sem inniheldur ídúrónidasa erfðavísi manna	Meðferð við slímsykrukvilla gerð I