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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 alpha L-iduronidase gene for the treatment of mucopolysaccharidosis type I

On 17 January 2018, orphan designation (EU/3/17/1955) 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 alpha L-iduronidase gene (also known as SB-318) for the treatment of mucopolysaccharidosis type I.

What is mucopolysaccharidosis type I?

Mucopolysaccharidosis type I is an inherited disease that is 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 GAGs down properly, GAGs gradually 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, progressive 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 0.05 in 10,000 people in the European Union (EU). This was equivalent to a total of around 3,000 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 Aldurazyme (laronidase) was authorised in the EU to treat some of the symptoms of mucopolysaccharidosis type I by replacing the missing enzyme (enzyme replacement therapy). 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 I 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 alpha-L-iduronidase enzyme, which is lacking in patients with mucopolysaccharidosis type I. 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 I had been started.

At the time of submission, 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 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.

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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	Adeno-associated viral vector serotype 2/6 encoding zinc-finger nucleases and the human alpha L-iduronidase gene	Treatment of mucopolysaccharidosis type I
Bulgarian	Адено-асоцииран вирусен вектор серотип 2/6, кодиращ цинкови пръстови нуклеази и човешки алфа L-идуронидазен ген	Лечение на мукополизахаридоза тип I
Croatian	Adeno-povezani virusni vektor serotipa 2/6 koji kodira nukleaze prstiju cinka i ljudski gen za alfa L-iduronidazu	Liječenje mukopolisaharidoze tipa I
Czech	Adeno-asociovaný virový vektorový sérotyp 2/6 kódující nukleázy prstu zinku a lidský alfa L-iduronidázový gen	Léčba mukopolysacharidozy typu I
Danish	Adeno-associeret viral vektor serotype 2/6, der koder for zinkfinger-nukleaser og det humane alfa L-iduronidase-gen	Behandling af mucopolysaccharidose type I
Dutch	Adeno-geassocieerde virale vector serotype 2/6 die coderen voor zinkvinger nucleasen en het humane alfa L-iduronidase gen	Behandeling van mucopolysacharidose type I
Estonian	Adenoviirusega assotsieerunud viirusvektori serotüüp 2/6, mis kodeerib tsink-sõrm nukleaase ja inimese alfa-L-iduronidaasi geeni	I-tüüpi mukopolüsahharidoosi ravi
Finnish	Adenoassosiotu serotyypin 2/6 virusvektori, joka koodittaa sinkkisorminukleaaseja ja ihmisen alfa-L-iduronidaasi-geeniä	Tyypin I mukopolysakkaridoosin hoito
French	Vecteur viral adéno-associé serotype 2/6 codant des nucléases à doigts de zinc et le gène de l'alpha-L-iduronidase humaine	Traitement de la mucopolysaccharidose de type I
German	Adeno-assoziierte viraler Vektor-Serotyp 2/6, der für Zinkfingernukleasen und das menschliche alpha-L-Iduronidasegen kodiert	Behandlung der Mukopolysaccharidose Typ I
Greek	Αδενοσυνδεδεμένος ιικός φορέας οροτύπου 2/6 που κωδικοποιεί νουκλεάσες δακτύλου ψευδαργύρου και το ανθρώπινο γονίδιο άλφα L-ιδουρονιδάσης	Θεραπεία βλεννοπολυσακχαρίδωσης, τύπου I
Hungarian	Adeno-asszociált virális vektor 2/6-os szerotípus, amely cink ujj-nukleázokat kódol, és a humán alfa-L-iduronidáz gént	I-1-es típusú mucopolisaccharidosis kezelése
Italian	dVettore virale adeno-associato di sierotipo 2/6 codificante nucleasi a dita di zinco ed il gene umano dell'alfa-L-iduronidasi	Trattamento della mucopolisaccaridosi di tipo I
Latvian	Adeno saistītā vīrusa serotipa 2/6vektors, kas kodē cinka pirkstu nukleāzes un cilvēka alfa L-iduronidāzes gēnu	I tipa mukopolisaharidozes ārstēšana

[1] At the time of designation

Language	Active ingredient	Indication
Lithuanian	Adenoasocijuoto viruso vektoriaus serotipas 2/6, koduojantis cinko pirštelių nukleazės ir žmogaus alfa L-iduronidazės geną	Mukopolisacharidozės(I tipo) gydymas
Maltese	Vettur tal-virus assoċjat ma' adeno serotip 2/6 li jikkodifika n-nukleażi tas-swaba taż-żingu u l-ġene alfa umana L-iduronidażi	Kura tal-mukopolisakkaridożi tat-tip I
Polish	Wektor wirusowy związany z adenowirusami serotypu 2/6 kodujący nukleazy z motywem palca cynkowego i ludzki gen alfa L-iduronidazy	Leczenie mukopolisacharydozy typu I
Portuguese	Vírus viral adeno-associado serotipo 2/6 que codifica nucleases de dedo de zinco e o gene da alfa L-iduronidase humana	Tratamento da mucopolissacaridose, tipo I
Romanian	Vector viral adeno-asociat de serotip 2/6 care codifică nucleazele "deget de zinc" și gena alfa-L-iduronidazei umane	Tratamentul mucopolizaharidozei de tip I
Slovak	Adeno-asociovaný vírusový vektor sérotypu 2/6 kódujúci nukleázy prstového zinku a gén ľudskej alfa L-iduronidázy	Liečba mukopolysacharidózy typu I
Slovenian	Adeno-povezan virusni vektor serotipa 2/6, ki kodira nukleazo cinkovih prstov in humani alfa L-iduronidazni gen	Zdravljenje mukopolisaharidoze vrste I
Spanish	El vector viral adeno-asociado serotipo 2/6 que codifica las nucleasas de dedo de zinc y el gen alfa L-iduronidasa humana	Tratamiento de la mucopolisacaridosis tipo I
Swedish	Adeno-associerad viral vektor serotyp 2/6 som kodar för zinkfinger-nukleaser och den humana alfa L-iduronidas-genen	Behandling av mukopolysackaridos typ I
Norwegian	Adenoassosiert virusvektor serotype 2/6 som koder for sinkfingernukleaser og det humane alfa L-iduronidase-genet	Behandling av mukopolysakkaridose type I
Icelandic	Adenó- tengd veiruferja af sermisgerð 2/6 sem kóðar fyrir sinkfingurnúkleasa og manna alfa L-ídúrónídasa geni	Meðferð við slímsykrukvilla gerð I