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Public summary of opinion on orphan designation

Adeno-associated viral vector serotype S3 encoding human alpha-galactosidase A cDNA for the treatment of Fabry disease

On 28 February 2020, orphan designation EU/3/20/2248 was granted by the European Commission to Freeline Therapeutics (Ireland) Limited, Ireland, for adeno-associated viral vector serotype S3 encoding human alpha-galactosidase A cDNA (also known as FLT190) for the treatment of Fabry disease.

What is Fabry disease?

Fabry disease is an inherited disease that is caused by the lack of an enzyme called alpha galactosidase A, which breaks down and removes Gb3, a complex molecule containing sugars and fats.

In patients with this condition, large amounts of Gb3 build up in tissues of vital organs, such as the kidneys and heart, leading to kidney failure and heart problems. Gb3 also builds up in the tissues of the skin, eye and nervous system leading to skin damage, clouding of the front part of the eye, pain in the hands and feet and complications affecting the brain.

Fabry disease is a long-term debilitating disease due to recurrent episodes of severe pain not responding to painkillers. It is also life-threatening due to kidney problems, heart attack and stroke.

What is the estimated number of patients affected by the condition?

At the time of designation, Fabry disease affected approximately 2.6 in 10,000 people in the European Union (EU). This was equivalent to a total of around 135,000 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).

What treatments are available?

At the time of designation, Fabrazyme (agalsidase beta), Galafold (migalastat) and Replagal (agalsidase alfa) were authorised in the EU to treat Fabry disease.

*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 519,200,000 (Eurostat 2020).

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The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with Fabry disease. Laboratory studies indicate that a single dose of the medicine could increase activity of alpha-galactosidase A for a long time and thereby reduce the need for regular treatment. 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 up of a virus that contains the gene for alpha-galactosidase A, the enzyme the patient lacks. When given by injection, it is expected that the virus will carry the gene into the patient's liver cells, allowing the patient to start producing the missing enzyme and thereby relieve symptoms of the disease.

The 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 adeno-associated viral vector serotype S3 encoding human alpha-galactosidase A cDNA have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with this medicine in patients with Fabry disease were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for the treatment of Fabry disease or designated as an orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000, the COMP adopted a positive opinion on 22 January 2020, 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.

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 S3 encoding human alpha-galactosidase A cDNA	Treatment of Fabry disease
Bulgarian	Адено-асоцииран вирусен вектор серотип S3, кодиращ човешка комплементарна ДНК на алфа-галактозидаза А	Лечение на болест на Fabry
Croatian	Adeno-pridruženi virusni vektor serotipa S3 koji kodira cDNA humane alfa- galaktozidaze	Liječenje Fabryjeve bolesti
Czech	Adeno-asociovaný virový vektor sérotypu S3 kódující cDNA lidské alfa-galaktosidázy A	Léčba Fabryho choroby
Danish	Adeno-associeret viral vektor serotype S3 kodende for human alpha-galactosidase A cDNA	Behandling af Fabrys sygdom
Dutch	Adeno-geassociëerde virale vector serotype S3 coderend voor humaan alpha-galactosidase A cDNA	Behandeling van de ziekte van Fabry
Estonian	Inimese alfa-galaktosidaas A cDNA-d kodeeriv adeno-assotsieerunud viirusvektori serotüüp S3.	Fabry tõve ravi
Finnish	Adeno-assosioitunut serotyypin S3 virusvektori, joka koodaa ihmisen alfa-galaktosidaasi A:n cDNA:ta	Fabryn taudin hoito
French	Vecteur viral adéno-associé de sérotype S3 codant pour l'ADNc de l'alpha-galactosidase A humaine	Traitement de la maladie de Fabry
German	Adeno-assoziierter viraler Vektor vom Serotyp S3 der humane Alpha-Galactosidase A cDNA enthält	Behandlung des Fabry-Syndroms
Greek	Αδενο-σχετιζόμενος ιϊκός φορέας οροτύπου S3 που κωδικοποιεί το cDNA της ανθρώπινης α-γαλακτοσιδάσης Α	Θεραπεία της νόσου του Fabry
Hungarian	Humán alfa-galaktozidáz A cDNS-t kódoló S3 szerotípusú adeno-asszociált virus vektor	Fabry betegség kezelése
Italian	Vettore virale adeno-associato di serotipo S3 che codifica per il cDNA dell'alfa-galattosidasi A umana.	Trattamento della malattia di Fabry
Latvian	Cilvēka alfa-galaktozidāzes A cDNS kodējošs adenoasociētais vīrusa vektora seroptips S3	Fabrī slimības ārstēšana
Lithuanian	Su adeno virusu susijusio vektoriaus S3 serotipas, koduojantis žmogaus alfa-galaktozidazės A cDNR	Fabry ligos gydymas

[1] At the time of designation

Language	Active ingredient	Indication
Maltese	Vettur virali serotip S3 assoċjat ma' adeno li jikkodifika l-alfa galaktosidaži A cDNA tal-bniedem	Kura tal-marda ta' Fabry
Polish	Wektor wirusowy związany z adenowirusami serotypu S3 kodujący cDNA ludzkiej alfa-galaktozydazy A	Leczenie choroby Fabry'ego
Portuguese	Vetor viral adeno-associado de serotipo S3 que codifica o cDNA da alfa-galactosidase A humana	Tratamento da doença de Fabry
Romanian	Vector viral adeno-asociat de serotip S3 ce codifică ADNc al alfa-galactozidazei A umane	Tratamentul bolii Fabry
Slovak	Adeno-asociovaný vírusový vektor sérotypu S3 kódujúci cDNA ľudskej alfa-galaktozidázy A	Liečba Fabryho choroby
Slovenian	Adeno-pridružen virusni vector serotipa S3 kodiran za cDNA humane alfa-galaktozidaze	Zdravljenje Fabryjeve bolezni
Spanish	Vector viral adeno-associado de serotipo S3 que codifica el cDNA de la alfa-galactosidase A humana	Tratamiento de la enfermedad de Fabry
Swedish	Adenoassocierad virusvektor serotyp S3 kodande för humant alfagalaktosidas A cDNA	Behandling av Fabrys sjukdom
Norwegian	Adenoassosiert virusvektor serotype S3 som koder for humant alfa-galaktosidase A cDNA	Behandling av Fabrys sykdom
Icelandic	Adenótengd veirugenaferja af sermisgerð S3 sem táknar fyrir manna alfa-galaktósídasa A cDNA	Meðferð Fabry-sjúkdóms