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Committee for Orphan Medicinal Products

# Public summary of opinion on orphan designation

## Adeno-associated viral vector serotype 8 containing the human alpha-galactosidase A gene for treatment of Fabry disease

On 20 March 2017, orphan designation (EU/3/17/1849) was granted by the European Commission to Freeline Therapeutics Ltd, United Kingdom, for adeno-associated viral vector serotype 8 containing the human alpha-galactosidase A gene for 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 lesions on the skin, 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 analgesics. It is also life-threatening due to kidney, heart and brain complications.

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

At the time of designation, Fabry disease affected less than 2.6 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 134,000 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 515,700,000 (Eurostat 2017).

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The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with the condition. Laboratory studies indicate that a single dose of the medicine could restore 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 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 Fabry disease had been started.

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

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 16 February 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 8 containing the human alpha-galactosidase A gene | Treatment of Fabry disease |
| Bulgarian | Адено-свързан вирусен вектор серотип 8, съдържащ гена на човешката алфа-галактозидаза А | Лечение на болест на Fabry |
| Croatian | Adeno-vezani virusni vektor serotipa 8 koji sadrži ljudski gen za alfa-galaktozidazu A | Liječenje Fabryjeve bolesti |
| Czech | Adeno-asociovaný virový vektor sérotypu 8obsahující gen pro humánní alfa-galaktosidázu A | Léčba Fabryho choroby |
| Danish | Adenoassocieret viral serotype 8 vektor, indeholdende det humane alfa-galaktosidase A-gen | Behandling af Fabrys sygdom |
| Dutch | Adeno-geassocieerde virale vector serotype 8 welke het humaan alfa-galactosidase A gen bevat | Behandeling van de ziekte van Fabry |
| Estonian | Inimese alfagalaktosidaas A geeni sisaldav adenoviirusega assotsieerunud viirusvektori serotüüp 8 | Fabry tõve ravi |
| Finnish | Adenoassosioitu virusvektori, serotyyppi 8, joka sisältää ihmisen alfa-galaktosidaasi-geenin | Fabryn taudin hoito |
| French | Vecteur viral adéno-associé de sérotype 8 contenant le gène du alpha-galactosidase A humain | Traitement de la maladie de Fabry |
| German | Adeno-assoziierter viraler Vektor vom Serotyp 8, der das humane Alpha-Galactosidase A-Gen enthält | Behandlung des Fabry-Syndroms |
| Greek | Αδενοσχετιζόμενος ιικός φορέας οροτύπου 8 που περιέχει το ανθρώπινο γονίδιο της α-γαλακτοσιδάσης Α | Θεραπεία της νόσου του Fabry |
| Hungarian | Humán alfa-galaktozidáz A gént tartalmazó 8-as szerotípusú adeno-asszociált vírusvektor | Fabry betegség kezelése |
| Italian | Vettore virale adeno-associato di sierotipo 8 contenente il gene del alfa-galattosidasi A umano | Trattamento della malattia di Fabry |
| Latvian | Adeno-asociētā vīrusa 8. seroptipa vektors, kas satur cilvēka α-galaktozidāzes A gēnu | Fabrī slimības ārstēšana |
| Lithuanian | Adenoasocijuoto viruso vektoriaus 8 serotipas, turintis žmogaus alfa-galaktozidazės A geną | Fabry ligos gydymas |
| Maltese | Vettur virali tas-serotip 8 assoċjat ma' adeno li fih il-ġene uman ta' alfa-galaktożidaži | Kura tal-marda ta' Fabry |
| Polish | Wektor wirusowy związany z adenowirusami serotypu 8 zawierający gen ludzkiej alfa galaktozydazy A | Leczenie choroby Fabry'ego |
| Portuguese | Vetor viral de serotipo 8 adeno-associado contendo o gene da alfa-galactosidase A humana | Tratamento da doença de Fabry |

[1] At the time of designation

| Language | Active ingredient | Indication |
|---|---|---|
| Romanian | Vector viral adeno-asociat de serotip 8 care conţine gena alfa-galactozidazei A umane | Tratamentul bolii Fabry |
| Slovak | Adeno-asociovaný vírusový vektor sérotypu 8 obsahujúci gén ľudskej alfa-galaktozidázy A | Liečba Fabryho choroby |
| Slovenian | Adenovirusni vektor serotipa 8, ki vsebuje gen za humano alfa-galaktozidazo A | Zdravljenje Fabryjeve bolezni |
| Spanish | Vector viral adenoasociado recombinante serotipo 8 que contiene el gen del alfa-galactosidasa A humano | Tratamiento de la enfermedad de Fabry |
| Swedish | Adenoassocierad virusvektor serotyp 8 innehållande genen för humant alpha-galaktosidas A | Behandling av Fabrys sjukdom |
| Norwegian | Adenoassosiert virusvektor serotype 8 som inneholder genet for human alfa-galaktosidase A | Behandling av Fabrys sykdom |
| Icelandic | Adenótengd veiruferja af sermisgerð 8 sem inniheldur manna tákna-bættan erfðavísi fyrir alfa-galaktósíðasa A | Meðferð Fabry-sjúkdóms |