



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

## Public summary of opinion on orphan designation

(3S)-1-azabicyclo[2.2.2]oct-3-yl{2-[2-(4-fluorophenyl)-1,3-thiazol-4-yl]propan-2-yl} carbamate for the treatment of Fabry disease

On 22 August 2014, orphan designation (EU/3/14/1310) was granted by the European Commission to Genzyme Europe BV, the Netherlands, for (3S)-1-azabicyclo[2.2.2]oct-3-yl{2-[2-(4-fluorophenyl)-1,3-thiazol-4-yl]propan-2-yl} carbamate 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. This enzyme is contained in lysosomes (part of the body's cells that break down nutrients and other materials) where it breaks down and removes globotriaosylceramide (Gb3, a complex molecule of sugars and a fatty substance stored in the body). In patients who lack this enzyme, 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 neurological 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 2.3 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 118,000 people<sup>\*</sup>, 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).

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<sup>\*</sup>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 511,100,000 (Eurostat 2014).



## What treatments are available?

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

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with Fabry disease because early studies in experimental models suggest that it could improve the outcome of patients when used in combination with current therapies. 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 expected to work by blocking the enzyme glucosylceramide synthase, which is involved in producing Gb3. By blocking the production of Gb3, the medicine is expected to slow down its build up in patients with Fabry disease, who lack alpha-galactosidase A and therefore cannot break Gb3 down. This is expected to lead to a reduction in Gb3, thereby reducing the symptoms of Fabry disease.

## 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 Fabry disease were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for Fabry's 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 10 July 2014 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:

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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<sup>1</sup>, Norwegian and Icelandic

Language	Active ingredient	Indication
English	(3S)-1-azabicyclo[2.2.2]oct-3-yl{2-[2-(4-fluorophenyl)-1,3-thiazol-4-yl]propan-2-yl} carbamate	Treatment of Fabry disease
Bulgarian	(3S)-1-азабицикло[2.2.2]окт-3-ил{2-[2-(4-флуорофенил)-1,3-тиазол-4-ил]пропан-2-ил} карбамат	Лечение на болест на Fabry
Croatian	(3S)-1-azabiciкло[2.2.2]okt-3-il{2-[2-(4-fluorofenil)-1,3-tiazol-4-il]propan-2-il} karbamat	Liječenje Fabryjeve bolesti
Czech	(3S)-1-azabicyklo[2.2.2]okt-3-yl{2-[2-(4-fluorofenyl)-1,3-thiazol-4-yl]propan-2-yl} karbamát	Léčba Fabryho choroby
Danish	(3s)-1-azabicyclo[2.2.2]oct-3-yl{2-[2-(4-fluorophenyl)-1,3-thiazol-4-yl]propan-2-yl} carbamat	Behandling af Fabrys sygdom
Dutch	(3S)-1-azabicyclo[2.2.2]oct-3-yl{2-[2-(4-fluorophenyl)-1,3-thiazol-4-yl]propaan-2-yl} carbamaat	Behandeling van de ziekte van Fabry
Estonian	(3S)-1-asabitsüklo[2.2.2]okt-3-üül{2-[2-(4-fluorofenüül)-1,3-tiasool-4-üül]propaan-2-üül} karbamaat	Fabry tõve ravi
Finnish	(3S)-1-atsabisyklo[2.2.2]okt-3-yyli-{2-[2-(4-fluorifenyyli)-1,3-tiatsol-4-yyli]propan-2-yyli} karbamaatti	Fabryn taudin hoito
French	(3S)-1-azabicyclo[2.2.2]oct-3-yl{2-[2-(4-fluorophényl)-1,3-thiazol-4-yl]propan-2-yl} carbamate	Traitement de la maladie de Fabry
German	(3S)-1-Azabicyclo[2,2,2]oct-3-yl {2-[2-(4-fluorophenyl)-1,3-thiazol-4-yl]propan-2-yl} carbamat	Behandlung des Fabry-Syndroms
Greek	(3S)-1-αζαδίκυκλο[2.2.2]όκτα-3-υλο-{2-[2-(4-φθοροφαίνυλο)-1,3-θειαζολ-4-υλο]προπαν-2-υλοκαρβαμικό	Θεραπεία της νόσου του Fabry
Hungarian	(3S)-1-azabicyclo[2.2.2]oct-3-yl{2-[2-(4-fluorophenyl)-1,3-thiazol-4-yl]propán-2-yl} karbamát	Fabry betegség kezelése
Italian	(3S)-1-azabiciiclo[2.2.2]oct-3-il {2-[2-(4-fluorofenil)-1,3-tiazol-4-il]propan-2-il} carbamato	Trattamento della malattia di Fabry
Latvian	(3S)-1-azabiciķlo[2.2.2]okt-3-il{2-[2-(4-fluorfenil)-1,3-tiazol-4-il]propān-2-il} karbamāts	Fabrī slimības ārstēšana
Lithuanian	(3S)-1-azabiciķlo[2.2.2]okt-3-il{2-[2-(4-fluorofenil)-1,3-tiazol-4-il]propan-2-il} karbamatas	Fabry ligos gydymas

<sup>1</sup> At the time of designation

Language	Active ingredient	Indication
Maltese	(3S)-1-azabicyclo[2.2.2]oct-3-yl{2-[2-(4-fluorophenyl)-1,3-thiazol-4-yl]propan-2-yl} carbamate	Kura tal-marda ta' Fabry
Polish	(3S)-1-azabicyklo[2.2.2]okt-3-yl{2-[2-(4-fluorofenyl)-1,3-tiazol-4-yl]propan-2-ylo} karbaminian	Leczenie choroby Fabry'ego
Portuguese	(3S)-1-azabicyclo[2.2.2]oct-3-il{2-[2-(4-fluorofenil)-1,3-tiazol-4-il]propan-2-il} carbamato	Tratamento da doença de Fabry
Romanian	(3S)-1-azabicyclo[2.2.2]oct-3-il{2-[2-(4-fluorofenil)-1,3-tiazol-4-il]propan-2-il} carbamat	Tratamentul bolii Fabry
Slovak	(3S)-1-azabicyklo[2,2,2]okt-3-yl{2-[2-(4-fluorofenyl)-1,3-tiazol-4-yl]propán-2-yl} karbamát	Liečba Fabryho choroby
Slovenian	(3S)-1-azabicyklo[2.2.2]oct-3-il{2-[2-(4-fluorofenil)-1,3-tiazol-4-il]propan-2-il} karbamat	Zdravljenje Fabryjeve bolezni
Spanish	(3S)-1-azabicyclo[2.2.2]oct-3-il{2-[2-(4-fluorofenil)-1,3-tiazol-4-il]propan-2-il} carbamato	Tratamiento de la enfermedad de Fabry
Swedish	(3S)-1-azabicyklo[2.2.2]okt-3-yl{2-[2-(4-fluorofenyl)-1,3-tiazol-4-yl]propan-2-yl} karbamat	Behandling av Fabrys sjukdom
Norwegian	(3S)-1-azabicyklo[2.2.2]okt-3-yl{2-[2-(4-fluorofenyl)-1,3-tiazol-4-yl]propan-2-yl} karbamát	Behandling av Fabrys sykdom
Icelandic	(3S)-1-azabícykló[2.2.2]oct-3-yl{2-[2-(4-flúórófenýl)-1,3-thíazól-4-ýl]própan-2-ýl} carbamat	Meðferð Fabry-sjúkdóms