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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Recombinant human alpha-glucosidase conjugated with multiple copies of synthetic bismannose-6-phosphate-tetra-mannose glycan for the treatment of glycogen storage disease type II (Pompe's disease)

On 26 March 2014, orphan designation (EU/3/14/1251) was granted by the European Commission to Genzyme Europe BV, the Netherlands, for recombinant human alpha-glucosidase conjugated with multiple copies of synthetic bismannose-6-phosphate-tetra-mannose glycan for the treatment of glycogen storage disease type II (Pompe's disease).

What is glycogen storage disease type II?

Glycogen storage disease type II, also known as Pompe's disease, is an inherited disorder that is caused by the lack of an enzyme called acid alpha glucosidase (GAA). This enzyme is contained in lysosomes (part of the body's cells that break down nutrients and other materials). GAA breaks down glycogen (a complex sugar stored in the body) into glucose. When this enzyme is lacking, large amounts of glycogen build up in the muscles, including the heart muscle and diaphragm (the main breathing muscle under the lungs). The progressive build-up of glycogen causes a wide range of signs and symptoms, including heart problems, breathing difficulties and muscle weakness.

Glycogen storage disease type II is a long-term debilitating and life-threatening disease because it causes breathing and heart problems and is associated with premature death.

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

At the time of designation, glycogen storage disease type II affected not more than 1 in 10,000 people in the European Union (EU). This was equivalent to a total of not more than 51,000 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 511,100,000 (Eurostat 2014).

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What treatments are available?

At the time of designation, Myozyme (alglucosidase alfa) was authorised for the treatment of glycogen storage disease type II in the EU. Myozyme is an 'enzyme replacement therapy' that works by replacing the missing GAA enzyme.

The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with glycogen storage disease type II because early studies in experimental models show that it might improve muscle function of patients with this 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?

Like Myozyme, this medicine is an enzyme replacement therapy that works by replacing the missing GAA enzyme in patients with glycogen storage disease type II. It is a copy of human GAA, which is produced by a method known as 'recombinant DNA technology': it is made by cells into which a gene (DNA) has been introduced that makes them able to produce the enzyme. The replacement enzyme helps to break down glycogen and stops its build up in the cells.

The GAA in this medicine is attached to several molecules called 'bismannose-6-phosphate-tetra-mannose glycan'. This is expected to increase the uptake of the enzyme by skeletal muscles (muscles used for movement), thereby improving muscle coordination and strength of patients with glycogen storage disease type II.

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, a clinical trial with the medicine in patients withglycogen storage disease type II was ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for glycogen storage disease type II 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 6 February 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[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	Recombinant human alpha-glucosidase conjugated with multiple copies of synthetic bismannose-6-phosphate-tetra-mannose glycan	Treatment of glycogen storage disease type II (Pompe's disease)
Bulgarian	рекомбинантна човешка алфа-глюкозидаза, конюгирана с множество копия на синтетичен бис-маноза-6-фосфат-тетра-маноза гликан	Лечение на тип 2 гликогеноза (Болест на Помпе)
Czech	Rekombinantní lidská alfa-glukosidáza konjugovaná s mnohonásobnými kopiemi syntetického bis-manóza-6-fosfát-tetra-manóza glykanu	Léba glykogenózy typu II (Pompeho choroba)
Croatian	Rekombinantna ljudska alfa-glukozidaza konjugirana s višestrukim kopijama sintetskog bis-manoza-6-fosfat-tetra-manoza glikana	Liječenje bolesti nagomilavanja glikogena tip II (Pompeova bolest)
Danish	Rekombinant human alfa-glucosidase konjugeret med multiple kopier af syntetisk bis-mannose- 6-phosphat-tetra-mannose glycan	Behandling af glycogenose type II (Pompes sygdom)
Dutch	Recombinant humaan alfa-glucosidase geconjugeerd met meerdere kopieën van synthetisch bis-mannose-6-fosfaat-tetra-mannose glycaan	Behandeling van de glycogeenstapelingsziekte type II (Pompe-ziekte)
Estonian	Rekombinantne inimese alfa-glükosidaas konjugeeritud sünteetilise bis-mannoos-6-fosfaat-tetra-mannoos glükaani hulgikoopiatega	Glükogenoos II (Pompe tõve) ravi
Finnish	Rekombinantti ihmisen alfaglukosidaasi konjugoituna useisiin synteettisen bis-mannoosi-6-fosfaatti-tetra-mannoosi-glykaanin kopioihin	Tyyppi II glykogenoosin (Pompen tauti) hoito
French	Alpha-glucosidase recombinante humaine conjuguée à de multiples copies de bis-mannose-6-phosphate-tétra-mannose-glycane de synthèse	Traitement de la glycogénose de type II (maladie de Pompe)
German	Rekombinante humane alpha-Glukosidase konjugiert mit mehreren Einheiten synthetischer bis-Mannose-6-phosphat-tetra-Mannose-Glykane	Behandlung der Glykogenspeicherkrankheit Typ II (Pompe-Krankheit)
Greek	Ανασυνδυασμένη ανθρώπινη άλφα-γλυκοσιδάση συνδεδεμένη με πολλαπλά αντίγραφα συνθετικής δι-6-φωσφορικής-μαννόζο-τέτρα-μαννόζο γλυκάνης	Θεραπεία της Γλυκογόνωσης τύπου II (Νόσος του Pompe)
Hungarian	Rekombináns humán alfa-glükozidáz szintetikus bisz-mannóz-6-foszfát-tetra-mannóz glikán többszörös kópiájához kapcsolva	II-es típusú glikogéntárolási betegség (Pompe-kór) kezelése
Italian	Alfa-glucosidasi umana ricombinante coniugata con copie multiple di bis-mannosio-6-fosfato-tetra mannosio glicano di sintesi	Trattamento della glicogenosi, tipo II (malattia di Pompe)

[1] At the time of designation

Language	Active ingredient	Indication
Latvian	Ar vairākām sintētiska bis-mannozes-6-fosfāt-tetra-mannozes glikāna kopijām konjugēta rekombinanta cilvēka alfa-glikozidāze	Glikogēna uzkrāsanas II tipa traucējumu (Pompe slimība) ārstēšana
Lithuanian	Rekombinantinė žmogaus alfa-gliukozidazė su dauginėmis sintetinio bis-manozės-6-fosfato-tetra-manozės glikano kopijomis	II tipo glikogenozės (Pompe ligos) gydymas
Maltese	Alfa-glucosidase uman rikombinanti kkonġugat ma' kopji multipli ta' bismannose-6-phosphate-tetra-mannose glycan sintetiku	Kura tal-glikoġenożi tat-tip II (marda ta' Pompe)
Polish	Rekombinowana ludzka alfa-glukozydaza sprzężona z multiplikowanym syntetycznym bis-mannozo-6-fosforanem-tetra-mannozo glukanem	Leczenie choroby spichrzania glikogenu typu II (choroby Pompego)
Portuguese	Alfa-glucosidase humana recombinante conjugada com cópias múltiplas de bis-manose-6-fosfato-tetra-manose glicano sintético	Tratamento da glicogenose de tipo II (Doença de Pompe)
Romanian	Alfa-glucozidază umană recombinantă conjugată cu multiple copii de bi-manozo-6-fosfat-tetra-manozo-glican de sinteză	Tratamentul glicogenozei tip II (boala Pompe)
Slovak	Rekombinantná ľudská alfa-glukozidáza konjugovaná s mnohonásobnými kópiami syntetického bis-manóza-6-fosfát-tetra-manózoglykánu	Liečba glykogenózy typ II (Pompeho choroba)
Slovenian	Rekombinantna humana alfa-glukozidaza konjugirana z večkratnimi kopijami sintetičnega bis-manoza-6-fosfat-tetra-manoza glikana	Zdravljenje glikogenoze tipa II (Pompejeva bolezen)
Spanish	Alfa-glucosidasa humana recombinante conjugada con múltiples copias de glicano sintético bis-manosa-6-fosfato-tetra-manosa	Tratamiento de la enfermedad de almacenamiento del glucógeno tipo II (enfermedad de Pompe)
Swedish	Rekombinant humant alfa-glukosidas konjugerat med multipla kopior av syntetisk bis-mannos-6-fosfat--tetra-mannos glykan	Behandling av glykogen upplagringssjukdom typ II (Pompes sjukdom)
Norwegian	Rekombinant humant alfa-glukosidase konjugert med flere kopier av syntetisk bis-mannose-6-fosfat-tetra-mannose glukan	Behandling av glykogenose type II (Pompes sykdom)
Icelandic	Raðbrigða manna alfa-glúkósídasi tengdur mörgum eintökum af samtengdum bis-mannósa-6-fosfat-tetra-mannósaglýkani	Meðferð á glýkógenupphleðslu sjúkómi af gerð II (Pompes sjúkdómur)