



## **Committee for Orphan Medicinal Products**

### **Public summary of positive opinion for orphan designation of recombinant human acid sphingomyelinase for the treatment of Niemann-Pick disease, type B**

On 19 September 2001, orphan designation (EU/3/01/056) was granted by the European Commission to Genzyme B.V., The Netherlands, for recombinant human acid sphingomyelinase for the treatment of Niemann-Pick disease, type B.

The sponsorship was transferred to Genzyme Europe B.V., The Netherlands, in April 2002.

#### **What is Niemann-Pick disease, type B?**

Niemann-Pick disease refers to a group of inherited metabolic disorders that belong to the larger family of lysosomal storage diseases (LSDs). Niemann-Pick diseases are classified in a subgroup of LSDs lipid storage diseases in which harmful quantities of fatty substances, called lipids, accumulate in the spleen, liver, lungs, bone marrow, and brain. There are four types of Niemann-Pick, all having in common the lack or very low activity of the lysosomal enzyme "acid sphingomyelinase". LSDs are divided in four categories; primary deficiency in acid sphingomyelinase (type A and B) and defective transport of cholesterol (type of fat) across the lysosomal membrane (type C and D). Type A and B are caused by different mutations in the same gene which encodes the enzyme acid sphingomyelinase (ASM), responsible for breaking down a lipid (fatty substance) called sphingomyelin. Niemann-Pick disease varies in age of onset and severity. As it progresses it may lead to abnormal enlargement of the liver, liver disease, development of foam cells (cells with accumulated fat) in the liver and lungs, causing lung disease. Niemann-Pick disease type B is chronically debilitating and life threatening.

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

At the time of designation Niemann-Pick disease, type B affected less than 0.04 in 10,000 people in the European Union (EU)\*. This is based on the information provided by the sponsor and knowledge of the Committee for Orphan Medicinal Products (COMP). This is below the threshold for orphan designation which is 5 in 10,000. This is equivalent to a total of around 1,500 people.

#### **What treatments are available?**

At the time of submission of application for orphan drug designation there was no satisfactory treatment of Niemann-Pick disease, type B in the European Union.

Treatment included symptomatic treatment such as lipid-lowering medicines, antibiotics and oxygen. Surgery to remove the spleen, an organ which is part of the immune system, was performed in some cases.

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\*Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed based on data from the European Union. This represents a population of 377,000,000 (Eurostat 2001).

**How is this medicine expected to work?**

The recombinant human acid sphingomyelinase is produced in laboratories by chinese hamster ovary cells expressing the human sphingomyelinase gene. According to the sponsor, the activity of the enzyme could prevent or ameliorate the accumulation of sphingomyelin by removing it from the liver, lung and other visceral tissues.

**What is the stage of development of this medicine?**

The effects of recombinant human acid sphingomyelinase were evaluated in experimental models.

At the time of submission of the application for orphan designation, no clinical trials in patients with Niemann-Pick disease, type B were initiated.

Recombinant human acid sphingomyelinase was not authorised anywhere worldwide for treatment of Niemann-Pick disease, type B, at the time of submission. Orphan designation of recombinant human acid sphingomyelinase was granted in the United States for treatment of acid sphingomyelinase deficiency (Niemann-Pick disease).

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 18 July 2001 a positive opinion recommending the grant of the above-mentioned 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;
- and either the rarity of the condition (affecting not more than five in 10,000 people in the Community) or the 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 the quality, safety and efficacy is necessary before a product can be granted a marketing authorisation.

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### Translations of the active ingredient and indication in all EU languages

Language	Active Ingredient	Indication
English	Recombinant human acid sphingomyelinase	Treatment of Niemann-Pick Disease, Type B
Danish	Rekombinant human sur sphingomyelinase	Behandling af Niemann-Pick, type B
Dutch	Recombinant humaan zuur sfingomyelinase	Behandeling van de ziekte van Niemann-Pick, type B
Finnish	Rekombinantti ihmisen hapan sfingomyelinaasi	Tyypin B Nieman-Pick:in taudin hoito
French	Sphingomyélinase acide humaine recombinante	Traitement de la maladie de Niemann-Pick de types B
German	Rekombinante menschliche Säure-Sphingomyelinase	Behandlung der Niemann-Pick-Krankheit Typ B
Greek	Ανθρώπινη ανασυνδυασμένη όξινη σφιγγομυελινάση	Θεραπεία της νόσου Niemann-Pick, Τύπου Β
Italian	Sfingomielinasi acida ricombinante umana	Trattamento della malattia di Niemann-Pick, tipo B
Portuguese	Esfingomielinase ácida humana recombinante	Tratamento da doença de Niemann-Pick, tipos B
Spanish	Esfingomielinasa ácida humana recombinante	Tratamiento de la enfermedad de Niemann-Pick, tipos B
Swedish	Surt sfingomyelinas av human typ framställt med rekombinantteknik	Behandling av Niemann-Pick, typ B