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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

1,5-(butylimino)-1,5-dideoxy, D-glucitol for the treatment of Gaucher disease

Please note that this product was withdrawn from the Community Register of designated orphan medicinal products in November 2012 at the end of the period of market exclusivity.

On 18 October 2000, orphan designation (EU/3/00/006) was granted by the European Commission to Oxford GlycoSciences (UK) Ltd, United Kingdom, for 1,5-(butylimino)-1,5-dideoxy, D-glucitol for the treatment of Gaucher disease.

The sponsorship was transferred to Actelion Registration Limited, United Kingdom, in March 2003.

What is Gaucher Disease?

Gaucher disease is characterised by the accumulation of specific chemical substances (glucocerebrosides) in several types of cells of the immune system (the body's natural defence system) that are localised throughout the body, but particularly in the spleen, liver and bone marrow, and cells of the nervous system (neurons). The disorder results from decreased activity of an enzyme (a protein that can trigger a chemical reaction in the body), called glucocerebrosidase or acid β–glucosidase; this enzyme normally degrades the glucocerebrosides. Since glucocerebrosides are not cleared, they progressively accumulate in the cells. The disorder has a genetic origin, so it is caused by damage in a gene that carries the information necessary for the production of the enzyme. The severity of Gaucher disease is extremely variable; some patients present in childhood with virtually all the complications of Gaucher disease, while others remain asymptomatic for more than 70 years.

Gaucher disease has traditionally been divided into the following 3 clinical subtypes, according to the absence or presence of damage to the nerves and its progression:

- Type 1 - Non-neuronopathic form (the most common and least severe form);
- Type 2 - Acute neuronopathic form (the most severe form, usually diagnosed shortly after birth);
- Type 3 - Chronic neuronopathic form (a form of intermediate severity between Type 1 and Type 2).

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8416
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union

However, some cases do not fit precisely into one of these categories. Gaucher disease can be life-threatening (Type 2 and 3) or chronically debilitating (Type 1).

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

At the time of designation, Gaucher disease affected less than 0.6 in 10,000 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 23,000 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 submission of application for orphan drug designation, there were only medicinal products authorised for the treatment of type 1 Gaucher disease. These products aimed to replace the missing or defective enzyme. Some patients were treated symptomatically with splenectomy (surgical removal of the spleen) or bone marrow transplantation.

Satisfactory argumentation has been submitted by the sponsor to justify the assumption that 1,5-(butylimino)-1,5-dideoxy, D-glucitol might be of potential significant benefit for the treatment of Gaucher disease, mainly because it may be of major contribution to patient care. This assumption will have to be confirmed at the time of marketing authorisation. This will be necessary to maintain the orphan status.

How is this medicine expected to work?

1,5-(butylimino)-1,5-dideoxy, D-glucitol is structurally similar to glucose, a sugar that is used by the body to make glucocerebrosides. According to the sponsor, 1,5-(butylimino)-1,5-dideoxy, D-glucitol will bind to the enzyme that produces the harmful accumulating glucocerebrosides and thus reduces them in the body.

What is the stage of development of this medicine?

The effects of 1,5-(butylimino)-1,5-dideoxy, D-glucitol were evaluated in experimental models.

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

1,5-(butylimino)-1,5-dideoxy, D-glucitol was not authorised anywhere worldwide for the treatment of Gaucher disease, at the time of submission. Orphan designation of 1,5-(butylimino)-1,5-dideoxy, D-glucitol was granted in the United States for the treatment of Gaucher disease, among other indications.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 13 September 2000 recommending the granting of this designation.

[*] 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.
At the time of designation, this represented a population of 375,500,000 (Eurostat 2000).

Update: 1,5-(butylimino)-1,5-dideoxy, D-glucitol (Zavesca) has been authorised in the EU since 20 November 2002 for the oral treatment of mild to moderate type 1 Gaucher disease. Zavesca may be used only in the treatment of patients for whom enzyme replacement therapy is unsuitable.

More information on Zavesca can be found in the European public assessment report (EPAR) on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European Public Assessment Reports

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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:

Actelion Registration Limited
BSI Building 13th floor
389 Chiswick High Road
London W4 4AL
United Kingdom
Telephone: + 44 208 987 3320
Telefax: + 44 208 987 3322

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	1,5-(Butylimino)-1,5-dideoxy, D-glucitol	Treatment of Gaucher Disease
Danish	1,5-(butylimino)-1,5-dideoxy, D-glucitol	Behandling af Gauchers sygdom
Dutch	1,5-(Butylimino)-1,5-dideoxy, D-glucitol	Behandeling van de ziekte van Gaucher
Finnish	1,5-(butyyli-imino)-1,5-dideoksi, D-glusitoli	Gaucherin taudin hoito
French	1,5-(Butylimino)-1,5-didésoxy, D-glucitol	Traitement de la maladie de Gaucher
German	1,5-(Butylimino)-1,5-didesoxy, D-Glucitol	Behandlung der Gaucher-Krankheit
Greek	1,5-(Butylimino)-1,5-dideoxy, D-glucitol	Θεραπευτική αγωγή για την νόσο του Gaucher
Italian	1,5-(Butilimino)-1,5-dideoxi, D-glucitol	Trattamento della malattia di Gaucher
Portuguese	1,5-(Butilimino)-1,5-dideoxi, D-glucitol	Tratamento da doença de Gaucher
Spanish	1,5-(Butilimino)-1,5-didesoxi,D-glucitol	Tratamiento de la enfermedad de Gaucher
Swedish	1,5-(butylimino)-1,5-dideoxi, D-glucitol	Behandling av Gauchers sjukdom

[1] At the time of designation