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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Sodium phenylbutyrate for the treatment of ornithine transcarbamylase deficiency

First publication	29 February 2012
Rev.1: withdrawal from the Community Register	23 July 2013
Rev.2: administrative update	3 October 2013

Disclaimer

Please note that revisions to the Public Summary of Opinion are purely administrative updates. Therefore, the scientific content of the document reflects the outcome of the Committee for Orphan Medicinal Products (COMP) at the time of designation and is not updated after first publication.

Please note that this product was withdrawn from the Community Register of designated Orphan Medicinal Products in July 2013 on request of the Sponsor.

On 9 February 2012, orphan designation (EU/3/12/950) was granted by the European Commission to Lucane Pharma SA, France, for sodium phenylbutyrate for the treatment of ornithine transcarbamylase deficiency.

What is ornithine transcarbamylase deficiency?

Ornithine transcarbamylase deficiency is one of the inherited disorders known as 'urea cycle disorders', which cause ammonia to accumulate in the blood. Patients with ornithine transcarbamylase deficiency lack 'ornithine transcarbamylase', one of the liver enzymes that are needed to get rid of excess nitrogen. In the absence of this enzyme, excess nitrogen accumulates in the body in the form of ammonia, which can be toxic at high levels, especially to the brain. Symptoms of the disease usually appear in the first few days of life and include lethargy (lack of energy), vomiting, loss of appetite, seizures (fits) and coma.

Ornithine transcarbamylase deficiency is a long-term debilitating and life-threatening disease that leads to mental retardation and is associated with poor overall survival.

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

At the time of designation, ornithine transcarbamylase deficiency affected less than 0.1 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 5,000 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, sodium phenylbutyrate was already authorised in the EU for the treatment of some urea cycle disorders, including ornithine transcarbamylase deficiency. This medicine is known to have a bitter taste which may decrease compliance with treatment. In addition, patients were advised to control their dietary intake of proteins, which are rich in nitrogen, to reduce the amount of ammonia formed in the body.

The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with ornithine transcarbamylase deficiency because it is a new tasteless granule formulation of sodium phenylbutyrate developed to mask its bitter taste, which is expected to help patients to follow their 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?

After it is ingested, sodium phenylbutyrate is converted into a substance called phenylacetate in the body. Phenylacetate attaches to the amino acid glutamine, which contains nitrogen, forming a substance that is eliminated in the urine. This allows the levels of nitrogen in the body to decrease, reducing the amount of ammonia produced.

This medicine is a new formulation of sodium phenylbutyrate in which the granules are coated in a way that masks the bitter taste of the medicine, making it more palatable.

What is the stage of development of this medicine?

The effects of sodium phenylbutyrate 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 ornithine transcarbamylase deficiency had been started.

At the time of submission, this medicine was not authorised anywhere in the EU for ornithine transcarbamylase deficiency 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 7 December 2011 recommending the granting of this designation.

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[*]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 27), Norway, Iceland and Liechtenstein.
At the time of designation, this represented a population of 509,000,000 (Eurostat 2012).

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	Sodium phenylbutyrate	Treatment of ornithine transcarbamylase deficiency
Bulgarian	Натриев фенилбутират	Лечение на дефицит на орнитин транскарбамилаза
Czech	Natrium-fenylbutyrát	Léčba nedostatku transkarbamylázy ornithinu
Danish	Natriumphenylbutyrat	Behandling af ornithin transcarbamylase defekt
Dutch	Natriumfenylbutyraat	Behandeling van ornithine transcarbamylase deficiëntie
Estonian	Naatriumfenüülbutüraat	Ornitiintranskarbamülaasi puudulikkuse ravi
Finnish	Natriumfenyylibutyraatti	Ornitiinitranskarbamylaasin puutoksen hoito
French	Phénylbutyrate de sodium	Traitement du déficit en ornithine transcarbamylase
German	Natriumphenylbutyrat	Behandlung des Ornithintranscarbamylase-Mangels
Greek	Φαινυλοβουτυρικό νάτριο	Αγωγή για την έλλειψη της τρανσκαρβαμυλάσης της ορνιθίνης
Hungarian	Nátrium-fenilbutirát	Ornitin transzkarbamiláz hiány kezelése
Italian	Fenilbutirrato di sodio	Trattamento del deficit di ornitina-transcarbamilasi
Latvian	Nātrija fenilbutirāts	Ornitīna transkarbamilāzes nepietiekamības ārstēšana
Lithuanian	Natrio fenilbutiratas	Ornitintranskarbamilazės stokos gydymas
Maltese	Sodium phenylbutyrate	Kura ta' defiċjenza ta’ l-Ornithine Transcarbamylase
Polish	Fenylomaślan sodu	Leczenie pacjentów z niedoborem transkarbamylazy ornitynowej
Portuguese	Fenilbutirato de sódio	Tratamento da deficiência de ornitina-transcarbamilase
Romanian	Fenilbutirat de sodiu	Tratamentul deficitului de ornitin-transcarbamilază
Slovak	Fenylbutyrát sodný	Liečba nedostatku transkarbamylázy ornitínu
Slovenian	Natrijev fenilbutirat	Zdravljenje pomanjkanja ornitin-transkarbamilaze
Spanish	Fenilbutirato de sodio	Tratamiento de la deficiencia de ornitina transcarbamilasa
Swedish	Natriumfenylbutyrat	Behandling av brist på ornitintranskarbamylas
Norwegian	Natriumfenylbutyrat	Behandling av ornitintranskarbamylase-mangel
Icelandic	Natríum phenýlbútýrat	Meðferð við skorti á ornitín transkarbamýlasa

[1] At the time of designation