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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Sodium phenylbutyrate for the treatment of citrullinaemia type 1

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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Please note that this product was withdrawn from the Community Register of designated Orphan Medicinal Products in July 2013 on request of the Sponsor.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/3/12/949) was granted by the European Commission to Lucane Pharma SA, France, for sodium phenylbutyrate for the treatment of citrullinaemia type 1.

What is citrullinaemia type 1?

Citrullinaemia type 1 is one of the inherited disorders known as 'urea cycle disorders', which cause ammonia to accumulate in the blood. Patients with citrullinaemia type 1 lack 'argininosuccinate synthase', 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.

Citrullinaemia type 1 is a long-term debilitating and life-threatening disease that leads to mental retardation and is associated with poor overall survival.

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

At the time of designation, citrullinaemia type 1 affected less than 0.24 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 12,000 people*, and is below the

*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).

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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 citrullinaemia type 1. 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 citrullinaemia type 1 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 citrullinaemia type 1 had been started.

At the time of submission, this medicine was not authorised anywhere in the EU for citrullinaemia type 1 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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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 citrullinaemia type 1
Bulgarian	Натриев фенилбутират	Лечение на цитрилинемия тип 1
Czech	Natrium-fenylbutyrát	Léčba citrulinémie typu 1
Danish	Natriumphenylbutyrat	Behandling af citrullinæmi type 1
Dutch	Natriumfenylbutyraat	Behandeling van citrullinemia type1
Estonian	Naatriumfenüülbutüraat	1.tüüpi tsitrullineemia ravi
Finnish	Natriumfenyylibutyraatti	1-Tyypin sitrullinemian hoito
French	Phénylbutyrate de sodium	Traitement de la citrullinémie de type 1
German	Natriumphenylbutyrat	Behandlung einer Citrullinämie Typ 1
Greek	Φαινυλοβουτυρικό νάτριο	Θεραπεία της κιτρουλιναιμίας τύπου 1.
Hungarian	Nátrium-fenilbutirát	1-es típusú citrullinaemia kezelésére
Italian	Fenilbutirrato di sodio	Trattamento della citrullinemia di tipo 1
Latvian	Nātrija fenilbutirāts	1. tipa citrulinēmijas ārstēšana
Lithuanian	Natrio fenilbutiratas	Citrulinemijos 1 tipo gydymas
Maltese	Sodium phenylbutyrate	Kura taċ-ċitrullinemija tat-tip 1
Polish	Fenylomaślan sodu	Leczenie cytrulinemii typu 1
Portuguese	Fenilbutirato de sódio	Tratamento da citrulimémia Tipo 1
Romanian	Fenilbutirat de sodiu	Tratamentul citrulinemiei de tip 1
Slovak	Fenylbutyrát sodný	Liečba citrulinémie 1. typu
Slovenian	Natrijev fenilbutirat	Zdravljenje citrulinemije tipa 1
Spanish	Fenilbutirato de sodio	Tratamitento de la citrulinemia de tipo 1
Swedish	Natriumfenylbutyrat	Behandling av citrullinemi typ 1
Norwegian	Natriumfenylbutyrat	Behandling av citrullinemi type 1
Icelandic	Natríum phenýlbútýrat	Meðferð á cítrúllíndreyra gerð 1

[1] At the time of designation