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Committee for Orphan Medicinal Products

# Public summary of opinion on orphan designation

## Sodium phenylbutyrate for the treatment of 5q spinal muscular atrophy

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On 11 January 2012, orphan designation (EU/3/11/948) was granted by the European Commission to GMP-Orphan SAS, France, for sodium phenylbutyrate for the treatment of 5q spinal muscular atrophy.

### What is 5q spinal muscular atrophy?

5q spinal muscular atrophy is an inherited disease that affects the motor neurons (nerves from the brain and spinal cord that control muscle movements). Patients with the disease lack a protein called 'survival motor neuron' (SMN), which is essential for the normal functioning and survival of motor neurons. Without this protein, the motor neurons deteriorate and eventually die. This causes the muscles to fall into disuse, leading to muscle wasting (atrophy) and weakness. Muscle weakness is usually more severe in the proximal musculature (the muscles closest to the trunk). The disease is linked to a defect on chromosome 5q and is usually diagnosed in the first year of life.

5q spinal muscular atrophy disease is a long-term debilitating and life-threatening disease because it causes breathing problems and paralysis that worsens over time.

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

At the time of designation, 5q spinal muscular atrophy affected approximately 0.3 in 10,000 people in the European Union (EU)[*]. This is equivalent to a total of around 15,000 people, and is below the ceiling for orphan designation, which are 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, no satisfactory methods were authorised in the EU for the treatment of 5q spinal muscular atrophy. Patients received supportive treatment to help them and their families cope with the symptoms of the disease. This included chest physiotherapy and physical aids to support muscular function, and ventilators to help with breathing.

[*]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. This represents a population of 506,300,000 (Eurostat 2011).

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## How is this medicine expected to work?

The SMN protein is made from two genes, the SMN1 and SMN2 genes. Most patients with 5q spinal muscular atrophy lack the SMN1 gene but have the SMN2 gene, which mostly produces a 'short' SMN protein which cannot work properly.

Sodium phenylbutyrate is expected to make the SMN2 gene produce adequate levels of SMN protein of normal length, thereby increasing the survival of motor neurons. It is expected to do this by blocking enzymes called histone deacetylases (HDAC), which are involved in turning genes 'on' and 'off' within cells. In 5q spinal muscular atrophy, sodium phenylbutyrate is expected to keep the SMN2 gene switched 'on'. This is expected to lead to an increased production of the normal-length SMN protein.

## 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, clinical trials with sodium phenylbutyrate in patients with 5q spinal muscular atrophy were ongoing.

At the time of submission, sodium phenylbutyrate was authorised in the EU for the treatment of urea cycle disorders.

At the time of submission, sodium phenylbutyrate was not authorised anywhere in the EU for 5q spinal muscular atrophy 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 9 November 2011 recommending the granting of this designation.

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.

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## 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.

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## 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 5q spinal muscular atrophy |
| Bulgarian | Натриев фенилбутират | Лечение на 5q спинална мускулна атрофия |
| Czech | Natrium-fenylbutyrát | Léčba 5q spinální muskulární atrofie |
| Danish | Natriumphenylbutyrat | Behandling af 5q spinal muskelatrofi |
| Dutch | Natriumfenylbutyraat | Behandeling van 5q spinale spieratrofie |
| Estonian | Naatriumfenüülbutüraat | 5q spinaalse lihasatroofia ravi |
| Finnish | Natriumfenyylibutyraatti | 5q-kromosomiin liittyvä motoneuronitauti |
| French | Phénylbutyrate de sodium | Traitement de l'amyotrophie spinale 5q |
| German | Natriumphenylbutyrat | Behandlung der 5q spinalen Muskelatrophie |
| Greek | Φαινυλοβουτυρικό νάτριο | Θεραπεία της νωτιαίας μυϊκής ατροφίας (5q) |
| Hungarian | Nátrium-fenilbutirát | 5q spinális izomatrophia kezelése |
| Italian | Fenilbutirrato di sodio | Trattamento dell'atrofia muscolare spinale 5q |
| Latvian | Nātrija fenilbutirāts | 5q spinālas muskuļu atrofijas ārstēšana |
| Lithuanian | Natrio fenilbutiratas | Spinalinės raumenų atrofijos gydymas, esant 5q delecijoms |
| Maltese | Sodium phenylbutyrate | Kura tal-atrofija muskolari spinali 5q |
| Polish | Fenylomaślan sodu | Leczenie rdzeniowego zaniku mięśni 5q |
| Portuguese | Fenilbutirato de sódio | Tratamento da atrofia muscular espinal 5q |
| Romanian | Fenilbutirat de sodiu | Tratamentul amiotrofiei spinale 5q |
| Slovak | Fenylbutyrát sodný | Liečba 5q spinálnej svalovej atrofie |
| Slovenian | Natrijev fenilbutirat | Zdravljenje 5q spinalne mišične atrofije |
| Spanish | Fenilbutirato de sodio | Tratamiento de la atrofia muscular espinal 5q |
| Swedish | Natriumfenylbutyrat | Behandling av 5q spinal muskelatrofi |
| Norwegian | Natriumfenylbutyrat | Behandling av 5q spinal muskelatrofi |
| Icelandic | Natríum phenýlbútýrat | Meðferð við 5q mænuvöðvarýrnun |

[1] At the time of designation