6 August 2020
EMADOC-628903358-2376

# Public summary of opinion on orphan designation

## Sodium phenylbutyrate, tauroursodeoxycholic acid for the treatment of amyotrophic lateral sclerosis

On 4 June 2020, orphan designation EU/3/20/2284 was granted by the European Commission to Drug Development and Regulation S.L., Spain, for sodium phenylbutyrate, tauroursodeoxycholic acid (also known as AMX0035) for the treatment of amyotrophic lateral sclerosis.

### What is amyotrophic lateral sclerosis?

Amyotrophic lateral sclerosis (ALS) is a progressive disease of the nervous system, where nerve cells in the brain and spinal cord that control voluntary movement gradually deteriorate, causing loss of muscle function and paralysis. The exact causes are unknown but are believed to include genetic and environmental factors. The symptoms of ALS depend on which muscles weaken first, and include loss of balance, loss of control of hand and arm movement, and difficulty speaking, swallowing and breathing. ALS usually starts in midlife and men are more likely to develop the disease than women.

ALS is a debilitating and life-threatening disease because of the gradual loss of function and its paralysing effect on muscles used for breathing, which usually leads to death from respiratory failure.

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

At the time of designation, ALS affected approximately 1 in 10,000 people in the European Union (EU). This was equivalent to a total of around 52,000 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, riluzole was authorised in the EU to treat ALS. Patients also received supportive treatment, such as physiotherapy and breathing support, to relieve the symptoms of the disease.

*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, Iceland, Liechtenstein, Norway and the United Kingdom. This represents a population of 519,200,000 (Eurostat 2020).

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The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with ALS. Studies showed that the medicine could improve strength of arms and lung function in patients being treated with riluzole. 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?

The medicine is made up of two substances: sodium phenylbutyrate and tauroursodeoxycholic acid. How the medicine works is not fully clear, but it is expected to reduce nerve cell stress and prevent nerve cells from dying. This is expected to improve symptoms of the disease.

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

The effects of sodium phenylbutyrate and tauroursodeoxycholic acid have been evaluated in experimental models.

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

At the time of submission, the medicine was not authorised anywhere in the EU for the treatment of ALS. Orphan designation had been granted in the United States for this condition.

In accordance with Regulation (EC) No 141/2000, the COMP adopted a positive opinion on 23 April 2020, 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:

Contact details of the current sponsor for this orphan designation can be found on EMA website.

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, tauroursodeoxycholic acid | Treatment of amyotrophic lateral sclerosis |
| Bulgarian | Натриев фенилбутират, тауроурсодеоксихолева киселина | Лечение на амиотрофична латерална склероза |
| Croatian | Natrijev fenilbutirat, tauroursodeoksikolična kiselina | Liječenje amiotrofične lateralne skleroze |
| Czech | Natrium-fenylbutyrát, kyselina tauroursodeoxycholová | Léčba amyotrofické laterální sklerózy (ALS) |
| Danish | Natriumphenylbutyrat, tauroursodeoxoycholsyre | Behandling af amyotrofisk lateralsklerose |
| Dutch | Natriumfenylbutyraat, tauroursodeoxycholiczuur | Behandeling van amyotrofe lateraalsclerose |
| Estonian | Naatriumfenüülbutüraat, tauroursodeoksükoolhape | Amüotroofilise lateraalskleroosi ravi |
| Finnish | Natriumfenyylibutyraatti, tauroursodeoksikoolihappo | Amyotrofisen lateraaliskleroosin hoito |
| French | Phénylbutyrate de sodium, acide tauroursodésoxycholique | Traitement de la sclérose latérale amyotrophique |
| German | Natriumphenylbutyrat, Tauroursodeoxycholic-Säure | Behandlung der amyotrophen Lateralsklerose |
| Greek | Φαινυλοβουτυρικό νάτριο-ταυροουρσοδεοξυχολικό οξύ | Θεραπεία πλάγιας μυοατροφικής σκλήρυνσης |
| Hungarian | Nátrium-fenilbutirát-tauroursodeoxycholsav | Amyotrophiás lateral sclerosis kezelése |
| Italian | Fenilbutirrato di sodio, acido tauroursodesossicolico | Trattamento della sclerosi laterale amiotrofica |
| Latvian | Nātrija fenilbutirāts, tauroursodeoksiholskābe | Amiotrofiskās laterālās sklerozes ārstēšana |
| Lithuanian | Natrio fenilbutiratas, tauroursodeoksicholio rūgštis | Šoninės amiotrofinės sklerozės gydymas |
| Maltese | Aċidu tawrursodeoksikoliku fenilbutiriku tas-sodju | Kura tas-sklerosi laterali amjotrofika |
| Polish | Fenylomaślan sodu, kwas tauroursodeoksycholowy | Leczenie stwardnienia bocznego zanikowego |
| Portuguese | Fenilbutirato de sódio, ácido tauroursodesoxicólico | Tratamento da esclerose lateral amiotrófica |
| Romanian | Fenilbutirat de sodiu, acid tauroursodeoxicolic | Tratamentul sclerozei laterale amiotrofice |
| Slovak | Fenylbutyrát sodný, tauroursodeoxycholová kyselina | Liečba amyotrofickej laterálnej sklerózy |

[1] At the time of designation

| Language | Active ingredient | Indication |
|---|---|---|
| Slovenian | Natrijev fenilbutirat, tauroursodeoksiholna kislina | Zdravljenje amiotrofične lateralne skleroze |
| Spanish | Fenilbutirato de sodio, ácido tauroursodesoxicólico | Tratamiento de la esclerosis lateral amiotrófica |
| Swedish | Natriumfenylbutyrat, tauroursodeoxykolsyra | Behandling av amyotrofisk lateralskleros |
| Norwegian | Natriumfenylbutyrat, tauroursodeoksykolsyre | Behandling av amyotrofisk lateralsklerose |
| Icelandic | Natríum phenýlbútýrat, tauroúrsódeoxýckólolic sýra | Meðferð við blandaðri hreyfitaugahrörnun |