



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Sodium benzoate for the treatment of argininosuccinic aciduria

On 11 January 2016, orphan designation (EU/3/15/1601) was granted by the European Commission to Syri Limited, United Kingdom, for sodium benzoate for the treatment of argininosuccinic aciduria.

What is argininosuccinic aciduria?

Argininosuccinic aciduria is one of the inherited disorders known as 'urea-cycle disorders', which cause ammonia to accumulate in the blood. Patients with this disorder lack 'argininosuccinate lyase', one of the liver enzymes that are needed to get rid of excess nitrogen. In the absence of this liver 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.

Argininosuccinic aciduria is a long-term debilitating and life-threatening disease that leads to mental disability and is associated with a high mortality rate.

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

At the time of designation, argininosuccinic aciduria 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, Ravicti (glycerol phenylbutyrate) was authorised in the EU for the treatment of urea cycle disorders including argininosuccinic aciduria. Patients were generally advised to control their dietary intake of proteins, which are rich in nitrogen, to reduce the amount of ammonia formed in the body. Ravicti is for use in patients who cannot be managed by changes in their diet alone.

*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 28), Norway, Iceland and Liechtenstein. This represents a population of 512,900,000 (Eurostat 2015).



The sponsor has provided sufficient information to show that sodium benzoate might be of significant benefit for patients with argininosuccinic aciduria because it could be used together with the currently authorised treatment, and could be beneficial when treating acute forms of the condition. 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?

Sodium benzoate has been used as an unlicensed treatment for hyperammonaemia (high levels of ammonia in the blood).

It works by combining with the amino acid glycine, which contains nitrogen, to form a substance that can be removed from the body by the kidneys. This allows the levels of nitrogen in the body to decrease, reducing the amount of ammonia produced and therefore the damage to the brain and other organs.

What is the stage of development of this medicine?

At the time of submission of the application for orphan designation, no clinical trials with sodium benzoate in patients with argininosuccinic aciduria had been started. The sponsor presented data from the published literature on the use of sodium benzoate in urea cycle disorders.

At the time of submission, sodium benzoate was not authorised anywhere in the EU for argininosuccinic aciduria 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 10 December 2015 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.

For more information

Sponsor's contact details:

Contact details of the current sponsor for this orphan designation can be found on EMA website, on the medicine's [rare disease designations page](#).

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 languages¹, Norwegian and Icelandic

| Language | Active ingredient | Indication |
|------------|--------------------|---------------------------------------------|
| English | Sodium benzoate | Treatment of argininosuccinic aciduria |
| Bulgarian | Натриев бензоат | Лечение на аргининосукцининова ацидурия |
| Croatian | Natrijev benzoat | Liječenje argininosukcinske acidurije |
| Czech | Benzoát sodný | Léčba argininosukcinátové acidurie |
| Danish | Natriumbenzoat | Behandling af argininravsyreuri |
| Dutch | Natriumbenzoaat | Behandeling van argininosuccinic aciduria |
| Estonian | Naatriumbenzoaat | Argininosuktsiin-atsiduuria ravi |
| Finnish | Natriumbentsoatti | Argininosukkinaattiasidurian hoito |
| French | Benzoate de sodium | Traitement de l'acidurie argininosuccinique |
| German | Natriumbenzoat | Behandlung einer Argininosukzinoazidurie |
| Greek | Βενζοϊκό νάτριο | Θεραπεία της αργινοηλεκτρικής οξυουρίας. |
| Hungarian | Nátrium benzoát | Argininoszukcinin anuria kezelésére |
| Italian | Benzoato di sodio | Trattamento dell'aciduria argininosuccinica |
| Latvian | Nātrija benzoāts | Arginīna sukcināta acidūrijas ārstēšana |
| Lithuanian | Natrio benzoatas | Arginino sukcininės acidurijos gydymas |
| Maltese | Sodium benzoate | Kura tal-aċidurja argininosuċċinika |
| Polish | Benzoesan sodu | Leczenie acydurii argininobursztynianowej |
| Portuguese | Benzoato de sódio | Tratamento da acidúria argininosuccínica |
| Romanian | Benzoat de sodiu | Tratamentul aciduriei argininosuccinice |
| Slovak | Benzoan sodný | Liečba arginínosukcinátovej acidúrie |
| Slovenian | Natrijev benzoat | Zdravljenje argininsukcinilne acidurije |
| Spanish | Benzoato de sodio | Tratamiento de la aciduria argininsuccínica |
| Swedish | Natriumbenzoat | Behandling av argininbarnstensätsaciduri |
| Norwegian | Natriumbenzoat | Behandling av argininsuccinaturiravsyreuil |
| Icelandic | Natríumbenzóat | Meðferð á argínínósúksíníksýrumígu |

¹ At the time of designation