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Public summary of opinion on orphan designation

Bacillus subtilis oxalate decarboxylase for the treatment of primary hyperoxaluria

On 17 July 2017, orphan designation (EU/3/17/1891) was granted by the European Commission to Allena Pharmaceuticals Ireland Limited, Ireland, for *Bacillus subtilis* oxalate decarboxylase (also known as ALLN-177) for the treatment of primary hyperoxaluria.

What is primary hyperoxaluria?

Primary hyperoxaluria is an inherited disease in which patients suffer from recurring kidney and bladder stones which lead to pain, blood in the urine and frequent urinary tract infections. The disease is caused by the lack of certain enzymes produced by the liver that are needed to breakdown a substance called glyoxylate in the body. Instead of being converted into the amino acid glycine, glyoxalate is therefore converted into excess oxalate. This can form calcium oxalate deposits, which cause kidney and bladder stones and may damage the kidneys and other organs.

Primary hyperoxaluria is long-term debilitating and life threatening because of the high rate of kidney failure seen in patients with the condition.

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

At the time of designation, primary hyperoxaluria affected approximately 0.1 in 10,000 people in the European Union (EU). This was equivalent to a total of around 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, no satisfactory methods were authorised in the EU for treating primary hyperoxaluria. Different treatments were used to prevent the accumulation of calcium oxalate such as dietary changes, drinking plenty of fluids and taking vitamin B6. Kidney and liver transplantation have been possible options in patients with kidney failure.

[*]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 515,700,000 (Eurostat 2017).

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How is this medicine expected to work?

The medicine contains an enzyme capable of breaking down oxalate that was originally derived from the bacterium *Bacillus subtilis*. When the medicine is swallowed the enzyme passes through the gut and breaks down oxalate present in food that would otherwise be absorbed, as well as oxalate that passes from the body into the gut. This action is expected to lower levels of oxalate in the body and so help reduce the formation of kidney and bladder stones.

What is the stage of development of this medicine?

The effects of the medicine have been evaluated in experimental models.

At the time of submission of the application for orphan designation, no clinical trials with *Bacillus subtilis* oxalate decarboxylase in patients with primary hyperoxaluria had yet started.

At the time of submission, this medicine was not authorised anywhere in the EU for primary hyperoxaluria. Orphan designation of the medicine had been granted in the United States for both primary and paediatric hyperoxaluria.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 15 June 2017 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, 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 languages[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	*Bacillus subtilis* oxalate decarboxylase	Treatment of primary hyperoxaluria
Bulgarian	*Оксалат* декарбоксилаза от *Bacillus subtilis*	Лечение на първична хипероксалурия
Croatian	Oksalatna dekarboksilaza bakterije *Bacillus subtilis*	Liječenje primarne hiperoksalurije
Czech	Oxalát dekarboxyláza *Bacillus subtilis*	Léčba primární hyperoxalurie
Danish	Oxalat decarboxylase fra *Bacillus subtilis*	Behandling af primær hyperoxaluri
Dutch	*Bacillus subtilis*-oxalaatdecarboxylase	Behandeling van primaire hyperoxalurie
Estonian	Bakteri *Bacillus subtilis* oksalaadi dekarboksülaas	Esmase hüperoksaluuria ravi
Finnish	*Bacillus subtilis*-oksalaattidekarboksylaasi	Primaarisen hyperoksalurian hoito
French	Oxalate décarboxylase de *Bacillus subtilis*	Traitement de l'hyperoxalurie primaire
German	*Bacillus subtilis* Oxalat-Decarboxylase	Behandlung der primären Hyperoxalurie
Greek	Οξαλική αποκαρβοξυλάση από *Bacillus subtilis*	Θεραπεία της πρωτοπαθούς υπεροξαλουρίας
Hungarian	*Bacillus subtilis* eredetű oxalát-dekarboxiláz	Primer hiperoxaluria kezelésére
Italian	Ossalato decarbossilasi da *Bacillus subtilis*	Trattamento delll'iperossaluria primaria
Latvian	*Bacillus subtilis* oksalāta dekarboksilāze	Primāras hiperoksalūrijas ārstēšana
Lithuanian	*Bacillus subtilis* oksalato dekarboksilazė	Pirminės hiperoksalurijos gydymas
Maltese	Oxalate decarboxylase ta' *Bacillus subtilis*	Kura ta' iperoxalurja primarja
Polish	Dekarboksylaza szczawianowa *Bacillus subtilis*	Leczenie pierwotnej hiperoksalurii
Portuguese	Oxalato descarboxilase de *Bacillus subtilis*	Tratamento da hiperoxalúria primária
Romanian	Oxalat decarboxilază a *Bacillus subtilis*	Tratamentul hiperoxaluriei primare
Slovak	Oxalát dekarboxylázy *Bacillus subtilis*	Liečba primárnej hyperoxalúrie typu 1
Slovenian	Oksalat-dekarboksilaza *Bacillus subtilisa*	Zdravljenje primarne hiperoksalurije
Spanish	Oxalato descarboxilasa de *Bacillus subtilis*	Tratamiento de la hiperoxaluria primaria
Swedish	*Bacillus subtilis*-oxalatdekarboxylas	Behandling av primär hyperoxaluri

[1] At the time of designation

Language	Active ingredient	Indication
Norwegian	Oksalatdekarboksylase fra *Bacillus subtilis*	Behandling av primær hyperoksaluri
Icelandic	*Bacillus subtilis* oxalat dekarboxýlasi	Meðferð við prímeri oxalatmigu