10 February 2021
EMADOC-628903358-3055

Public summary of opinion on orphan designation

Poly(oxy-1,2-ethanediyl), alpha-(carboxymethyl)-omega-methoxy-, amide with cystathionine γ-lyase [pyridoxal 5'-phosphate cofactor] (synthetic engineered human), tetramer for the treatment of homocystinuria

On 19 October 2020, orphan designation EU/3/20/2348 was granted by the European Commission to Aeglea BioTherapeutics UK Limited, United Kingdom, for poly(oxy-1,2-ethanediyl), alpha-(carboxymethyl)-omega-methoxy-, amide with cystathionine γ-lyase [pyridoxal 5'-phosphate cofactor] (synthetic engineered human), tetramer (also known as ACN00177) for the treatment of homocystinuria.

What is homocystinuria?

Homocystinuria is an inherited disorder in which a substance called homocysteine builds up in the blood and urine because the patient lacks an enzyme to break it down. The excess homocysteine can be toxic. In patients with this condition, symptoms usually appear in the first few days of life and long-term consequences include learning disabilities, brittle bones, problems with vision and blood disorders.

Homocystinuria is a long-term debilitating and life-threatening disease that leads to blood clots and problems with the heart and blood vessels and is associated with poor overall survival.

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

At the time of designation, homocystinuria affected less than 0.4 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 21,000 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).

*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).

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

What treatments are available?

At the time of designation, betaine was authorised in the EU for the treatment of homocystinuria. Vitamin B6 (pyridoxine) and cobalamin were also used to treat some patients with the condition.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with homocystinuria. Laboratory studies indicate that it might improve survival when used together with betaine. The medicine might also benefit patients for whom pyridoxine and cobalamin do not work.

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 contains an enzyme (cystathionine gamma-lyase) that has been engineered to be able break down homocysteine. It is expected to help eliminate the excess homocysteine in the body and thereby reduce symptoms of the disease.

What is the stage of development of this medicine?

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

At the time of submission of the application for orphan designation, no clinical trials in patients with homocystinuria had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for the treatment of homocystinuria or designated as an orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000, the COMP adopted a positive opinion on 10 September 2020, 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

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.