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Public summary of opinion on orphan designation

2’-O-(2-methoxyethyl) modified antisense oligonucleotide targeting glycogen synthase 1 pre-mRNA for the treatment of progressive myoclonic epilepsy type 2 (Lafora disease)

On 9 December 2020, orphan designation EU/3/20/2377 was granted by the European Commission to Ionis Development (Ireland) Limited, Ireland, for 2’-O-(2-methoxyethyl) modified antisense oligonucleotide targeting glycogen synthase 1 pre-mRNA (also known as ION283) for the treatment of progressive myoclonic epilepsy type 2 (Lafora disease).

What is progressive myoclonic epilepsy type 2 (Lafora disease)?

Lafora disease is an inherited brain disease marked by epileptic seizures (fits) and worsening intellectual function. Patients usually have their first fit between 10 and 20 years of age. This is followed by worsening of the functioning of the brain and spinal cord, which causes severe epilepsy, difficulty walking, depression and dementia, and eventually leads to death. Lafora disease is caused by a mutation (change) in one of two genes, called EPM2A and EPM2B, which are involved in the handling of glycogen, a substance the body uses to store energy.

Lafora disease is a debilitating and life-threatening disease that usually leads to death within 10 years of diagnosis.

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

At the time of designation, progressive myoclonic epilepsy type 2 (Lafora disease) affected approximately 0.04 in 10,000 people in the European Union (EU). This was equivalent to a total of around 2,000 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).

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What treatments are available?

At the time of designation, no satisfactory methods were authorised in the EU for treating Lafora disease. Medicines to control seizures were given, but their effectiveness was limited and did not last long, and they did not stop the disease from getting worse.

How is this medicine expected to work?

Lafora disease is caused by the build-up of abnormal forms of glycogen in the brain. The medicine is an 'antisense oligonucleotide', a short single strand of synthetic genetic material. It has been designed to stop an earlier stage in production of brain glycogen. It does this by reducing production of GYS1, a protein involved in glycogen production in the brain. By reducing GYS1 production in patients with Lafora disease, the medicine is expected to help control the condition, improve symptoms and slow the progression of Lafora 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 progressive myoclonic epilepsy type 2 (Lafora disease) had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for the treatment of progressive myoclonic epilepsy type 2 (Lafora disease) 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 5 November 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.