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Public summary of opinion on orphan designation

Sulindac for the treatment of fragile X syndrome

On 9 December 2020, orphan designation EU/3/20/2384 was granted by the European Commission to Aparito Netherlands B.V., Netherlands, for sulindac for the treatment of fragile X syndrome.

What is fragile X syndrome?

Fragile X syndrome is an inherited disease characterised by learning disability. Other symptoms include difficulty communicating and socialising, anxiety, hyperactivity (restlessness), and repetitive and stereotyped behaviours.

The disease is caused by a defect in a gene on the X chromosome. The gene is responsible for the production of a protein called fragile X mental retardation protein (FMRP), which is necessary for the normal development of the brain. In patients with fragile X syndrome, the defective gene cannot produce normal levels of the FMRP protein, and this leads to learning disability and other symptoms relating to the brain or nerves. Women are normally less severely affected than men, because they have a second X chromosome that usually has a normal copy of the gene.

Fragile X syndrome is a long-term debilitating disease because it causes severe behavioural problems and learning disabilities.

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

At the time of designation, fragile X syndrome affected less than 3 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 156,000 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 the treatment of fragile X syndrome. Patients were given general support, such as behavioural therapy and special education, and in some cases medicines to treat the symptoms of the disease, such as

*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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antidepressants, medicines for attention-deficit hyperactivity disorder and antipsychotics. Genetic counselling (discussion of the risks of passing on the condition to children) was recommended for families with a history of fragile X syndrome.

How is this medicine expected to work?

Sulindac works by blocking an enzyme called cyclo-oxygenase that produces prostaglandins, substances involved in the inflammation process. The medicine may also stimulate a protein called PPAR-gamma, which is found in the brain and plays a role in protecting brain cells from inflammation and helping with the normal development of the brain.

By reducing the production of prostaglandins in the brain cells and stimulating PPAR-gamma, sulindac may reduce inflammation in these cells and protect against further damage to the brain. These effects are expected to improve symptoms in people with fragile X syndrome.

What is the stage of development of this medicine?

The effects of sulindac for fragile X syndrome have been evaluated in experimental models.

At the time of submission of the application for orphan designation, no clinical trials with sulindac in patients with fragile X syndrome had started.

At the time of submission, sulindac was authorised in some countries of the EU for rheumatoid arthritis, osteoarthritis, acute gouty arthritis, ankylosing spondylitis and musculoskeletal and periarticular disorders such as tendinitis, tenosynovitis and bursitis.

At the time of submission, the medicine was not authorised anywhere in the EU for the treatment of fragile X syndrome 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.