



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

10 May 2021
EMADOC-628903358-3725

Public summary of opinion on orphan designation

(R)-3-(1-(2,3-dichloro-4-(pyrazin-2-yl)phenyl)-2,2,2-trifluoroethyl)-1-methyl-1-(1-methylpiperidin-4-yl)urea fumarate for the treatment of Prader-Willi syndrome

On 9 December 2020, orphan designation EU/3/20/2367 was granted by the European Commission to Helsinn Birex Pharmaceuticals Limited, Ireland, for (R)-3-(1-(2,3-dichloro-4-(pyrazin-2-yl)phenyl)-2,2,2-trifluoroethyl)-1-methyl-1-(1-methylpiperidin-4-yl)urea fumarate (also known as HM04 Fumarate or 12-HM04) for the treatment of Prader-Willi syndrome.

What is Prader-Willi syndrome?

Prader-Willi syndrome is an inherited condition caused by defects in specific regions of chromosome 15. This causes a wide range of symptoms, some of which can appear at birth, such as feeding problems, small size and reduced muscle strength. During childhood further symptoms develop, including increased appetite leading to constant eating and severe obesity, short stature, incomplete sexual development, learning difficulties and behavioural problems, such as aggression and stubbornness.

Prader-Willi syndrome is a life-long debilitating and life-threatening disease because of its serious symptoms, particularly learning difficulties, behavioural problems and obesity.

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

At the time of designation, Prader-Willi Syndrome affected approximately 0.3 in 10,000 people in the European Union (EU). This was equivalent to a total of around 16,000 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).



What treatments are available?

At the time of designation, growth hormone was authorised in the EU for treating Prader-Willi syndrome. In addition, symptoms were treated or managed in various ways, including supervised access to food to prevent obesity.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with Prader-Willi syndrome, with laboratory data showing that it may reduce excessive food intake – a benefit not seen with growth hormone therapy. 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?

Patients affected by Prader-Willi syndrome have high blood levels of a substance named ghrelin, a hormone mainly produced by the stomach wall. By binding to its receptor (target), ghrelin may alter the perception of hunger and promote overeating.

The medicine is expected to bind to the ghrelin receptors and block them, which may result in reduction of the appetite and food intake.

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 the medicine in patients with Prader-Willi syndrome had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for the treatment of Prader-Willi 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.