10 May 2021
EMADOC-628903358-3729

Public summary of opinion on orphan designation

4-[(3S)-3-aminopyrrolidin-1-yl]-6-cyano-5-(3,5-difluorophenyl)-N-[(2S)-1,1,1-trifluoropropan-2-yl]pyridine-3-carboxamide for the treatment of congenital hyperinsulinism

On 9 December 2020, orphan designation EU/3/20/2376 was granted by the European Commission to Scendea (NL) B.V., Netherlands, for 4-[(3S)-3-aminopyrrolidin-1-yl]-6-cyano-5-(3,5-difluorophenyl)-N-[(2S)-1,1,1-trifluoropropan-2-yl]pyridine-3-carboxamide (also known as CRN04777) for the treatment of congenital hyperinsulinism.

What is congenital hyperinsulinism?

Congenital hyperinsulinism is an inherited disorder in which the body releases insulin even when it is not needed. Insulin is a hormone that helps control levels of blood glucose (sugar) by increasing absorption of glucose into the cells of the body. In hyperinsulinism, the increased amount of insulin makes too much glucose enter the cells and causes hypoglycaemia (low blood glucose levels).

The severity of congenital hyperinsulinism varies among patients and some patients develop episodes of hypoglycaemia shortly after birth. Repeated episodes of hypoglycaemia increase the risk of serious complications such as seizures (fits), mental disability, breathing difficulties and coma.

Congenital hyperinsulinism is a long-term debilitating condition because of the effects of long-term hypoglycaemia on the brain, such as mental disability and seizures.

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

At the time of designation, congenital hyperinsulinism 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).

*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 medicines were authorised in the EU for the treatment of congenital hyperinsulinism. Products such as diazoxide and octreotide were used to reduce insulin release, and glucagon and glucose were used in emergencies to increase blood glucose levels short-term in patients with congenital hyperinsulinism. However, these medicines were not authorised specifically for use in this condition. Some patients were treated by surgical removal of part or all of the pancreas.

How is this medicine expected to work?

This medicine acts on a target called somatostatin receptor type 5 (SST5), which is involved in controlling the amount of insulin in the body. By targeting SST5 and reducing insulin levels, it is expected to raise blood glucose levels and relieve symptoms of the disease.

What is the stage of development of this medicine?

At the time of submission of the application for orphan designation, the evaluation of the effects of the medicine in experimental models was ongoing.

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

At the time of submission, the medicine was not authorised anywhere in the EU for the treatment of congenital hyperinsulinism 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.