10 February 2020
EMADOC-628903358-1570

Public summary of opinion on orphan designation

Exendin (9-39) for the treatment of congenital hyperinsulinism

On 13 November 2019, orphan designation EU/3/19/2223 was granted by the European Commission to Eigerbio Europe Limited, Ireland, for exendin (9-39) (also known as avexitide) 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 0.15 in 10,000 people in the European Union (EU). This was equivalent to a total of around 8,000 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 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

*Disclaimer: 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 (EU 28), Norway, Iceland and Liechtenstein. This represents a population of 518,400,000 (Eurostat 2019).

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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?

The medicine is a small protein fragment that binds to and blocks GLP-1r. GLP-1r is a receptor (target) on the surface of pancreatic cells that plays a role in releasing insulin from the pancreas. By blocking its action, the medicine is expected to reduce the amount of insulin released, thereby improving the symptoms of the disease.

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, clinical trials with the medicine in patients with congenital hyperinsulinism were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for the treatment of congenital hyperinsulinism. Orphan designation of exendin (9-39) had been granted in the United States for hyperinsulinemic hypoglycemia.

In accordance with Regulation (EC) No 141/2000, the COMP adopted a positive opinion on 10 October 2019, 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

Sponsor's contact details:

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.

Translations of the active ingredient and indication in all official EU languages[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	Exendin (9-39)	Treatment of congenital hyperinsulinism
Bulgarian	Ексендин (9-39)	Лечение на вроден хиперинсулинизъм
Croatian	Eksendin (9-39)	Liječenje prirođene hiperinzulinemije
Czech	Exendin (9-39)	Léčba kongenitálního hyperinzulinismu
Danish	Exendin (9-39)	Behandling af kongenit hyperinsulinisme
Dutch	Exendine (9-39)	Behandeling van congenitaal hyperinsulinisme
Estonian	Exendiin (9-39)	Kaasasündinud hüperinsulinismi ravi
Finnish	Eksendiini (9-39)	Synnynnäisen hyperinsulinismin hoito
French	Exendin (9-39)	Traitement de l'hyperinsulinisme congénital
German	Exendin (9-39)	Behandlung des kongenitalen Hyperinsulinismus
Greek	Εξενδίνη (9-39)	Θεραπεία του συγγενούς υπερινσουλινισμού
Hungarian	Exendin (9-39)	Congenitalis hyperinsulinismus kezelése
Italian	Exendin (9-39)	Trattamento dell' iperinsulinemia congenita
Latvian	Eksendīns (9-39)	Iedzimtas hiperinsulinēmijas ārstēšana
Lithuanian	Eksendinas (9-39)	Įgimto hiperinsulinizmo gydymas
Maltese	Exendin (9-39)	Kura ta' iperinsulinimja konġenitali
Polish	Eksendyna (9-39)	Leczenie wrodzonego hiperinsulinizmu
Portuguese	Exendina (9-39)	Tratamento do hiperinsulinismo congénito
Romanian	Exendină (9-39)	Tratamentul hiperinsulinismului congenital
Slovak	Exendin (9-39)	Liečba kongenitálneho hyperinzulinizmu
Slovenian	Eksendin (9-39)	zdravljenje prirojenega hiperinzulinizma
Spanish	Exendina (9-39)	Tratamiento del hiperinsulinismo congénito
Swedish	Exendin (9-39)	Behandling av medfödd hyperinsulinism
Norwegian	Eksendin (9-39)	Behandling av medfødt hyperinsulinisme
Icelandic	Exendin (9-39)	Meðferð á meðfæddu insúlínóhófi

[1] At the time of designation