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Public summary of opinion on orphan designation

Glucagon analogue linked to a human immunoglobulin Fc fragment for the treatment of congenital hyperinsulinism

On 25 May 2018, orphan designation (EU/3/18/2022) was granted by the European Commission to Hanmi Europe Limited, United Kingdom, for glucagon analogue linked to a human immunoglobulin Fc fragment (also known as HM15136) 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 1 in 10,000 people in the European Union (EU). This was equivalent to a total of less than 52,000 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 517,400,000 (Eurostat 2018).

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

with congenital hyperinsulinism. However, these medicines were not authorised specifically for use in this condition.

How is this medicine expected to work?

The medicine contains a copy of the hormone glucagon, which is naturally produced by the body. It acts like natural glucagon and releases glucose from the liver, which increases blood glucose levels thereby reducing the symptoms of the disease.

The glucagon in the medicine is combined with a type of protein called immunoglobulin G4 fragment, which helps the hormone stay active in the body for longer. This allows the medicine to be given less frequently than natural glucagon.

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 with the medicine in patients with congenital hyperinsulinism had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for congenital hyperinsulinism. Orphan designation of the medicine had been granted in the United States for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 19 April 2018 recommending the granting of this designation.

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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, on the medicine's rare disease designations page.

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	Glucagon analogue linked to a human immunoglobulin Fc fragment	Treatment of congenital hyperinsulinism
Bulgarian	Аналог на глюкагон, свързан към Fc фрагмент на човешки имуноглобулин	Лечение на вроден хиперинсулинизъм
Croatian	Analog glukagona vezan na Fc fragment ljudskog imunoglobulina	Liječenje prirođene hiperinzulinemije
Czech	Analog glukagonu spojený s Fc fragmentem lidského imunoglobulinu	Léčba kongenitálního hyperinzulinismu
Danish	Glucagon analog bundet til et humant immunoglobulin Fc-fragment	Behandling af kongenit hyperinsulinisme
Dutch	Glucagonanaloog gekoppeld aan een humaan immunoglobuline Fc fragment	Behandeling van congenitaal hyperinsulinisme
Estonian	Inimese immuunglobuliini Fc-fragmendiga seotud glükagooni analoog	Kaasasündinud hüperinsulinismi ravi
Finnish	Glukagonin analogi, joka on kytkeytynyt ihmisen immunoglobuliinin Fc-osaan	Synnynnäisen hyperinsulinismin hoito
French	Glucagon analogue lié au fragment Fc de l'immunoglobuline humaine	Traitement de l'hyperinsulinisme congénital
German	Glukagon-Analogon verbunden mit einem Human-Immunglobulin-Fc-Fragment	Behandlung des kongenitalen Hyperinsulinismus
Greek	Ανάλογο γλυκαγόνης συνδεδεμένο με το Fc τμήμα ανθρώπινης ανοσοσφαιρίνης	Θεραπεία του συγγενούς υπερινσουλινισμού
Hungarian	Humán immunglobulin Fc-fragmentumához kötött glukagon analóg	Congenitalis hyperinsulinismus kezelése
Italian	Analogo del glucagone legato a un frammento Fc dell'immunoglobulina umana	Trattamento dell' iperinsulinemia congenita
Latvian	Glikagona analogs, kas piesaistīts cilvēka imūnglobulīna Fc fragmentam	Iedzimtas hiperinsulinēmijas ārstēšana
Lithuanian	Gliukagono analogas sujungtas su žmogaus imunoglobulino Fc fragmentu	Įgimto hiperinsulinizmo gydymas
Maltese	Analogu ta' glukagon marbut ma' framment Fc ta' immunoglobulina umana	Kura ta' iperinsulinimja kongenitali
Polish	Analog glukagonu powiązany z fragmentem Fc ludzkiej immunoglobuliny	Leczenie wrodzonego hiperinsulinizmu
Portuguese	Análogo do glucagon ligado a um fragmento Fc da imunoglobulina humana	Tratamento do hiperinsulinismo congénito
Romanian	Analog al glucagonului legat de un fragment Fc de imunoglobulină umană	Tratamentul hiperinsulinismului congenital
Slovak	Analóg glukagónu viazaný na Fc fragment ľudského imunoglobulínu	Liečba kongenitálneho hyperinzulinizmu

[1] At the time of designation

Language	Active ingredient	Indication
Slovenian	Analog glukagona, vezan na Fc fragment humanega imunoglobulina	zdravljenje prirojenega hiperinzulinizma
Spanish	Análogo de glucagón ligado a un fragmento Fc de la inmunoglobulina humana	Tratamiento del hiperinsulinismo congénito
Swedish	Glukagonanalog länkad till ett humant Fc-immunglobulinfragment	Behandling av medfödd hyperinsulinism
Norwegian	Glukagonanalog bundet til et humant immunglobulin Fc-fragment	Behandling av medfødt hyperinsulinisme
Icelandic	Glúkagon hliðstæða tengd Fc-hluta manna ónæmisglóbúlíns	Meðferð á meðfæddu insúlínóhófi