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Public summary of opinion on orphan designation

Synthetic glucagon analogue modified to contain 7 amino acid substitutions for the treatment of congenital hyperinsulinism

On 20 June 2017, orphan designation (EU/3/17/1887) was granted by the European Commission to Zealand Pharma A/S, for synthetic glucagon analogue modified to contain 7 amino acid substitutions 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 blood glucose (sugar) levels by driving glucose into the cells of the body. In hyperinsulinism, the increased amount of insulin 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 0.2 in 10,000 people in the European Union (EU). This was equivalent to a total of around 10,000 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, glucagon and glucose were used in patients with congenital hyperinsulinism to increase blood glucose levels.

[*]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 515,700,000 (Eurostat 2017).

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The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with the condition. Unlike other glucagon preparations, this medicine has been modified to improve its stability making it more suitable for long-term use. 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?

This medicine is a synthetic copy of the natural hormone glucagon that counteracts the effects of insulin by raising blood glucose levels. It does this by breaking down glycogen (the form in which glucose is stored in the liver), and by stimulating the production of glucose in the liver. The medicine is therefore expected to prevent hypoglycaemic episodes and organ damage due to congenital hyperinsulinism.

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 congenital hyperinsulinism were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for congenital hyperinsulinism or designated as an orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 12 May 2017 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	Synthetic glucagon analogue modified to contain 7 amino acid substitutions	Treatment of congenital hyperinsulinism
Bulgarian	Синтетичен аналог на глюкагон модифициран да съдържа 7 аминокиселинни заместявания	Лечение на вроден хиперинсулинизъм
Croatian	Sintetski analog glukagona modificiran da sadrži 7 supstitucija aminokiselina	Liječenje prirođene hiperinzulinemije
Czech	Syntetický analog glukagonu modifikovaný substitucí 7 aminokyselin	Léčba kongenitálního hyperinzulinismu
Danish	Syntetisk glucagon analog, modificeret med 7 aminosyre substitutioner	Behandling af kongenit hyperinsulinisme
Dutch	Synthetisch glucagonanaloog gemodifiëerd zodat het 7 aminozuursubstituties bevat	Behandeling van congenitaal hyperinsulinisme
Estonian	Seitsme aminohappe asendusega modifitseeritud sünteetiline glükagooni analoog	Kaasasündinud hüperinsulinismi ravi
Finnish	Synteettinen glukagonin analogi, joka on muokattu sisältämään 7 aminohapposubstituutiota	Synnynnäisen hyperinsulinismin hoito
French	Glucagon synthetique analogue modifie avec 7 acide amines de substitution	Traitement de l'hyperinsulinisme congénital
German	Synthetisches Glucagon Analog, das mit 7 Aminosäuren- Substitutionen modifiziert ist	Behandlung des kongenitalen Hyperinsulinismus
Greek	Συνθετικό ανάλογο γλυκαγόνης τροποποιημένο με 7 αντικαταστημένα αμινοξέα	Θεραπεία του συγγενούς υπερινσουλινισμού
Hungarian	Szintetikus glukagon analóg, ami módosítás után 7 aminosav szubsztitúciót tartalmaz	Congenitalis hyperinsulinismus kezelése
Italian	Analogo sintetico del glucagone, modificato con sette sostituzioni aminoacidiche	Trattamento dell' iperinsulinemia congenita
Latvian	Modificēts, sintētisks glukagona analogs, kas satur 7 aminskābju substitūcijas	Iedzimtas hiperinsulinēmijas ārstēšana
Lithuanian	Sintetinis gliukagono analogas, modifikuotas septynių aminorūgščių pakaita	Įgimto hiperinsulinizmo gydymas
Maltese	Analogu ta' glukagon sintetiku modifikat biex ikun fih 7 sostituzzjonijiet ta' amminoaċidu	Kura ta' iperinsulinimja konġenitali
Polish	Syntetyczny analog glukagonu zmodyfikowany 7-ma substytucjami aminokwasów	Leczenie wrodzonego hiperinsulinizmu
Portuguese	Análogo sintético do glucagon modificado para conter 7 substituições de aminoácidos	Tratamento do hiperinsulinismo congénito
Romanian	Analog sintetic al glucagonului, modificat cu şapte substituţii aminoacidice	Tratamentul hiperinsulinismului congenital
Slovak	Syntetický analóg glukagónu modifikovaný o 7 aminokyselinových substitúcií	Liečba kongenitálneho hyperinzulinizmu

[1] At the time of designation

Language	Active ingredient	Indication
Slovenian	Sintetični analog glukagona, modifciran s 7 nadomestnimi aminokislinami	zdravljenje prirojenega hiperinzulinizma
Spanish	Analogo sintetico de glucagon modificado para contener 7 substituiçiones de acidos aminos	Tratamiento del hiperinsulinismo congénito
Swedish	Syntetisk glukagonanalog modifierad med 7 aminosyrasubstitutioner.	Behandling av medfödd hyperinsulinism
Norwegian	Syntetisk glukagonanalog modifisert til å inneholde 7 aminosyresubstitusjoner	Behandling av medfødt hyperinsulinisme
Icelandic	Tilbúin glúkagon hliðstæða breytt til að innihalda 7 amínó sýru skiptiefnahvörf	Meðferð á meðfæddu insúlínóhófi