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Public summary of opinion on orphan designation

Glucagon analogue linked to a human immunoglobulin Fc fragment for the treatment of insulin autoimmune syndrome

On 22 April 2020, orphan designation EU/3/20/2275 was granted by the European Commission to JVM Europe B.V, Netherlands, for glucagon analogue linked to a human immunoglobulin Fc fragment (also known as HM15136) for the treatment of insulin autoimmune syndrome.

What is insulin autoimmune syndrome?

Insulin autoimmune syndrome is a condition in which the immune system (the body's defences) abnormally makes antibodies which attach to insulin and stop it from working, causing a temporary increase in blood sugar. The antibodies then start releasing the insulin, leading to a sudden rise in insulin levels that causes an excessive fall in blood sugar (hypoglycaemia).

Insulin autoimmune syndrome most commonly develops in adults. Patients have hypoglycaemia and high levels of antibodies against insulin and, over time, the condition can damage the pancreas, the gland which produces insulin. Signs of hypoglycaemia include sweating, light-headedness, weakness and tiredness. Hypoglycaemia caused by high levels of insulin can lead to effects on the brain including fits, cerebral palsy (poor coordination and muscle control) and blindness.

The disease is seriously debilitating and life-threatening because of its serious effects on the brain.

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

At the time of designation, insulin autoimmune syndrome affected less than 0.01 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 500 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 submission of the application for orphan drug designation, no medicine was authorised for the condition. Patients were treated with corticosteroids to reduce the production of antibodies and with medicines to reduce absorption of sugar from the digestive tract and so reduce the release of insulin from the pancreas.

How is this medicine expected to work?

The medicine is made up of a protein (called human immunoglobulin G4 fragment) attached to a copy of the natural hormone, glucagon. In the body, glucagon prevents severe hypoglycaemia but it is present only for a few minutes. It is expected that the protein attachment will allow the medicine to work for much longer so that it would need to be given just once a week.

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 insulin autoimmune syndrome were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for the treatment of insulin autoimmune syndrome or designated as an orphan medicinal product elsewhere for this condition. It has been granted orphan designation in the EU for the treatment of congenital hyperinsulinism.

In accordance with Regulation (EC) No 141/2000, the COMP adopted a positive opinion on 19 March 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

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	Glucagon analogue linked to a human immunoglobulin Fc fragment	Treatment of insulin autoimmune syndrome
Bulgarian	Аналог на глюкагон, свързан към Fc фрагмент на човешки имуноглобулин	Лечение на инсулинов автоимунен синдром
Croatian	Analog glukagona vezan na Fc fragment ljudskog imunoglobulina	Liječenje inzulinskog autoimunog sindroma
Czech	Analog glukagonu spojený s Fc fragm entem lidského imunoglobulinu	Léčba inzulinového autoimunitního syndromu
Danish	Glucagon analog bundet til et humant immunoglobulin Fc-fragment	Behandling af insulin autoimmun syndrom
Dutch	Glucagonanaloog gekoppeld aan een humaan immunoglobuline Fc fragment	Behandeling van insuline-auto immuunsyndroom
Estonian	Inimese immuunglobuliini Fc-fragmendiga seotud glükagooni analoog	Insuliini autoimmuunsündroomi ravi
Finnish	Glukagonin analogi, joka on kytkeytynyt ihmisen immunoglobuliinin Fc-osaan	Insuliiniin liittyvän autoimmuunisyndrooman hoito
French	Glucagon analogue lié au fragment Fc de l'immunoglobuline humaine	Traitement du syndrome auto-immun anti-insuline
German	Glukagon-Analogon verbunden mit einem Human-Immunglobulin-Fc-Fragment	Behandlung des Insulin-Autoimmunsyndroms
Greek	Ανάλογο γλυκαγόνης συνδεδεμένο με ενα Fc τμήμα ανθρώπινης ανοσοσφαιρίνης	Θεραπεία του αυτοάνοσου συνδρόμου ινσουλίνης
Hungarian	Humán immunglobulin Fc-fragmentumához kötött glukagon analóg	Inzulin autoimmun szindróma kezelése
Italian	Analogo del glucagone legato a un frammento Fc dell'immunoglobulina umana	Trattamento della sindrome insulinica autoimmune
Latvian	Glikagona analogs, kas piesaistīts cilvēka imūnglobulīna Fc fragmentam	Insulīna autoimūnā sindroma ārstēšana
Lithuanian	Gliukagono analogas sujungtas su žmogaus imunoglobulino Fc fragmentu	Insulino autoimuninio sindromo gydymas

[1] At the time of designation

Language	Active ingredient	Indication
Maltese	Analogu ta' glukagon marbut ma' framment Fc ta' immunoglobulina umana	Trattament tas-sindrome awtoimmuni tal-insulina
Polish	Analog glukagonu powiązany z fragmentem Fc ludzkiej immunoglobuliny	Leczenie autoimmunologicznego zespołu insulinowego
Portuguese	Análogo do glucagon ligado ao fragmento Fc da imunoglobulina humana	Tratamento da síndrome autoimune da insulina
Romanian	Analog al glucagonului legat de fragmentul Fc al unei immunoglobuline umană	Tratamentul sindromului insulinic autoimun
Slovak	Analóg glukagónu viazaný na Fc fragment ľudského imunoglobulínu	Liečba inzulínového autoimunitného syndrómu
Slovenian	Analog glukagona, vezan na Fc fragment humanega imunoglobulina	Zdravljenje insulinskega avtoimunskega sindroma
Spanish	Análogo de glucagón ligado a un fragmento Fc de la inmunoglobulina humana	Tratamiento del síndrome de autoinmunidad a la insulina
Swedish	Glukagonanalog länkad till ett humant Fc-immunglobulinfragment	Behandling av autoimmunt insulinsyndrom
Norwegian	Glukagon analog bundet til et humant immunglobulin Fc-fragment	Behandling av autoimmunt insulinsyndrom
Icelandic	Glúkagonhliðstæða tengd Fc-hluta manna ónæmisglóbúlíns	Meðferð við insúlín sjálfnæmisheilkenni