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Public summary of opinion on orphan designation

Lys^{40}(NODAGA-^{68}Ga)NH_2-exendin-4 for the diagnosis of insulinoma

On 26 June 2020, orphan designation EU/3/20/2295 was granted by the European Commission to Stichting Katholieke Universiteit, Netherlands, for Lys^{40}(NODAGA-^{68}Ga)NH_2-exendin-4 for the diagnosis of insulinoma.

What is insulinoma?

Insulinoma is one of a group of so-called neuroendocrine tumours (NETs) that arise from hormone producing cells, usually in the digestive system. In the case of insulinoma, the tumour is formed from cells that produce insulin, which are normally found in the pancreas.

The cancer cells produce excess insulin, the hormone that controls levels of glucose (sugar) in the blood, resulting in abnormally low blood glucose levels (hypoglycaemia).

The condition is debilitating and potentially life-threatening due to the symptoms of hypoglycaemia, which can include fainting, seizures (fits), coma and brain damage.

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

At the time of designation, the number of patients affected by insulinoma was estimated to be approximately 0.3 people in 10,000 in the European Union (EU). This was equivalent to a total of around 16,000 people per year* and is below the ceiling for orphan designation. This is based on the information provided by the sponsor and the knowledge of the Committee for Orphan Medicinal Products (COMP).

What methods of diagnosis are available?

At the time of designation, insulinomas were diagnosed using various methods. These included histopathology (examining a tissue under the microscope) and biochemical testing (measuring substances produced by neuroendocrine tumours), as well as imaging methods such as magnetic resonance imaging (MRI) and computer tomography (CT) to visualise the location of the tumour. Medicines that attached to specific targets on the tumour cells and contained small amounts of

*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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radioactivity that could be detected on an imaging scan (scintigraphy), allowing the tumour to be located, were authorised for some types of NETs, but not specifically for insulinoma.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with insulinoma because early results in patients suggest it could be used to detect the condition in patients who could not be diagnosed using existing methods.

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 to be used for an imaging method called positron emission tomography (PET). It consists of a radioactive element, gallium (^{68}Ga), attached to a derivative of exenatide, a substance similar to a natural hormone called glucagon-like peptide (GLP-1) and which is licensed in the EU to treat diabetes. Insulinomas have high numbers of receptors (targets) for GLP-1 on their surface. The medicine is expected to attach to these GLP-1 receptors in the insulinoma, emitting radiation that can be detected by the PET imaging scan. This makes it possible to see the location of the tumour.

What is the stage of development of this medicine?

The effects of Lys^{40}(NODAGA-^{68}Ga)NH_2-exendin-4 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 insulinoma were ongoing.

At the time of submission, this medicine was not authorised anywhere in the EU for the diagnosis of insulinoma 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 20 May 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.

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

Language	Active ingredient	Indication
English	Lys^{40}(NODAGA-^{68}Ga)NH_2-exendin-4	Diagnosis of insulinoma
Bulgarian	Lys40(NODAGA-68Ga)NH2-ексендин-4	Диагностика на инсулином
Croatian	Lys40(NODAGA-68Ga)NH2-eksendin-4	Dijagnoza inzulinoma
Czech	Lys40(NODAGA-68Ga)NH2-exendin-4	Diagnóza inzulinomu
Danish	Lys40(NODAGA-68Ga)NH2-exendin-4	Diagnostisering af insulinom
Dutch	Lys40(NODAGA-68Ga)NH2-exendin-4	Diagnose van insulinoma
Estonian	Lys40(NODAGA-68Ga)NH2-eksendiin-4	Insulinoomi diagnoosimine
Finnish	Lys40(NODAGA-68Ga)NH2-eksendiini-4	Insulinooman diagnosointi
French	Lys40(NODAGA-68Ga)NH2-exendine-4	Diagnosis of insulinoma
German	Lys40(NODAGA-68Ga)NH2-Exendin-4	Diagnose des Insulinoms
Greek	Lys40(NODAGA-68Ga)NH2-εξενδίνη-4	Διάγνωση του ινσουλινώματος
Hungarian	Lys40(NODAGA-68Ga)NH2-exendin-4	Inzulinóma diagnosztizálása
Italian	Lys40(NODAGA-68Ga)NH2-exendina-4	Diagnosi dell'insulinoma
Latvian	Lys40(NODAGA-68Ga)NH2-eksendīns-4	Insulinomas diagnostika
Lithuanian	Lys40(NODAGA-68Ga)NH2-eksendinas-4-4	Insulinomos diagnozė
Maltese	Lys40(NODAGA-68Ga)NH2-eżendin-4	Dijanjożi ta' insulinoma
Polish	Lys40(NODAGA-68Ga)NH2-eksendyna-4	Diagnozowanie insulinomy
Portuguese	Lys40(NODAGA-68Ga)NH2-exendin-4	Diagnóstico de insulinoma
Romanian	Lys40(NODAGA-68Ga)NH2-exendină-4	Diagnosticul insulinomului
Slovak	Lys40(NODAGA-68Ga)NH2-exendin-4	Diagnóza inzulinómu
Slovenian	Lys40(NODAGA-68Ga)NH2-eksendin-4	Diagnosticiranje insulinoma
Spanish	Lys40(-NODAGA-68Ga)NH2-exendin-4	Diagnostico para insulinoma
Swedish	Lys40(NODAGA-68Ga)NH2-exendin-4	Diangons av insulinom
Norwegian	Lys40(NODAGA-68Ga)- NH2exendin-4	Diagnostisering av insulinom
Icelandic	Lys40(NODAGA-68Ga)NH2-exendín-4	Til sjúkdómsgreiningar á insúlínæxli

[1] At the time of designation