



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

## Public summary of opinion on orphan designation

Gallium [Ga-68]-N-[(4,7,10-Tricarboxymethyl-1,4,7,10-tetraazacyclododec-1-yl)acetyl]-D-phenylalanyl-L-cysteinyl-L-tyrosyl-D-tryptophanyl-L-lysyl-L-threoninyl-L-cysteinyl-L-threonine-cyclic(2-7)disulfide for the diagnosis of gastro-entero-pancreatic neuroendocrine tumours

On 19 February 2014, orphan designation (EU/3/14/1237) was granted by the European Commission to Advanced Accelerator Applications SA, France, for Gallium [Ga-68]-N-[(4,7,10-Tricarboxymethyl-1,4,7,10-tetraazacyclododec-1-yl)acetyl]-D-phenylalanyl-L-cysteinyl-L-tyrosyl-D-tryptophanyl-L-lysyl-L-threoninyl-L-cysteinyl-L-threonine-cyclic(2-7)disulfide for the diagnosis of gastro-entero-pancreatic neuroendocrine tumours.

### What are gastro-entero-pancreatic neuroendocrine tumours?

Gastro-entero-pancreatic neuroendocrine tumours (GEP-NETs) are tumours that arise from neuroendocrine cells in the gut. These cells release hormones that control various functions of the digestive system. The symptoms of GEP-NETs depend on where the tumour is located within the gut and on whether it produces excess hormones. Often by the time of diagnosis the tumours have spread to other organs such as the liver.

GEP-NETs are debilitating as they often produce excess hormones that may cause severe symptoms. They are life-threatening if they spread to other organs in the body.

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

At the time of designation, GEP-NETs affected less than 2.8 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 143,000 people<sup>\*</sup>, 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).

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<sup>\*</sup>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 511,100,000 (Eurostat 2014).



## What methods of diagnosis are available?

At the time of designation, GEP-NETs were diagnosed using various methods. They 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. Somatostatin receptor scintigraphy was a commonly used imaging technique, employing a radioactive tracer to obtain an image. At the time of designation, <sup>111</sup>In-DTPA-pentetreotide (Octreoscan) was authorised in the EU for use in scintigraphy.

The sponsor has provided sufficient information to show that the medicinal product might be of significant benefit for patients with GEP-NETs because early studies indicate that it may improve the accuracy of detecting those GEP-NETs that have a certain protein known as 'somatostatin receptors' on their surface (somatostatin receptor positive tumours). 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 (<sup>68</sup>Ga), attached to a substance containing a somatostatin analogue, a substance similar to a natural hormone called somatostatin. Most GEP-NETs have high amounts of somatostatin receptors on their surface. The product is expected to attach to these somatostatin receptors and to accumulate in the GEP-NETs cells. These cells are then expected to emit radiation that can be detected by the PET imaging method, thereby allowing the tumour to be diagnosed.

## 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 product in experimental models was ongoing.

At the time of submission, no clinical trials with the product in patients with GEP-NETs had been started.

At the time of submission, the product was not authorised anywhere in the EU for diagnosing GEP-NETs or designated as an orphan medicinal product elsewhere for this indication.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 9 January 2014 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:

Advanced Accelerator Applications SA  
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01630 Saint-Genis-Pouilly  
France  
Tel. +33 450 99 30 76  
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E-mail: [Regulatory\\_Affairs@adacap.com](mailto:Regulatory_Affairs@adacap.com)

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<sup>1</sup>, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Gallium [Ga-68]-N-[(4,7,10-tricarboxymethyl-1,4,7,10-tetraazacyclododec-1-yl)acetyl]-D-phenylalanyl-L-cysteinyl-L-tyrosyl-D-tryptophanyl-L-lysyl-L-threoninyl-L-cysteinyl-L-threonine-cyclic(2-7)disulfide	Diagnosis of gastro-entero-pancreatic neuroendocrine tumours
Bulgarian	галий (68Ga)-N-[(4,7,10-Трикарбоксиметил-1,4,7,10-тетраазациклододек-1-ил) ацетил]-D-фенилаланил-L-цистеинил-L-тирозил-D-триптофанил-L-лизил-L-треонинил-L-цистеинил-L-треонин-цикличен(2-7) дисулфид	Диагностициране на гастро-ентеро-панкреатични невроендокринни тумори
Czech	kovový prvek (68Ga)-N-[(4,7,10-trikarboxymethyl-1,4,7,10-tetraazacyklododec-1-yl)acetyl]-D-fenylalanyl-L-cysteinyl-L-tyrosyl-D-tryptofanyl-L-lysyl-L-threoninyl-L-cysteinyl-L-threonin-cyklo(2-7)disulfid	Diagnostika gastroenteropankreatických neuroendokrinních tumorů
Croatian	Galij (68Ga)-N-[(4,7,10-Trikarboksimetil-1,4,7,10-tetraazaciklododec-1-il) acetil]-D-fenilalanil-L-cisteinil-L-tirozil-D-triptofanil-L-lizil-L-treoninil-L-cisteinil-L-treonin-ciklički (2-7) disulfid	Dijagnoza gastroenteropankreatičnih neuroendokrinih tumora
Danish	Gallium(68Ga)-N-[(4,7,10-Tricarboxymethyl-1,4,7,10-tetraazacyclododec-1-yl)acetyl]-D-phenylalanyl-L-cysteinyl-L-tyrosyl-D-tryptophanyl-L-lysyl-L-threoninyl-L-cysteinyl-L-threonin-cyclisk(2-7)disulfid	Diagnose af gastroentero pankreatiske neuroendokrine tumorer
Dutch	Gallium(68Ga)-N-[(4,7,10-Tricarboxymethyl-1,4,7,10-tetraazacyclododec-1-yl)acetyl]-D-fenylalanyl-L-cysteinyl-L-tyrosyl-D-tryptofanyl-L-lysyl-L-threoninyl-L-cysteinyl-L-threonin-cyclisk(2-7)disulfide	Diagnose van gastro-entero-pancreatische neuro-endocriene tumoren
Estonian	Gallium(68Ga)-N-[(4,7,10-trikarboksümetüül-1,4,7,10-tetra-asa-tsüklododek-1-üül)atsetüül]-D-fenüülalanüül-L-tsüsteinüül-L-türosüül-D-trüptofanüül-L-lüsüül-L-treoninüül-L-tsüsteinüül-L-treoniin-tsükliiline(2-7)disulfiid	Gastroenteropankreaatiliste neuroendokriintuumorite diagnoosimine
Finnish	Gallium(68Ga)-N-[(4,7,10-trikarboksिमetyyli-1,4,7,10-tetra-atsasyklododek-1-yyl)asetyyli]-D-fenyylialaniyli-L-kysteinyyli-L-tyrosyyli-D-tryptofanyyli-L-lysyli-L-treoninyyli-L-kysteinyyli-L-treoniini-syklinen (2-7)disulfidi	Maha-suolikanavan ja haiman neuroendokriinisten kasvainten diagnosointi

<sup>1</sup> At the time of designation

Language	Active ingredient	Indication
French	(2-7) Disulfure cyclique de N-[(4,7,10-tricarboxyméthyl-1,4,7,10-tétrazacyclododécyl-1)acétyl]-D-phénylalanil-L-cystéinyl-L-tyrosyl-D-tryptophanyl-L-lysyl-L-thréoninyl-L-cystéinyl-L-thréonine marqué au gallium 68	Diagnostic des tumeurs neuro-endocrines gastro-entéro-pancréatiques
German	Gallium(68Ga)-N-[(4,7,10-Tricarboxymethyl-1,4,7,10-tetraazacyclododec-1-yl)acetyl]-D-phenylalanil-L-cysteinyl-L-tyrosyl-D-tryptophanyl-L-lysyl-L-threoninyl-L-cysteinyl-L-threonin-cyclisches(2-7)Disulfid	Diagnose von gastro-entero-pankreatischen neuroendokrinen Tumoren
Greek	γάλλιο (Ga-68)-N-[(4,7,10-τρικαρβοξυμεθυλ-1,4,7,10-τετραζακυκλοδωδεκ-1-υλ)ακετυλ]-D-φαινυλαλανυλ-L-κυστεϊνυλ-L-τυροσυλ-D-τρυπτοφανυλ-L-λυσυλ-L-θρεονινυλ-L-κυστεϊνυλ-L-θρεονίνο-κυκλικό(2-7)δισουλφίδιο	Διάγνωση των γαστρεντεροπαγκρεατικών νευροενδοκρινικών όγκων
Hungarian	Gallium(68Ga)-N-[(4,7,10-trikarboximetil-1,4,7,10-tetraazaciklododec-1-il)acetyl]-D-fenilalanil-L-ciszteinil-L-tirozil-D-triptofanil-L-lizil-L-treoninil-L-ciszteinil-L-treonin-ciklikus(2-7)disulfid	Gastro-entero-pancreaticus neuroendokrin tumorok diagnosztikája
Italian	Gallio(68Ga)-N-[(4,7,10-Tricarbossimetil-1,4,7,10-tetraazaciclododec-1-il)acetyl]-D-fenilalanil-L-cisteinil-L-tirosil-D-triptofanil-L-lisil-L-treoninil-L-cisteinil-L-treonin-(2-7)disolfuro ciclico	Diagnosi dei tumori neuroendocrini gastroenteropancreatici
Latvian	Gallija(Ga-68)-N-[(4,7,10-trikarboksimetil-1,4,7,10-tetraazaciklododec-1-il)acetyl]-D-fenilalanil-L-cisteinil-L-tirozil-D-triptofanil-L-lizil-L-treoninil-L-cisteinil-L-treonīna-cikliskais(2-7)disulfids	Kuņģa-zarnu trakta-aizkuņģa dziedzera neiroendokrīnu audzēju diagnostikai
Lithuanian	Galio[Ga-68]-N-[(4,7,10-trikarboksilmetil-1,4,7,10-tetraazaciklododek-1-ilo)acetyl]-D-fenilalanil-L-cisteinil-L-tirosil-D-triptofanil-L-lizil-L-treoninil-L-cisteinil-L-treonino-ciklinis(2-7)disulfidas	Skrandžio, žarnų, kasos neuroendokrininių navikų diagnostikai
Maltese	Gallium [Ga-68]-N-[(4,7,10-tricarboxymethyl-1,4,7,10-tetraazacyclododec-1-yl)acetyl]-D-phenylalanil-L-cysteinyl-L-tyrosyl-D-tryptophanyl-L-lysyl-L-threoninyl-L-cysteinyl-L-threonine-cyclic(2-7)disulfide	Dijanjosi ta' tumuri newroendokrini gastro-entero-pankrejatiċi
Polish	Gal(68Ga)-N-[(4,7,10-trikarboksymetylo-1,4,7,10-tetraazacyklododec-1-yl)acetylo]-D-fenylalanylo-L-cysteinylo-L-tyrozylo-D-tryptofanylo-L-lizylo-L-treoninylo-L-cysteinylo-L-treoniny-cyklicznej(2-7) disiarczek	Diagnostyka guzów neuroendokrynych przewodu pokarmowego i trzustki

Language	Active ingredient	Indication
Portuguese	Gálio (68Ga)-N-[(4,7,10-Tricarboximetil-1,4,7,10-tetraazaciclododec-1-il)acetil]-D-fenilalanil-L-cisteinil-L-tirosil-D-triptofanil-L-lisil-L-treoninil-L-cisteinil-L-treonina-cíclico(2-7)dissulfureto	Diagnóstico de tumores neuroendócrinos gastro-entero-pancreáticos
Romanian	(2-7) Disulfură ciclică de N-[(4,7,10-Tricarboximetil-1,4,7,10-tetraazaciclododeca-1-il)acetil]-D-fenilalanil-L-cisteinil-L-tirosil-D-triptofanil-L-lisil-L-treoninil-L-cisteinil-L-treonin-(2-7) marcata cu Galiu [Ga-68]	Diagnosticul tumorilor neuroendocrine gastro-entero-pancreatice
Slovak	Gálium [Ga-68]-N-[(4,7,10-trikarboxymetyl-1,4,7,10-tetraazacyklododek-1-yl)acetyl]-D-fenylalanil-L-cysteinyl-L-tyrosyl-D-tryptofanyl-L-lysyl-L-treoninyl-L-cysteinyl-L-treonin-cyclo(2-7)disulfid	Diagnóza gastroentero-pankreatických neuroendokrinných tumorov
Slovenian	Galijev [Ga-68]-N-[(4,7,10-trikarboksimetil-1,4,7,10-tetraazaciclododeka-1-il)acetil]-D-fenilalanil-L-cisteinil-L-tirozil-D-triptofanil-L-lisil-L-treoninil-L-cisteinil-L-treonin-ciklični(2-7)disulfid	Diagnostika gastroenteropankreatičnih neuroendokrinih tumorjev
Spanish	Galio(68Ga)-N-[(4,7,10-Tricarboximetil-1,4,7,10-tetraazaciclododec-1-il)acetil]-D-fenilalanil-L-cisteinil-L-tirosil-D-triptofanil-L-lisil-L-treoninil-L-cisteinil-L-treonina-cíclico(2-7)disulfuro	Diagnóstico de los tumores neuroendocrinos gastroenteropancreáticos
Swedish	Gallium(68Ga)-N-[(4,7,10-Trikarboxymetyl-1,4,7,10-tetraazacyklododek-1-yl)acetyl]-D-fenylalanil-L-cysteinyl-L-tyrosyl-D-tryptofanyl-L-lysyl-L-treoninyl-L-cysteinyl-L-treonin-cyklisk(2-7)disulfid	Diagnos av neuroendokrina tumörer i mage, tarm och bukspottkörtel
Norwegian	Gallium(68Ga)-N-[(4,7,10-trikarboksymetyl-1,4,7,10-tetraazasyklododek-1-yl)acetyl]-D-fenylalanil-L-cysteinyl-L-tyrosyl-D-tryptofanyl-L-lysyl-L-treoninyl-L-cysteinyl-L-treonin-syklisk(2-7)disulfid	Diagnose av gastroenteropankreatiske nevroendokrine tumorar
Icelandic	Gallíum (68Ga)-N-[(4,7,10-þrikarboxýmetyl-1,4,7,10-tetraazacyklódódek-1-yl)acetyl]-D-fenýlalanýl-L-cýsteinýl-L-týrósýl-D-trýptófanyl-L-lýsýl-L-treónínýl-L-cýsteinýl-L-treónín-hringtengt(2-7)tvísúlfið	Greining á maga-þarma- bris æxlum af taugainnkirtla-toga