



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Lutetium (^{177}Lu)-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 treatment of gastro-entero-pancreatic neuroendocrine tumours

On 31 January 2008, orphan designation (EU/3/07/523) was granted by the European Commission to BioSynthema Global Operations B.V, The Netherlands, for lutetium (^{177}Lu)-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 treatment of gastro-entero-pancreatic neuroendocrine tumours.

The sponsorship was transferred to Advanced Accelerator Applications, France, in September 2011.

What are gastro-entero-pancreatic neuroendocrine tumours?

Gastro-entero-pancreatic neuroendocrine tumours (GEP-NET) are a group of tumours that share a number of common characteristics, for example content of specific chemical substances called "neuroendocrine markers". There are two main types of GEP-NET: carcinoid tumours, and "pancreatic-type" endocrine tumours (these often occur in the pancreas, but also in other sites). GEP-NET are chronically debilitating as they often produce and secrete hormonal substances that may cause severe symptoms, and 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-NET affected approximately 1.6 in 10,000 people in the European Union (EU)*. This is equivalent to a total of around 80,000 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).

*Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed based on data from the European Union (EU 27), Norway, Iceland and Lichtenstein. This represents a population of 498,000,000 (Eurostat 2006). This estimate is based on available information and calculations presented by the sponsor at the time of the application).



What treatments are available?

At the time of the application for orphan designation, several products were authorised in the Community for the treatment of one or more of GEP-NET. In most cases, these products are active against the symptoms caused by the secretion of hormones, but are not active against the growth of the tumours. Commonly, surgery and treatment with so called somatostatin analogues were used. Somatostatin analogues are similar to a naturally occurring hormone in the body called somatostatin that prevents the release of many hormones.

Lutetium(¹⁷⁷Lu)-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 may be of potential significant benefit, as it is expected to kill tumour cells, and thus reduce tumour size and eventually improve the long term outcome of the patients. These assumptions will have to be confirmed at the time of marketing authorisation. This will be necessary to maintain the orphan status.

How is this medicine expected to work?

Lutetium(¹⁷⁷Lu)-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 contains a somatostatin analogue together with a radioactive form of a chemical called Lutetium (¹⁷⁷Lu). The product is expected to bind to the tumour cells thanks to the somatostatin analogue and to kill them with the radiation from the lutetium component.

What is the stage of development of this medicine?

The effects of lutetium (¹⁷⁷Lu)-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 were evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical studies in patients with GEP-NET were ongoing.

Lutetium(¹⁷⁷Lu)-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 was not authorised anywhere worldwide for GEP-NET or designated as orphan medicinal product elsewhere for this condition, at the time of submission.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 5 December 2007 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:

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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 languages¹, Norwegian and Icelandic

Language	Active Ingredient	Indication
English	Lutetium (¹⁷⁷ Lu)-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	Treatment of gastro-entero-pancreatic neuroendocrine tumours
Bulgarian	Лутетиум (¹⁷⁷ Lu)-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	Лечение на гастро-ентеро-панкреатични невроендокринни тумори
Czech	Lutecium (¹⁷⁷ Lu)-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	Léčba gastroenteropankreatických neuroendokrinních tumorů
Danish	Lutetium (¹⁷⁷ Lu)-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	Behandling af gastroentero pankreatiske neuroendokrine tumorer
Dutch	Lutetium (¹⁷⁷ Lu)-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	Behandeling van gastro-entero-pancreatische neuro-endocriene tumoren
Estonian	Luteetsium (¹⁷⁷ Lu)-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-tsükliline(2-7)disulfiid	Gastroenteropankreaatiliste neuroendokriintuumorite ravi
Finnish	Lutetium (¹⁷⁷ Lu)-N-[(4,7,10-trikarboksümetyyli-1,4,7,10-tetra-atsasyklododek-1-yyli)asetyyli]-D-fenyyialanyyli-L-kysteinyyli-L-tyrosyyli-D-tryptofanyyli-L-lysyli-L-treoninyyli-L-kysteinyyli-L-treoniini-syklinen (2-7)disulfidi	Maha-suolikanavan ja haiman neuroendokriinisten kasvainten hoito
French	(2-7) disulfure cyclique de N-[(4,7,10-tricarboxyméthyl-1,4,7,10-tétraazacyclododécyl-1)acétyl]-D-phénylalanyl-L-cystéinyl-L-tyrosyl-D-tryptophanyl-L-lysyl-L-thréoninyl-L-cystéinyl-L-thréonine marqué au ¹⁷⁷ Lutétium	Traitement des tumeurs neuro-endocrines gastro-entéro-pancréatiques

¹ At the time of designation

Language	Active Ingredient	Indication
German	Lutetium (¹⁷⁷ Lu)-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-cyclisches(2-7)disulfide	Behandlung von gastro-entero-pankreatischen neuroendokrinen Tumoren
Greek	Λουτήτιο (¹⁷⁷ Lu)-N-[(4,7,10-Τρικαρβοξυμεθυλ-1,4,7,10-τετρααζακυκλοδωδεκ-1-υλ)ακετυλ]-D-φαινυλαλανυλ-L-κυστεϊνυλ-L-τυροσυλ-D-τρυπτοφανυλ-L-λυσυλ-L-θρεονινυλ-L-κυστεϊνυλ-L-θρεονίνο-κυκλικό(2-7)δισουλφίδιο	Θεραπεία των γαστρεντεροπαγκρεατικών νευροενδοκρινικών όγκων
Hungarian	Lutécium (¹⁷⁷ Lu)-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)diszulfid	Gastro-entero-pancreaticus neuroendokrin tumorok kezelése
Italian	Lutezio (¹⁷⁷ Lu)-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	Trattamento dei tumori neuroendocrini gastroenteropancreatici
Latvian	Lutēcija(¹⁷⁷ Lu)-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)disulfīds	Kuņģa-zarnu trakta-aizkuņģa dziedzera neuroendokrīnu audzēju ārstēšana
Lithuanian	Liutecio (¹⁷⁷ Lu)-N-[(4,7,10-trikarboksilmetil-1,4,7,10-tetraazaciklododek-1-il)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 gydymas
Maltese	Lutetium (¹⁷⁷ Lu)-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	Kura ta' tumuri newroendokrini gastro-entero-pankrejatiċi
Polish	Lutetet (¹⁷⁷ Lu)-N-[(4,7,10-trikarboksymetylo-1,4,7,10-tetraazacyklododec-1-yl)acetylo]-D-fenyloalanylo-L-cysteinylo-L-tyrozylo-D-tryptofanylo-L-lizylo-L-treoninylo-L-cysteinylo-L-treoniny-cyklicznej(2-7) disiarczek	Leczenie pacjentów z guzami neuroendokrynnymi przewodu pokarmowego i trzustki
Portuguese	Lutécio (¹⁷⁷ Lu)-N-[(4,7,10-Tricarboximetil-1,4,7,10-tetraazaciclododec-1-il)acetyl]-D-fenilalanil-L-cisteinil-L-tirosil-D-triptofanil-L-lisil-L-treoninil-L-cisteinil-L-treonina-cíclico(2-7)dissulfureto	Tratamento de tumores neuroendócrinos gastro-entero-pancreáticos
Romanian	Lutețiu(¹⁷⁷ Lu)-N-[(4,7,10-tricarboximetil-1,4,7,10-tetraazaciclododec-1-il)acetyl]-D-fenilalanil-L-cisteinil-L-tirozil-D-triptofanil-L-lizil-L-treoninil-L-cisteinil-L-treonin-ciclic(2-7)disulfidă	Tratamentul tumorilor neuroendocrine gastro-entero-pancreatice

Language	Active Ingredient	Indication
Slovak	Lutécium(¹⁷⁷ Lu)-N-[(4,7,10-trikarboxymetyl-1,4,7,10-tetraazacyklododec-1-yl)acetyl]-D-fenylalanyl-L-cysteinyl-L-tyrozy-D-tryptofanyl-L-lyzyl-L-treoninyl-L-cysteinyl-L-treonín-cyklický(2-7)disulfid	Liečba gastroenteropankreatických neuroendokrinných tumorov
Slovenian	Lutecij(¹⁷⁷ Lu)-N-[(4,7,10-Trikarboksimetil-1,4,7,10-tetraazaciklododek-1-il)acetyl]-D-fenilalanil-L-cisteinil-L-tirosil-D-tripofanil-L-lisil-L-treoninil-L-cisteinil-L-treonin-ciklični(2-7)disulfid	Zdravljenje gastroenteropankreatičnih neuroendokrinih tumorjev
Spanish	N-[(4,7,10-Trikarboximetil-1,4,7,10-tetraazaciclododec-1-il)acetyl]-D-fenilalanil-L-cisteinil-L-tirosil-D-triptofanil-L-lisil-L-treoninil-L-cisteinil-L-treonin-ciclo(2-7)disulfido marcado con Lutecio (¹⁷⁷ Lu)	Tratamiento de los tumores neuroendocrinos gastroenteropancreáticos
Swedish	Lutetium (¹⁷⁷ Lu)-N-[(4,7,10-trikarboximetyl-1,4,7,10-tetraazacyclododec-1-yl)acetyl]-D-fenylalanyl-L-cysteinyl-L-tyrosyl-D-tryptofanyl-L-lysyl-L-treoninyl-L-cysteinyl-L-treonin-cyklisk(2-7)disulfid	Behandling av neuroendokrina tumörer i mage, tarm och bukspottkörtel
Norwegian	Lutetium (¹⁷⁷ Lu)-N-[(4,7,10- trikarboksymetyl -1,4,7,10-tetraazacyclododec-1-yl)acetyl]-D-fenylalanyl-L-cysteinyl-L-tyrosyl-D-tryptofanyl-L-lysyl-L-treoninyl-L-cysteinyl-L-treonin-cyklisk(2-7)disulfid	Behandling av gastro-enteropankreatiske neuroendokrine tumorar