

7 November 2016
EMA/615260/2016
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Lutetium-177(3+), S²,S⁷-cyclo[N-{4,7,10-tricarboxymethyl-1,4,7,10-tetraaza-cyclododecan-1-yl-acetyl}-4-chloro-L-phenylalanyl-D-cysteinyl-4-[(4S)-2,6-dioxo-1,3-diazinane-4-carboxamido]-L-phenylalanyl-4-(carbamoylamino)-D-phenylalanyl-L-lysyl-L-threonyl-L-cysteinyl-D-tyrosinamide] for the treatment of gastro-entero-pancreatic neuroendocrine tumours

On 14 October 2016, orphan designation (EU/3/16/1754) was granted by the European Commission to Ipsen Pharma, France, for lutetium-177(3+), S²,S⁷-cyclo[N-{4,7,10-tricarboxymethyl-1,4,7,10-tetraaza-cyclododecan-1-yl-acetyl}-4-chloro-L-phenylalanyl-D-cysteinyl-4-[(4S)-2,6-dioxo-1,3-diazinane-4-carboxamido]-L-phenylalanyl-4-(carbamoylamino)-D-phenylalanyl-L-lysyl-L-threonyl-L-cysteinyl-D-tyrosinamide] (also known as ¹⁷⁷Lu-OPS201) for the treatment of gastro-entero-pancreatic neuroendocrine tumours.

What are gastro-entero-pancreatic neuroendocrine tumours?

Gastro-entero-pancreatic neuroendocrine tumours (GEP-NETs) are tumours that usually arise from neuroendocrine cells in the gut or pancreas. These cells release hormones that control various functions of the digestive system. The symptoms of GEP-NETs depend on where the tumour is growing 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 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-NETs affected approximately 3.8 in 10,000 people in the European Union (EU). This was equivalent to a total of around 195,000 people*, and is below the ceiling for

*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 513,700,000 (Eurostat 2016).

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 the application for orphan designation, several products were authorised in the EU for treating GEP-NETs, including everolimus, lanreotide, octreotide and sunitinib. Surgery was also used to remove or reduce the size of tumours.

The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with GEP-NETs because early data in patients with advanced, inoperable disease showed that their condition stabilised or improved. 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 made of a somatostatin analogue combined with a radioactive substance. A somatostatin analogue attaches to the same receptors as the natural hormone somatostatin. Somatostatin receptors are found in high amounts on GEP-NET cells. By attaching to these receptors, the medicine is expected to bring the radioactivity to the tumour cells and kill them.

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 medicine in experimental models was ongoing.

At the time of submission of the application for orphan designation, clinical trials with the medicine in patients with GEP-NETs were ongoing.

At the time of submission, this medicine was not authorised anywhere in the EU for GEP-NETs 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 8 September 2016 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, 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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Lutetium-177(3+), S ² , S ⁷ -cyclo[N-{4,7,10-tricarboxymethyl-1,4,7,10-tetraaza-cyclododecan-1-yl-acetyl}-4-chloro-L-phenylalanyl-D-cysteiny]-4-[(4S)-2,6-dioxo-1,3-diazinane-4-carboxamido]-L-phenylalanyl-4-(carbamoylamino)-D-phenylalanyl-L-lysyl-L-threonyl-L-cysteiny]-D-tyrosinamide]	Treatment of gastro-entero-pancreatic neuroendocrine tumours
Bulgarian	Лутетий-177(3+), S ² , S ⁷ -цикло[N-{4,7,10-трикарбоксиметил-1,4,7,10-тетрааза-циклододекан-1-ил-ацетил}-4-хлоро-L-фенилаланил-D-цистеинил-4-[(4S)-2,6-диоксо-1,3-дiazинан-4-карбоксамидо]-L-фенилаланил-4-(карбамоиламино)-D-фенилаланил-L-лизил-L-треонил-L-цистеинил-D-тирозинамид]	Лечение на гастро-ентеро-панкреатични невроендокринни тумори
Croatian	Lutecij-177(3+), S ² , S ⁷ -ciklo[N-{4,7,10-trikarboksimetil-1,4,7,10-tetraaza-ciklododekan-1-il-acetil}-4-kloro-L-fenilalanil-D-cisteinil-4-[(4S)-2,6-diokso-1,3-diazinan-4-karboksamido]-L-fenilalanil-4-(karbamoilamino)-D-fenilalanil-L-lizil-L-treonil-L-cisteinil-D-tirozinamid]	Liječenje gastroenteropankreatičnih neuroendokrinih tumora
Czech	Lutecium-177(3+), S ² , S ⁷ -cyklo[N-{4,7,10-trikarboxymethyl-1,4,7,10-tetraaza-cyklo-dodekan-1-yl-acetyl}-4-chloro-L-fenylalanyl-D-cysteiny]-4-[(4S)-2,6-dioxo-1,3-diazinan-4-karboxamido]-L-fenylalanyl-4-(karbamoylamino)-D-fenylalanyl-L-lysyl-L-threonyl-L-cysteiny]-D-tyrosinamid]	Léčba gastro-entero-pankreatických neuroendokrinních tumorů
Danish	Lutetium-177(3+), S ² , S ⁷ -cyclo[N-{4,7,10-tricarboxymethyl-1,4,7,10-tetraaza-cyclododecan-1-yl-acetyl}-4-chloro-L-phenylalanyl-D-cysteiny]-4-[(4S)-2,6-dioxo-1,3-diazinane-4-carboxamido]-L-phenylalanyl-4-(carbamoylamino)-D-phenylalanyl-L-lysyl-L-threonyl-L-cysteiny]-D-tyrosinamid]	Behandling af gastro-entero-pancreatiske neuroendocrine tumorer
Dutch	Lutetium-177(3+), S ² , S ⁷ -cyclo[N-{4,7,10-tricarboxymethyl-1,4,7,10-tetra-aza-cyclododecaan-1-yl-acetyl}-4-chloor-L-fenylalanyl-D-cysteïnyl-4-[(4S)-2,6-dioxo-1,3-diazinane-4-carboxamido]-L-fenylalanyl-4-(carbamoylamino)-D-fenylalanyl-L-lysyl-L-threonyl-L-cysteïnyl-D-tyrosinamide]	Behandeling van gastro-entero-pancreatische neuroendocriene tumoren

¹ At the time of designation

Language	Active ingredient	Indication
Estonian	Luteetsium-177(3+), S ² ,S ⁷ -tsüklo[N-{4,7,10-trikarboksümetüül-1,4,7,10-tetra-asa-tsüklododekaan-1-üül-atsetüül}-4-kloro-L-fenüülalanüül-D-tsüsteinüül-4-[(4S)-2,6-diokso-1,3-diasinaan-4-karboksamido]-L-fenüülalanüül-4-(karbamoüülamino)-D-fenüülalanüül-L-lüsüül-L-treonüül-L-tsüsteinüül-D-türosinamiid]	Gastroenteropankreatiliste neuroendokriintuumorite ravi
Finnish	Lutetium-177(3+), S ² ,S ⁷ -syklo[N-{4,7,10-trikarboksümetyyli-1,4,7,10-tetra-atsa-syklododekaani-1-yyli-asetyyli}-4-kloro-L-fenyyialanyyli-D-kysteinyyli-4-[(4S)-2,6-diokso-1,3-diatsinaani-4-karboksiamido]-L-fenyyialanyyli-4-(karbamoyyliamino)-D-fenyyialanyyli-L-lysyli-L-treonyyli-L-kysteinyyli-D-tyrosinamidi]	Maha-suolikanavan ja haiman neuroendokriinisten kasvainten hoito
French	Lutétium-177(3+), S ² ,S ⁷ -cyclo[N-{4,7,10-tricarboxyméthyl-1,4,7,10-tétraaza-cyclododécane-1-yl-acétyl}-4-chloro-L-phénylalanil-D-cystéinyl-4-[(4S)-2,6-dioxo-1,3-diazinane-4-carboxamido]-L-phénylalanil-4-(carbamoylamino)-D-phénylalanil-L-lysyl-L-thréonyl-L-cystéinyl-D-tyrosinamide]	Traitement des tumeurs neuroendocrines gastroentéropancréatiques
German	Lutetium-177(3+), S ² ,S ⁷ -cyclo[N-{4,7,10-Tricarboxymethyl-1,4,7,10-tetraaza-cyclododecan-1-yl-acetyl}-4-chlor-L-phenylalanil-D-cysteinyl-4-[(4S)-2,6-dioxo-1,3-diazinan-4-carboxamido]-L-phenylalanil-4-(carbamoylamino)-D-phenylalanil-L-lysyl-L-threonyl-L-cysteinyl-D-tyrosinamid]	Behandlung von gastro-entero-pankreatischen neuroendokrinen Tumoren
Greek	Λουτέτιο -177(3+), S ² ,S ⁷ -κυκλο[N-{4,7,10-τρικαρβοξυμεθυλο-1,4,7,10-τετρααζα-κυκλοδωδεκανο-1-υλ-ακετυλο}-4-χλωρο-L-φαινυλαλανυλο-D-κυστεϊνυλο-4-[(4S)-2,6-διοξο-1,3-διαζινανο-4-καρβοξαμιδο]-L-φαινυλαλανυλο-4-(καρβαμοϋλαμινο)-D-φαινυλαλανυλο-L-λυσυλο-L-θρεονυλο-L-κυστεϊνυλο-D-τυροσιναμίδη]	Θεραπεία των γαστρεντεροπαγκρεατικών νευροενδοκρινικών όγκων
Hungarian	Lutécium-177(3+), S ² ,S ⁷ -ciklo[N-{4,7,10-trikarboximetil-1,4,7,10-tetraaza-ciklododekán-1-il-acetil}-4-kloro-L-fenilalanil-D-ciszteinil-4-[(4S)-2,6-dioxo-1,3-diazinán-4-karboxamido]-L-fenilalanil-4-(karbamoilamino)-D-fenilalanil-L-lizil-L-treonil-L-ciszteinil-D-tirozinamid]	Gasztro-entero-pankreatikus neuroendokrin tumorok kezelése
Italian	Lutezio-177(3+), S ² ,S ⁷ -ciclo[N-{4,7,10-tricarbossimetil-1,4,7,10-tetraaza-ciclododecan-1-il-acetil}-4-cloro-L-fenilalanil-D-cisteinil-4-[(4S)-2,6-diosso-1,3-diazinan-4-carbossamido]-L-fenilalanil-4-(carbamoilamino)-D-fenilalanil-L-lisil-L-treonil-L-cisteinil-D-tirosinamide]	Trattamento dei tumori gastro-entero-pancreatici neuroendocrini

Language	Active ingredient	Indication
Latvian	Lutēcija-177(3+), S ² ,S ⁷ -ciklo[N-{4,7,10-trikarboksimetil-1,4,7,10-tetraaza-ciklododekān-1-il-acetil}-4-hlor-L-fenilalanil-D-cisteinil-4-[(4S)-2,6-diokso-1,3-diazinān-4-karboksamido]-L-fenilalanil-4-(karbamoilamino)-D-fenilalanil-L-lizil-L-treonil-L-cisteinil-D-tirosinamīds]	Kuņģa-zarnu -aizkuņģa dziedzerā neiroendokrīnu audzēju ārstēšana
Lithuanian	Liutecis-177(3+), S ² ,S ⁷ -ciklo[N-{4,7,10-trikarboksimetil-1,4,7,10-tetraaza-ciklododekan-1-il-acetil}-4-chlor-L-fenilalanil-D-cisteinil-4-[(4S)-2,6-diokso-1,3-diazinan-4-karboksamid]-L-fenilalanil-4-(karbamoilamin)-D-fenilalanil-L-lizil-L-treonil-L-cisteinil-D-tirozinamidas]	Skrandžio-žarnyno-kasos neuroendokrininių navikų gydymas
Maltese	Lutetium-177(3+), S ² ,S ⁷ -cyclo[N-{4,7,10-tricarboxymethyl-1,4,7,10-tetraaza-cyclododecan-1-yl-acetyl}-4-chloro-L-phenylalanyl-D-cysteiny-4-[(4S)-2,6-dioxo-1,3-diazinane-4-carboxamido]-L-phenylalanyl-4-(carbamoylamino)-D-phenylalanyl-L-lysyl-L-threonyl-L-cysteiny-4-D-tyrosinamide]	Kura ta' tumuri newroendokrini gastro-entero-pankrejatiċi
Polish	kompleks lutetu-177(3+) i S ² ,S ⁷ -cyklo[N-{4,7,10-trikarboksymetylo-1,4,7,10-tetraaza-cyklododekan-1-ylo-acetylo}-4-chloro-L-feniloalano-D-cysteinylo-4-[(4S)-2,6-diokso-1,3-diazynano-4-karboksoamido]-L-feniloalano-4-(karbamoiłamino)-D-feniloalano-L-lizylo-L-treonilo-L-cysteinylo-D-tyrozynoamidu	Leczenie guzów neuroendokrynnych przewodu pokarmowego i trzustki
Portuguese	Lutécio-177(3+), S ² ,S ⁷ -ciclo[N-{4,7,10-tricarboximetil-1,4,7,10-tetraaza-ciclododecan-1-il-acetil}-4-cloro-L-fenilalanil-D-cisteinil-4-[(4S)-2,6-dioxo-1,3-diazinano-4-carboxamido]-L-fenilalanil-4-(carbamoilamino)-D-fenilalanil-L-lisil-L-treonil-L-cisteinil-D-tirosinamida]	Tratamento dos tumores neuroendócrinos gastro-entero-pancreáticos
Romanian	Lutețiu-177(3+), S ² ,S ⁷ -ciclo[N-{4,7,10-tricarboximetil-1,4,7,10-tetraazaciclododeca-1-il-acetil}-4-cloro-L-fenilalanil-D-cisteinil-4-[(4S)-2,6-dioxo-1,3-diazinan-4-carboxamido]-L-fenilalanil-4-(karbamoilamino)-D-fenilalanil-L-lisil-L-treonil-L-cisteinil-D-tirozinamidă]	Tratamentul tumorilor neuroendocrine gastro-entero-pancreatice
Slovak	Lutécium-177(3+), S ² ,S ⁷ -cyklo[N-{4,7,10-tricarboxymetyl-1,4,7,10-tetraaza-cyklododekán-1-yl-acetyl}-4-chlór-L-fenylalanyl-D-cysteiny-4-[(4S)-2,6-dioxo-1,3-diazinán-4-karboxamido]-L-fenylalanyl-4-(karbamoylamino)-D-fenylalanyl-L-lyzyl-L-treonyl-L-cysteiny-4-D-tyrozínamid]	Liečba gastroenteropankreatických neuroendokrinných nádorov
Slovenian	Lutecij-177(3+), S ² ,S ⁷ -ciklo[N-{4,7,10-trikarboksimetil-1,4,7,10-tetraaza-ciklododekan-1-yl-acetil}-4-kloro-L-fenilalanil-D-cisteinil-4-[(4S)-2,6-diokso-1,3-diazinan-4-karboksamido]-L-fenilalanil-4-(karbamoilamino)-D-fenilalanil-L-lizil-L-treonil-L-cisteinil-D-tirozinamid]	Zdravljenje gastro-entero-pancreatičnih neuroendokrinih tumorjev

Language	Active ingredient	Indication
Spanish	Lutecio-177(3+), S ² ,S ⁷ -ciclo[N-{4,7,10-tricarboximetil-1,4,7,10-tetraaza-ciclododecan-1-il-acetil}-4-cloro-L-fenilalanil-D-cisteínil-4-[(4S)-2,6-dioxo-1,3-diazinano-4-carboxamido]-L-fenilalanil-4-(carbamoilamino)-D-fenilalanil-L-lisil-L-treonil-L-cisteínil-D-tirosinamida]	Tratamiento de los tumores neuroendocrinos gastroenteropancreáticos
Swedish	Lutetium-177(3+), S ² ,S ⁷ -cyklo[N-{4,7,10-trikarboximetyl-1,4,7,10-tetraazacyklododekan-1-yl-acetyl}-4-klor-L-fenylalanyl-D-cysteiny-4-[(4S)-2,6-dioxo-1,3-diazinan-4-karboxamid]-L-fenylalanyl-4-(karbamoylamino)-D-fenylalanyl-L-lysyl-L-treonyl-L-cysteiny-D-tyrosinamid]	Behandling av gastroenteropankreatiska neuroendokrina tumörer
Norwegian	Lutetium-177(3+), S ² ,S ⁷ -syklo[N-{4,7,10-trikarboksymetyl-1,4,7,10-tetraaza-syklododekan-1-yl-acetyl}-4-klor-L-fenylalanyl-D-cysteiny-4-[(4S)-2,6-diokso-1,3-diazinan-4-karboksamid]-L-fenylalanyl-4-(karbamoylamin)-D-fenylalanyl-L-lysyl-L-treonyl-L-cysteiny-D-tyrosinamid]	Behandling av gastroenteropankreatiske nevroendokrine tumorer
Icelandic	Lútetíum-177(3+), S ² ,S ⁷ -sýkló[N-{4,7,10-Tríkarboxýmetyl-1,4,7,10-tetraaza-sýklódódekan-1-ýl-asetýl}-4-klóró-L-fenýlalanýl-D-sýsteinýl-4-[(4S)-2,6-díoxó-1,3-díazínan-4-karboxamíð]-L-fenýlalanýl-4-(karbamóýlamínó)-D-fenýlalanýl-L-lýsýl-L-treónýl-L-sýsteinýl-D-týrósinamíð]	Meðferð á maga-þarma- bris æxlum af taugainnkirtla-toga