



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

18 December 2019
EMADOC-628903358-1305

Public summary of opinion on orphan designation

Poly(oxy-1,2-ethanediyl), alpha-hydro-omega-hydroxy-,15,15'-diester with N-acetyl-L-isoleucyl-L-cysteinyl-L-valyl-1-methyl-L-tryptophyl-L-glutaminyl-L-alpha-aspartyl-L-tryptophylglycyl-L-alanyl-L-histidyl-L-arginyl-L-cysteinyl-L-threonyl-2-[2-(2-aminoethoxy)ethoxy]acetyl-N6-carboxy-L-lysine cyclic (2.fwdarw.12)-(disulfide); where two identical synthetic peptide domains are covalently linked at the ends of the polyethylene glycol chain for the treatment of C3 glomerulopathy

On 21 August 2019, orphan designation EU/3/19/2201 was granted by the European Commission to Apellis Ireland Limited, Ireland, for poly(oxy-1,2-ethanediyl), alpha-hydro-omega-hydroxy-,15,15'-diester with N-acetyl-L-isoleucyl-L-cysteinyl-L-valyl-1-methyl-L-tryptophyl-L-glutaminyl-L-alpha-aspartyl-L-tryptophylglycyl-L-alanyl-L-histidyl-L-arginyl-L-cysteinyl-L-threonyl-2-[2-(2-aminoethoxy)ethoxy]acetyl-N6-carboxy-L-lysine cyclic (2.fwdarw.12)-(disulfide); where two identical synthetic peptide domains are covalently linked at the ends of the polyethylene glycol chain (also known as APL-2) for the treatment of C3 glomerulopathy.

What is C3 glomerulopathy?

C3 glomerulopathy is a condition in which a part of the body's immune system (the body's natural defences) known as the complement system is overactive. As a result, breakdown products of a component of the system called C3 build up in the kidneys, damaging them and reducing their function.

Patients with C3 glomerulopathy usually have signs of problems relating to poor kidney function, such as blood or protein in urine, high blood pressure, blurred vision and swelling in the hands and feet.

C3 glomerulopathy is life threatening and debilitating in the long term because it can lead to kidney failure.



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

At the time of designation, C3 glomerulopathy affected approximately 0.8 in 10,000 people in the European Union (EU). This was equivalent to a total of around 41,000 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).

What treatments are available?

At the time of orphan designation, no satisfactory treatments were authorised in the EU for C3 glomerulopathy. Because the disease involves the body's immune system, immunosuppressant medicines (that reduce the activity of the immune system) were usually used. Other treatments included plasmapheresis (a procedure to remove unwanted substances from plasma, the liquid part of the blood), infusion of healthy plasma, and medicines to reduce blood pressure and protein in the urine. Some patients developing end-stage kidney disease received dialysis and kidney transplantation.

How is this medicine expected to work?

The medicine works by reducing the abnormal activity of the complement system, which reduces the breakdown of C3. This is expected to prevent C3 breakdown products building up in the kidneys thereby reducing damage in the kidneys and the problems caused by the kidneys not working well enough.

What is the stage of development of this medicine?

The effects of this medicine have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with this medicine in patients with C3 glomerulopathy were ongoing.

At the time of submission, this medicine was not authorised anywhere in the EU for the treatment of C3 glomerulopathy. Orphan designation had been granted in the United States for C3 glomerulopathy.

In accordance with Regulation (EC) No 141/2000, the COMP adopted a positive opinion on 18 July 2019, 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.

*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 518,400,000 (Eurostat 2019).

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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Poly(oxy-1,2-ethanediyl), alpha-hydro-omega-hydroxy-,15,15'-diester with N-acetyl-L-isoleucyl-L-cysteinyl-L-valyl-1-methyl-L-tryptophyl-L-glutaminy-L-alpha-aspartyl-L-tryptophylglycyl-L-alanyl-L-histidyl-L-arginyl-L-cysteinyl-L-threonyl-2-[2-(2-aminoethoxy)ethoxy]acetyl-N6-carboxy-L-lysineamide cyclic (2.fwdarw.12)-(disulfide); where two identical synthetic peptide domains are covalently linked at the ends of the polyethylene glycol chain	Treatment of C3 glomerulopathy
Bulgarian	Поли(окси-1,2-етанедиил), алфа-хидро-омега-хидрокси-,15,15'-диестер с N-ацетил-L-изолевцил-L-цистеинил-L-валил-1-метил-L-триптофил-L-глутаминил-L-алфа-аспартил-L-триптофилглицил-L-аланил-L-хистидил-L-аргинил-L-цистеинил-L-треонил-2-[2-(2-аминоетокси)етокси]ацетил-N6-карбоксо-L-лизинамид цикличен (2.fwdarw.12)-(дисулфид); където два идентични синтетични пептидни домейна са свързани ковалентно към краищата на полиетиленовата гликолова верига	Лечение на C3 гломерулопатия
Croatian	Poli (oksi-1,2-etandiil), alfa-hidro-omega-hidroksi-, 15, 15'-diester s N-acetil-L-izoleucil-L-cisteinil-L-valil-1-metil-L-triptofil -L-glutaminil-L-alfa-aspartil-L-triptofilglcil-L-alanil-L-histidil-L-arginil-l-cisteinil-L-treonil-2- [2- (2-aminoetoksi) etoksi] acetil-N6 - karboksi-L-lizinamid ciklički (2.fvdarv.12) - (disulfid); pri čemu su dvije identične sintetičke peptidne domene kovalentno povezane na krajevima lanca polietilen glikola	Liječenje C3 glomerulopatije
Czech	Poly(oxy-1,2-ethandiyl), alpha-hydro-omega-hydroxy-,15,15'-diester s N-acetyl-L-isoleucyl-L-cysteinyl-L-valyl-1-methyl-L-tryptophyl-L-glutaminy-L-alpha-aspartyl-L-tryptophylglycyl-L-alanyl-L-histidyl-L-arginyl-L-cysteinyl-L-threonyl-2-[2-(2-aminoethoxy)ethoxy]acetyl-N6-karboxy-L-lysineamid cyklický (2.fwdarw.12)-(disulfid); kde dvě identické syntetické peptidové domény jsou kovalentně navázány ke koncům polyethylenglykolového řetězce	Léčba C3 glomerulopatie

¹ At the time of designation

Language	Active ingredient	Indication
Danish	Poly(oxy-1,2-ethanediyl), alpha-hydro-omega-hydroxy-,15,15'-diester med N-acetyl-L-isoleucyl-L-cysteinyl-L-valyl-1-methyl-L-tryptophyl-L-glutaminy-L-alpha-aspartyl-L-tryptophylglycyl-L-alanyl-L-histidyl-L-arginyl-L-cysteinyl-L-threonyl-2-[2-(2-aminoethoxy)ethoxy]acetyl-N6-carboxy-L-lysynamide cyclic (2.fwdarw.12)-(disulfide); hvor to identiske syntetiske peptidomæner er kovalent bundet til enderne af polyethylenglycolkæden	Behandling af C3 glomerulopati
Dutch	Poly(oxy-1,2-ethanediyl), alpha-hydro-omega-hydroxy-,15,15'-diester met N-acetyl-L-isoleucyl-L-cysteinyl-L-valyl-1-methyl-L-tryptophyl-L-glutaminy-L-alpha-aspartyl-L-tryptophylglycyl-L-alanyl-L-histidyl-L-arginyl-L-cysteinyl-L-threonyl-2-[2-(2-aminoethoxy)ethoxy]acetyl-N6-carboxy-L-lysynamide cyclisch (2.fwdarw.12)-(disulfide); waarbij twee identieke synthetische peptide domeinen covalent zijn verbonden aan de uiteinden van de polyethyleenglycolketen	Behandeling van C3 glomerulopathie
Estonian	Polü(oksü-1,2-etanediüül), alfa-hüro-omega-hüdroksü-,15,15'-diester koos N-atsetüül-L-isoleutsüül-L-tsüsteinüül-L-valüül-1-metüül-L-trüptofüül-L-glutaminüül-L-alfa-aspartüül-L-trüptofüülglütsüül-L-alanüül-L-histidüül-L-arginüül-L-tsüsteinüül-L-treonüül-2-[2-(2-aminoetoksü)etoksü]atsetüül-N6-karboksü-L-lüsinamiid tsüklik (2.fwdarw.12)-(disulfiid); kus kaks identset sünteetilise peptiidi domeini on polüetüleenglükooli ahela otstes kovalentselt seotud	C3 glomerulopaatia ravi
Finnish	Poly(oksi-1,2-etanediyyli), alfa-hydro-omega-hydroksi-,15,15'-diesteri yhdessä N-asetyyli-L-isoleusyyli-L-kysteinyyli-L-valyyli-1-metyyli-L-tryptofyyli-L-glutaminyyli-L-alfa-aspartyyli-L-tryptofylglysyyli-L-alanyyli-L-histidyyli-L-arginyyli-L-kysteinyyli-L-treonyyli-2-[2-(2-aminoetoksi)etoksi]asetyyli-N6-karboksi-L-syklinen lysinamidi (2.fwdarw.12)-(disulfidi); jossa kaksi identtistä, synteettistä peptidi domeenia on kovalenttisesti yhdistettynä polyetyleeniglykoliketjun päihin	C3 glomerulopatian hoito

Language	Active ingredient	Indication
French	Poly (oxy-1,2-éthanediyl), alpha-hydro-oméga-hydroxy, 15,15'-diester avec N-acétyl-L-isoleucyl-L-cystéinyl-L-valyl-1-méthyl-L-tryptophyle -L-glutaminyL-L-alpha-aspartyl-L-tryptophylglycyl-L-alanyl-L-histidyl-L-arginyl-L-cystéinyl-L-thréonyl-2-[2-(2-aminoéthoxy)éthoxy]éthoxy] acétyl-N6 -carboxy-L-lysineamide cyclique (2.fwdarw.12) - (disulfure); où deux domaines peptidiques synthétiques identiques sont liés de manière covalente aux extrémités de la chaîne polyéthylène glycol	Traitement de la glomérulopathie à dépôts de C3
German	Poly(oxy-1,2-ethanediyl), alpha-hydro-omega-hydroxy-,15,15'-diester with N-acetyl-L-isoleucyl-L-cysteinyL-L-valyl-1-methyl-L-tryptophyl-L-glutaminyL-L-alpha-aspartyl-L-tryptophylglycyl-L-alanyl-L-histidyl-L-arginyl-L-cysteinyL-L-threonyl-2-[2-(2-aminoethoxy)ethoxy]acetyl-N6-carboxy-L-lysineamide cyclic (2.fwdarw.12)-(disulfide); wo zwei identische synthetische Peptid-Domänen kovalent verbunden sind am Ende einer Polyethylen-Glycol-Kette	Behandlung von C3 Glomerulopathie
Greek	Πολυ(οξυ-1,2-αιθανεδιυλ), α-υδρο-ω-υδροξυ-,15,15'-διεστέρας με Ν-ακετυλ-Λ-ισολευκυλ-Λ-κυστεϊνυλ-Λ-βαλυλ-1-μεθυλ-Λ-τρυπτοφυλ-Λ-γλυταμινυλ-Λ-α-ασπραρτυλ-Λ-τρυπτοφυλγλυκυλ-Λ-αλανυλ-Λ-ιστιδυλ-Λ-αργινυλ-Λ-κυστεϊνυλ-Λ-θρεονυλ-2-[2-(2-αμινοαιθοξυ)αιθοξυ]ακετυλ-Ν6-καρβοξυ-Λ-λυσιναμίδη κυκλική (2.fwdarw.12)-(δισουλφίδη) όπου δύο όμοιες περιοχές συνθετικού πεπτιδίου είναι οποιοπολικά συνδεόμενες στα άκρα της αλυσίδας πολυαιθυλενογλυκόλης	Θεραπεία της C3 σπειραματοπάθειας
Hungarian	Poli(oxi-1,2-etándiil), alfa-hidro-omega-hidroxi-, 15,15'-diészter; N-acetil-L-izoleucil-L-ciszteinil-L-valil-1-metil-L-triptofil-L-glutaminil-L-alfa-aszpartil-L-triptofilglicil-L-alanil-L-hisztidil-L-arginil-L-ciszteinil-L-treonil-2-[2-(2-aminoetoxi)etoxi]acetil-N6-karboxi-L-lizinamid ciklikus (2□12)-(diszulfid); amelyben két azonos szintetikus peptid domén kovalens kötéssel kapcsolódik a polietilén-glikol lánc végeihez	C3 glomerulopátia kezelése

Language	Active ingredient	Indication
Italian	Poli(ossi-1,2-etanedil), alfa-idro-omega-idrossi-,15,15'-diestere con N-acetil-L-isoleucil-L-cisteinil-L-valil-1-metil-L-triptofil-L-glutaminil-L-alfa-aspartil-L-triptofilglicil-L-alanil-L-istidil-L-arginil-L-cisteinil-L-treonil-2-[2-(2-aminoetossi)etossi]acetil-N6-carbossi-L-lisinamide ciclic (2.fwdarw.12)-(disulfide); in cui due domini peptidici sintetici identici sono legati covalentemente al terminale della catena polietilenglicolica.	Trattamento della glomerulopatia C3
Latvian	Poli(oksi-1,2-etāndiil), alfa-hidro-omega-hidroksi-,15,15'-diesters ar N-acetil-L-izoleicil-L-cisteīnil-L-valil-1-metil-L-triptofil-L-glutaminil-L-alfa-aspartil-L-triptofilglicil-L-alanil-L-histidil-L-arginil-L-cysteīnil-L-treonil-2-[2-(2-aminoetoksi)etoksi]acetil-N6-karboksi-L-lizīnamīda ciklisku (2.fwdarw.12)-(disulfīdu), kur divi identiski sintētiska peptīda domēni ir kovalenti saistīti polietilēna glikola ķēdes galos	C3 glomerulopātijas ārstēšana
Lithuanian	Poli(oksi-1,2-etanedil), alfa-hidro-omega-hidroksi-,15,15'-diesteris su N-acetil-L-isoleucil-L-cysteinil-L-valil-1-metil-L-triptofil-L-glutaminil-L-alfa-aspartil-L-triptofilglicil-L-alanil-L-histidil-L-arginil-L-cisteinil-L-treonil-2-[2-(2-aminoetoksi)etoksi]acetil-N6-karboksi-L-lizinamido ciklik (2.fwdarw.12)-(disulfidas); kur du identiškai sintetiniai peptidų domenai yra kovalentiškai sujungti galais politileno glikolio sekos	C3 glomerulopatijos gydymas
Maltese	Poli(ossi-1,2-etanedil), alfa-idro-omega-idrossi-,15,15'-diester bi N-aċetil-L-isolewċil-L-ċisteinil-L-valil-1-metil-L-triptofil-L-glutaminil-L-alfa-aspartil-L-triptofilglicil-L-alanil-L-istidil-L-arginil-L-cisteinil-L-treonil-2-[2-(2-aminoetossi)etossi]aċetil-N6-karbossi-L-lisinamur ċikliku (2.fwdarw.12)-(disulfur); fejn żewġ dominji ta' peptidi sintetici identici jkunu marbutin b'mod kovalenti fit-trufijiet tal-katina tal-polietilenglikol	Kura tal-glomerulopatija C3

Language	Active ingredient	Indication
Polish	Poli(oksy-1,2-etanodiyl), alfa-hydro-omega-hydroksy-,15,15'-diester z cyklicznym N-acetylo-L-izoleucylo-L-cysteinylo-L-walylo-1-metylo-L-tryptofylo-L-glutaminylo-L-alfa-aspartylo-L-tryptofylglycylo-L-alanylo-L-histidylo-L-arginylo-L-cysteinylo-L-treonylo-2-[2-(2-aminoethoksy)etoksy]acetylo-N6-carboksy-L-lizynamidem (2.strzałka w prawo. 12)-(dwusiarczanem); gdzie dwie identyczne syntetyczne domeny peptydowe są kowalentnie połączone na końcach łańcucha glikolu polientylenowego	Leczenie glomerulopatii C3
Portuguese	Poli (oxi-1,2-etanodiil), alfa-hidro-ômega-hidroxi, 15,15'-diéster com N-acetil-L-isoleucil-L-cisteinil-L-valil-1-metil-L-triptofil -L-glutaminil-L-alfa-aspartil-L-triptofilglicil-L-alanil-L- histidil-L-arginil-L-cisteinil-L-treonil-2- [2- (2- aminoetoxi) etoxi] acetil-N6 -carboxi-L-lisinamida cíclica (2.fwdarw.12) - (disulfureto); onde dois domínios peptídicos sintéticos idênticos estão covalentemente ligados nas extremidades da cadeia de polietilenoglicol	Tratamento da glomerulopatia por C3
Romanian	Poli (oxi-1,2-etanodiil), alfa-hidro-omega-hidroxi, 15,15'-diester cu N-acetil-L-isoleucil-L-cisteinil-L-valil-1-metil-L-triptofil -L-glutaminil-L-alfa-aspartil-L-triptofilglicil-L-alanil-L-histidil-L-arginil-L-cisteinil-L-treonil-2- [2- (2-aminoetoxi) etoxi] acetil-N6 -carboxi-L-lisinamidă ciclică (2.fwdarw.12) - (disulfid); unde două domenii peptidice sintetice identice sunt legate covalent de extremitățile lanțului de polietilenglicol	Tratamentul glomerulopatiei C3
Slovak	Poly(oxy-1,2-etánediyl), alfa-hydro-omega-hydroxy-,15,15'-diester s N-acetyl-L-izoleucyl-L-cysteinyl-L-valyl-1-metyl-L-tryptofyl-L-glutaminyl-L-alfa-aspartylo-L-tryptofylglycyl-L-alanyl-L-histidyl-L-arginyl-L-cysteinyl-L-threonyl-2-[2-(2-aminoetoxi)etoxi]acetyl-N6-karboxy-L-lyzínamid cyklický (2.fwdarw.12)-(disulfid); kde dve identické syntetické peptidové domény sú kovalentne viazané na koncoch polyetylénového reťazca	Liečba C3 glomerulopatie

Language	Active ingredient	Indication
Slovenian	Poli(oks-1,2-etandiil), alfa-hidro-omega-hidroksi-,15,15'-diester z N-acetil-L-izolevcil-L-cisteinil-L-valil-1-metil-L-triptofil-L-glutaminil-L-alfa-aspartil-L-triptofilglicinil-L-alanil-L-histidil-L-arginil-L-cisteinil-L-treonil-2-[2-(2-aminoetoksi)etoksi]acetil-N6-karboksi-L-lizinamid ciklični (2.fwdarw.12)-(disulfid); kjer sta dve identični sintetični peptidni domeni kovalentno vezani na koncih polietilenske glikolne verige	Zdravljenje C3 glomerulopatije
Spanish	Poli(oxi-1,2-ethanedil), alfa-hidro-omega-hidroxi-,15,15'-diester con N-acetil-L-isoileucil-L-cisteinil-L-valil-1-metil-L-triptofil-L-glutaminil-L-alfa-aspartil-L-triptofilglicil-L-alanil-L-histidil-L-arginil-L-cisteinil-L-treonil-2-[2-(2-aminoetoxi)etoxi]acetil-N6-carboxi-L-lisinamide ciclic (2.fwdarw.12)-(disulfide); donde dos peptidos dominios peptidos identicos estan vinculados covalentemente a los extremos por una cadena de polietilenglicol	Tratamiento de la glomerulopatía C3
Swedish	Poly(oxy-1,2-etanediyl), alfa-hydro-omega-hydroxy-,15,15'-diester med N-acetyl-L-isoileucyl-L-cysteinyl-L-valyl-1-metyl-L-tryptofyl-L-glutaminyll-alfa-aspartyl-L-tryptofylglycyl-L-alanyl-L-histidyl-L-arginyl-L-cysteinyl-L-treonyl-2-[2-(2-aminoethoxy)ethoxy]acetyl-N6-carboxy-L-lysinamid cyklisk (2.fwdarw.12)-(disulfid); dääärr två identiska syntetiska peptidomäner är kovalent länkade i slutet av polyetylenglycerolkedjorna	Behandling av C3-glomerulopati
Norwegian	Poly(oksý-1,2-etandiyl), alfa-hydro-omega-hydroksý-,15,15'-diester med N-acetyl-L-isoileucyl-L-cysteinyl-L-valyl-1-metyl-L-tryptofyl-L-glutaminyll-alfa-aspartyl-L-tryptofylglysyl-L-alanyl-L-histidyl-L-arginyl-L-cysteinyl-L-treonyl-2-[2-(2-aminoetoksy)etoksy]acetyl-N6-carboksy-L-lysinamid syklisk (2.-->.12)-(disulfid); der to identiske syntetiske peptid-domener er kovalent bundet ved endene av polyetylenglykolkjedenn	Behandling av C3-glomerulopati
Icelandic	Poly(oxy-1,2-ethanediyl), alpha-hydro-omega-hydroxy-,15,15'-diester with N-acetyl-L-isoileucyl-L-cysteinyl-L-valyl-1-methyl-L-tryptophyll-L-glutaminyll-L-alpha-aspartyl-L-tryptophylglycyl-L-alanyl-L-histidyl-L-arginyl-L-cysteinyl-L-threonyl-2-[2-(2-aminoethoxy)ethoxy]acetyl-N6-carboxy-L-lysinamide cyclic (2.fwdarw.12)-(disulfide); þar sem tvö eins samtengd peptíðhneppi eru samgildistengd við enda pólýetylenglýkól keðjunnar	Meðferð við C3 glomerulopathy

