



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Public summary of opinion on orphan designation

4-((E)-(5-(2-(2-((S)-2-((S)-1-(L-threonyl-L-lysyl)pyrrolidine-2-carboxamido)-5-guanidinopentanamido)acetamido)-2-carboxyethyl)-2-hydroxyphenyl)diazenyl)phenyl (2-(trimethylammonio)ethyl) phosphate for the treatment of non-infectious uveitis

On 13 November 2019, orphan designation EU/3/19/2219 was granted by the European Commission to Granzer Regulatory Consulting & Services, Germany, for 4-((E)-(5-(2-(2-((S)-2-((S)-1-(L-threonyl-L-lysyl)pyrrolidine-2-carboxamido)-5-guanidinopentanamido)acetamido)-2-carboxyethyl)-2-hydroxyphenyl)diazenyl)phenyl (2-(trimethylammonio)ethyl) phosphate (also known as TRS) for the treatment of non-infectious uveitis.

What is non-infectious uveitis?

Uveitis is inflammation of the uvea, the middle layer of the eye, just beneath the white part of the eye. The inflammation can affect one or both eyes, and may cause discomfort, pain, and blurring of vision. Non-infectious uveitis is usually caused by the body's immune system (the body's natural defences) attacking normal tissue; it is not due to infection.

Non-infectious uveitis is a long-term debilitating disease because it may lead to damage to the tissues of the eye including glaucoma (damage to the optic nerve) and partial or complete blindness.

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

At the time of designation, non-infectious uveitis affected approximately 3.8 in 10,000 people in the European Union (EU). This was equivalent to a total of around 197,000 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 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).



What treatments are available?

At the time of designation, several medicines were authorised in Member States of the EU for the treatment of non-infectious uveitis. The first treatment option was corticosteroids, which were used to reduce the inflammation by lowering the activity of the immune system. These included Ozurdex (dexamethasone) given by injection into the eye. Other immunosuppressant medicines such as ciclosporin and Idacio (adalimumab) were also authorised for use in non-infectious uveitis.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with non-infectious uveitis because laboratory data suggest that the medicine works in a different way to existing treatments and could be used in patients with advanced non-infectious uveitis who have developed glaucoma, for whom corticosteroid treatment is unsuitable.

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?

The medicine is made up from 2 components, phosphorylcholine and tuftsin, linked together into a single compound. Both phosphorylcholine and tuftsin act on the immune system and this combined action leads to the production of interleukin-10 which has a key role in reducing inflammation. By reducing inflammation in the eye, the medicine is expected to relieve the symptoms of the disease.

What is the stage of development of this medicine?

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

At the time of submission of the application for orphan designation, no clinical trials with the medicine in patients with non-infectious uveitis had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for the treatment of non-infectious uveitis 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 10 October 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.

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	4-((E)-(5-(2-(2-((S)-2-((S)-1-(L-threonyl-L-lysyl)pyrrolidine-2-carboxamido)-5-guanidinopentanamido)acetamido)-2-carboxyethyl)-2-hydroxyphenyl)diazenyl)phenyl (2-(trimethylammonio)ethyl) phosphate	Treatment of non-infectious uveitis
Bulgarian	4-((E)-(5-(2-(2-((S)-2-((S)-1-(L-треонил-L-лизил)пиролидин-2-карбоксамидо)-5-гуанидинопентанамидо)ацетамидо)-2-карбоксиетил)-2-хидроксифенил)дiazенил)фенил (2-(триметиламонио)етил) фосфат	Лечение на хроничен неинфекциозен увеит
Croatian	4-((E)-(5-(2-(2-((S)-2-((S)-1-(L-treonil-L-lizil)pirolidin-2-karboksamid)-5-gvanidino pentanamid)acetamid)-2-karboksietil)-2-hidroksifenil)diazenil) fenil(2-(trimetilamonij)etil)fosfat	Liječenje neinfektivnog uveitisa
Czech	4-((E)-(5-(2-(2-((S)-2-((S)-1-(L-threonyl-L-lysyl)pyrolidin-2-karboxamido)-5-guanidinopentanamido)acetamido)-2-karboxyethyl)-2-hydroxyfenyl)diazenyl)fenyl (2-(trimethylamonio)ethyl) fosfát	Léčba neinfekční uveitidy
Danish	4-((E)-(5-(2-(2-((S)-2-((S)-1-(L-threonyl-L-lysyl)pyrrolidin-2-carboxamido)-5-guanidinopentanamido)acetamido)-2-carboxyethyl)-2-hydroxyphenyl)diazenyl)phenyl (2-(trimethylammonio)ethyl) phosphat	Behandling af non-infektøs uveitis
Dutch	4-((E)-(5-(2-(2-((S)-2-((S)-1-(L-threonyl-L-lysyl)pyrrolidine-2-carboxamido)-5-guanidinopentanamido)acetamido)-2-carboxyethyl)-2-hydroxyphenyl)diazenyl)phenyl (2-(trimethylammonio)ethyl)-fosfaat	Behandeling van niet-infectieuze uveïtis
Estonian	4-((E)-(5-(2-(2-((S)-2-((S)-1-(L-treonüül-L-lüsüül)pürrolidiin-2-karboksamido)-5-guanidiinpentaanamiid)atseetamido)-2-karboksüetüül)-2-hüdroksüfenüül)diasenüül)fenüül(2-(trimetüülammoonium)etüül)fosfaat	Mitte-infektsioosse uveiidi ravi

¹ At the time of designation

Language	Active ingredient	Indication
Finnish	4-((E)-(5-(2-(2-((S)-2-((S)-1-(L-treonyyli-L-lysyli)pyrrolidiini-2-karboksamidi)-5-guanidiinipentanamidi)asetamidi)-2-karboksietyyli)-2-hydroksifenyyli)diatsenyyli)fenyyli (2-(trimetyyliammonium)etyyli)fosfaatti	Ei-infektioperäisen uveitin hoito
French	4-((E)-(5-(2-(2-((S)-2-((S)-1-(L-thréonyl-L-lysyl)pyrrolidine-2-carboxamido)-5-guanidinopentanamido)acétamido)-2-carboxyéthyl)-2-hydroxyphényl)diazényl)phényl (2-(triméthylammonio)éthyl) phosphate	Traitement de l'uvéite non infectieuse
German	4-((E)-(5-(2-(2-((S)-2-((S)-1-(L-Threonyl-L-lysyl)pyrrolidin-2-carboxamido)-5-guanidinopentanamido)acetamido)-2-carboxyethyl)-2-hydroxyphenyl)diazényl)phenyl (2-(trimethylammonio)ethyl)phosphat	Behandlung der nicht-infektiösen Uveitis
Greek	4-((E)-(5-(2-(2-((S)-2-((S)-1-(L-θρεονυλ-L-λυσυλ)πυρρολιδινο-2-καρβοξαμιδο)-5-γουανιδινοπενταναμιδο)ακεταμιδο)-2-καρβοξυαιθυλο)-2-υδροξυφαινυλο)διαζεφυλο)φαινυλο (2-(τριμεθυλαμμώνιο)αιθυλο) φωσφορικό	Θεραπεία της μη μολυσματικής ραγοειδίτιδας.
Hungarian	4-((E)-(5-(2-(2-((S)-2-((S)-1-(L-treonill-L-lizil)pirrolidin-2-karboxamid)-5-guanidino-pentánamid)acetamid)-2-karboxi-etil)-2-hidroxi-fenil) diazenil)fenil (2-(trimetil-ammónium)etil)-foszfát	Nem fertőzőes eredetű uveitis kezelése
Italian	4-((E)-(5-(2-(2-((S)-2-((S)-1-(L-treonil-L-lisil)pirrolidina-2-carbossammido)-5-guanidinopentanammido)acetammido)-2-carbossietil)-2-idrossifenil)diazénil)fenil (2-(trimetilammonio)etil) fosfato	Trattamento dell'uveite non infettiva
Latvian	4-((E)-(5-(2-(2-((S)-2-((S)-1-(L-treonil-L-lizil)pirolidīn-2-karboksam)-5-guanidīnpentanamīd)acetamīd)-2-karboksietil)-2-hidroksifenil)diazénil)fenil (2-(trimetilamonija)etil) fosfāts	Ne-infekciozā uveīta ārstēšana
Lithuanian	4-((E)-(5-(2-(2-((S)-2-((S)-1-(L-treonil-L-lizil)pirolidin-2-karboksamido)-5-guanidinopentanamido)acetamido)-2-karboksietil)-2-hidroksifenil)diazénil)fenil (2-(trimetilamonio)etil) fosfatas	Neinfekcinio uveito gydymas

Language	Active ingredient	Indication
Maltese	4-((E)-(5-(2-(2-((S)-2-((S)-1-(L-treonil-L-lisil)pirrolidina-2-karbossamidu)-5-gwanidinopentanamidu)acetamidu)-2-karbossietil)-2-idrossifenil)diazenil)fenil (2-(trimetilammonju)etil) fosfat	Kura ta' uveite mhux infettiva
Polish	Fosforan 4 - ((E) - (5- (2- (2- ((S) - 2 - ((S) - 1- (L-treonylo-L-lizylo) pirolidyno-2-karboksyamido) -5-guanidynopentanamido) acetamido) -2-karboksyetylo) -2-hydroksyfenylo) diazenylo) fenyl (2- (trimetyloamonio) etylu)	Leczenie nieinfekcyjnego zapalenia błony naczyniowej oka
Portuguese	Fosfato de 4-((E)-(5-(2-(2-((S)-2-((S)-1-(L-treonil-L-lisil)pirrolidina-2-carboxamido)-5-guanidinopentanamido)acetamido)-2-carboxietil)-2-hidroxifenil)diazenil)fenil (2-(trimetilamónio)etil)	Tratamento da uveíte não infecciosa
Romanian	4-((E)-(5-(2-(2-((S)-2-((S)-1-(L-treonil-L-lisil)pirolidin-2-carboxamido)-5-guanidinopentanamido)acetamido)-2-carboxiethyl)-2-hidroxifenil)diazenil)fenil (2-(trimetilamonio)etil) fosfat	Tratamentul uveitei non-infectioase
Slovak	4-((E)-(5-(2-(2-((S)-2-((S)-1-(L-treonyl-L-lyzyl)pyrolidín-2-karboxamido)-5-guanidínopentanamido)acetamido)-2-karboxyetyl)-2-hydroxyfenyl)diazenyl)fenyl (2-(trimetylamónio)etyl) fosfát	Liečba neinfekčnej uveitídy
Slovenian	4-((E)-(5-(2-(2-((S)-2-((S)-1-(L-treonil-L-lizil)pirolidin-2-karboksamido)-5-guanidinopentanamido)acetamido)-2-karboksietil)-2-hidroksifenil)diazenil)fenil (2-(trimetilamonio)etil) fosfat	Zdravljenje neinfekcijskega uveitis
Spanish	(2-(trimetilamonio)etil) fosfato de 4-((E)-(5-(2-(2-((S)-2-((S)-1-(L-treonil-L-lisil)pirrolidin-2-carboxamido)-5-guanidinopentanamido)acetamido)-2-carboxietil)-2-hidroxifenil)diazenil)fenilo	Tratamiento de la uveítis no infecciosa
Swedish	4-((E)-(5-(2-(2-((S)-2-((S)-1-(L-treonyl-L-lysyl)pyrrolidin-2-karboxamido)-5-guanidinopentanamido)acetamido)-2-karboxietyl)-2-hydroxifenyl)diazenyl)fenyl (2-(trimetylammonio)etyl)fosfat	Behandling av icke-infektiös uveit
Norwegian	4-((E)-(5-(2-(2-((S)-2-((S)-1-(L-treonyl-L-lysyl)pyrrolidin-2-karboksamido)-5-guanidinopentanamido)acetamido)-2-karboksyetyl)-2-hydroksyfenyl)diazenyl)fenyl (2-(trimetylammonio)etyl)fosfat	Behandling av ikke-infeksiøs uveitt

Language	Active ingredient	Indication
Icelandic	4-((E)-(5-(2-(2-((S)-2-((S)-1-(L- treónýl-L- lýsýl)pýrrólídín-2-karboxamíðó)-5-gúanidínpentanamíðó) asetamíðó)-2-karboxýetýl)-2-hýdroxýfenýl)díasenýl)fenýl (2-(trímetýlammóníó)etýl) fosfat	Meðferð á æðahjúpsbólgu án sýkingar