



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

14 October 2013
EMA/COMP/167445/2008 Rev.2
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Cyclo { {(E,Z)-(2S,3R,4R)-3-hydroxy-4-methyl-2-(methylamino)nona-6,8-dienoyl}-L-2-aminobutyryl-N-methyl-glycyl-N-methyl-L-leucyl-L-valyl-N-methyl-L-leucyl-L-alanyl-D-alanyl-N-methyl-L-leucyl-N-methyl-L-leucyl-N-methyl-L-valyl} for the treatment of chronic non-infectious uveitis

First publication	29 July 2008
Rev.1: withdrawal from the Community Register	4 December 2012
Rev.2: administrative update	14 October 2013
Disclaimer Please note that revisions to the Public Summary of Opinion are purely administrative updates. Therefore, the scientific content of the document reflects the outcome of the Committee for Orphan Medicinal Products (COMP) at the time of designation and is not updated after first publication.	

Please note that this product was withdrawn from the Community Register of designated orphan medicinal products in November 2012 on request of the sponsor

On 14 September 2007, orphan designation (EU/3/07/472) was granted by the European Commission to Lux Biosciences GmbH, Germany, for cyclo { {(E,Z)-(2S,3R,4R)-3-hydroxy-4-methyl-2-(methylamino)nona-6,8-dienoyl}-L-2-aminobutyryl-N-methyl-glycyl-N-methyl-L-leucyl-L-valyl-N-methyl-L-leucyl-L-alanyl-D-alanyl-N-methyl-L-leucyl-N-methyl-L-leucyl-N-methyl-L-valyl} for the treatment of chronic non-infectious uveitis.

What is chronic non-infectious uveitis?

Uveitis means inflammation of the uvea, the middle layer of the eye. This can be due to an infection by a foreign organism, such as bacteria, or caused by an autoimmune reaction (the body's own defence system attacking normal tissue). Most cases of uveitis are however idiopathic which means that the cause is unknown. Uveitis can affect one eye or both eyes and may cause varying degrees of discomfort or pain, with or without blurring of vision. Chronic non-infectious uveitis is chronically debilitating, in particular because it may increase the risk of visual impairment and subsequent blindness.



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

At the time of designation, chronic non-infectious uveitis affected approximately 4 in 10,000 people in the European Union (EU). This was equivalent to a total of around 200,000 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?

Several medicinal products were available for the treatment of chronic non-infectious uveitis and were authorised in some Member States in the Community at the time of submission of the application for orphan drug designation. Most treatments aim to suppress (weaken) the response of the immune system, the body's natural defence system, thus relieving the inflammation.

Satisfactory argumentation has been submitted by the sponsor to justify the assumption that cyclo { {(E,Z)-(2S,3R,4R)-3-hydroxy-4-methyl-2-(methylamino)nona-6,8-dienoyl}-L-2-aminobutyryl-N-methyl-glycyl-N-methyl-L-leucyl-L-valyl-N-methyl-L-leucyl-L-alanyl-D-alanyl-N-methyl-L-leucyl-N-methyl-L-leucyl-N-methyl-L-valyl} might be of potential significant benefit for the treatment of chronic non-infectious uveitis, mainly because it may provide a major contribution to patient care. This assumption 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?

The mechanism of action of cyclo { {(E,Z)-(2S,3R,4R)-3-hydroxy-4-methyl-2-(methylamino)nona-6,8-dienoyl}-L-2-aminobutyryl-N-methyl-glycyl-N-methyl-L-leucyl-L-valyl-N-methyl-L-leucyl-L-alanyl-D-alanyl-N-methyl-L-leucyl-N-methyl-L-leucyl-N-methyl-L-valyl} is to suppress (weaken) the immune system by targeting especially the so called T-lymphocytes, a type of white blood cells that are particularly active in inflammation. According to the sponsor this is thought to decrease the inflammation and thus the symptoms of chronic non-infectious uveitis.

What is the stage of development of this medicine?

The effects of cyclo { {(E,Z)-(2S,3R,4R)-3-hydroxy-4-methyl-2-(methylamino)nona-6,8-dienoyl}-L-2-aminobutyryl-N-methyl-glycyl-N-methyl-L-leucyl-L-valyl-N-methyl-L-leucyl-L-alanyl-D-alanyl-N-methyl-L-leucyl-N-methyl-L-leucyl-N-methyl-L-valyl} were evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials in patients with chronic non-infectious uveitis were ongoing.

Cyclo { {(E,Z)-(2S,3R,4R)-3-hydroxy-4-methyl-2-(methylamino)nona-6,8-dienoyl}-L-2-aminobutyryl-N-methyl-glycyl-N-methyl-L-leucyl-L-valyl-N-methyl-L-leucyl-L-alanyl-D-alanyl-N-methyl-L-leucyl-N-methyl-L-leucyl-N-methyl-L-valyl} was not authorised anywhere worldwide for the treatment of non-infectious uveitis nor 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 25 July 2007 recommending the granting of this designation.

*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 27), Norway, Iceland and Liechtenstein. At the time of designation, this represented a population of 500,300,000 (Eurostat 2007).

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

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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	Cyclo { { (E,Z)-(2s,3r,4r)-3-Hydroxy-4-Methyl-2-(Methylamino)Nona-6,8-Dienoyl } -L-2-Aminobutyryl-N-Methyl-Glycyl-N-Methyl-L-Leucyl-L-Valyl-N-Methyl-L-Leucyl-L-Alanyl-D-Alanyl-N-Methyl-L-Leucyl-N-Methyl-L-Leucyl-N-Methyl-L-Valyl }	Treatment of chronic non-infectious uveitis
Bulgarian	Цикло { { (E,Z)-(2s,3r,4r)-3-Хидроксн-4-Метил-2-(Метиламно)Нона-6,8-Днонол } -L-2-Амнобутнрнл-Н-Метнл-Глнцнл-Н-Метнл-L-Левцнл-L-Валнл-Н-Метнл-L-Левцнл-L-Аланнл-D-Аланнл-Н-Метнл-L-Левцнл-Н-Метнл-L-Левцнл-Н-Метнл-L-Валнл }	Леченне на хроннчен неннфекцнозен увеит
Czech	Cyklo { { (E,Z)-(2s,3r,4r)-3-Hydroxy-4-Methyl-2-(Methylamino)Nona-6,8-Dienoyl } -L-2-Aminobutyryl-N-Methyl-Glycyl-N-Methyl-L-Leucyl-L-Valyl-N-Methyl-L-Leucyl-L-Alanyl-D-Alanyl-N-Methyl-L-Leucyl-N-Methyl-L-Leucyl-N-Methyl-L-Valyl }	Léčba chronické neinfekční uveitidy
Danish	Cyclo { { (E,Z)-(2s,3r,4r)-3-Hydroxy-4-Methyl-2-(Methylamino)Nona-6,8-Dienoyl } -L-2-Aminobutyryl-N-Methyl-Glycyl-N-Methyl-L-Leucyl-L-Valyl-N-Methyl-L-Leucyl-L-Alanyl-D-Alanyl-N-Methyl-L-Leucyl-N-Methyl-L-Leucyl-N-Methyl-L-Valyl }	Behandling af kronisk ikke-infektiøs uveitis
Dutch	Cyclo { { (E,Z)-(2S,3R,4R)-3-hydroxy-4-methyl-2-(methylamino)nona-6,8-diēnoyl } -L-2-aminobutyryl-N-methyl-glycyl-N-methyl-L-leucyl-L-valyl-N-methyl-L-leucyl-L-alanyl-D-alanyl-N-methyl-L-leucyl-N-methyl-L-leucyl-N-methyl-L-valyl }	Behandeling van chronische niet-infectieuze uveitis
Estonian	Tsüklo { { (E,Z)-(2s,3r,4r)-3-hüdroksü-4-metüül-2-(metüülamino)nona-6,8-dienoüül } -L-2-aminobutürüül-N-metüül-glütsüül-N-metüül-L-leuküül-L-valüül-N-metüül-L-leuküül-L-alanüül-D-alanüül-N-metüül-L-leuküül-N-metüül-L-leuküül-N-metüül-L-valüül }	Kroonilise mitteinfektsioosse uveiidi ravi.
Finnish	Siklo { { (E,Z)-(2s,3r,4r)-3-hydroksi-4-metyyli-2-(metyyliamino)nona-6,8-dienoyyli } -L-2-aminobutyryyli-N-metyyli-glysyli-N-metyyli-L-leusyyli-L-valyyli-N-metyyli-L-leusyyli-L-alanyyli-D-alanyyli-N-metyyli-L-leusyyli-N-metyyli-L-leusyyli-N-metyyli-L-valyyli }	Kroonisen, ei-infektioperäisen uveitin hoito

¹ At the time of designation

Language	Active Ingredient	Indication
French	Cyclo { { (E,Z)-(2s,3r,4r)-3-Hydroxy-4-Méthyl-2-(Méthylamino)Nona-6,8-Diénoyl } -L-2-Aminobutyryl-N-Méthyl-Glycyl-N-Méthyl-L-Leucyl-L-Valyl-N-Méthyl-L-Leucyl-L-Alanyl-D-Alanyl-N-Méthyl-L-Leucyl-N-Méthyl-L-Leucyl-N-Méthyl-L-Valyl }	Traitement de l'uvéite chronique non infectieuse
German	Cyclo { { (E,Z)-(2s,3r,4r)-3-Hydroxy-4-Methyl-2-(Methylamino)Nona-6,8-Dienoyl } -L-2-Aminobutyryl-N-Methyl-Glycyl-N-Methyl-L-Leucyl-L-Valyl-N-Methyl-L-Leucyl-L-Alanyl-D-Alanyl-N-Methyl-L-Leucyl-N-Methyl-L-Leucyl-N-Methyl-L-Valyl }	Behandlung der chronischen nicht-infektiösen Uveitis
Greek	Κυκλο { { (E,Z)-(2s,3r,4r)-3-υδροξυ-4-μεθυλο-2-(μεθυλαμινο)εννεα-6,8-διενόλη } -L-2-αμινοβουτυρυλο-N-μεθυλο-γλυκυλο-N-μεθυλο-L-λευκυλο-L-βαλυλο-N-μεθυλο-L-λευκυλο-L-αλανυλ-D-αλανυλ-N-μεθυλο-L-λευκυλο-N-μεθυλο-L-λευκυλο-N-μεθυλο-L-βαλυλο }	Θεραπεία της χρόνιας μη μολυσματικής ραγοειδίτιδας.
Hungarian	Ciklo { { (E,Z)-(2s,3r,4r)-3-hidroxi-4-metil-2-(metilamino)-nona-6,8-dienoil } -L-2-aminobutiril-N-metil-glicil-N-metil-L-leucil-L-valil-N-metil-L-leucil-L-alanil-D-alanil-N-metil-L-leucil-N-metil-L-leucil-N-metil-L-valil }	Krónikus, nem fertőzőes eredetű uveitis kezelése
Italian	Ciclo { { (E,Z)-(2s,3r,4r)-3-idrossi-4-metil-2-(metilammino)nona-6,8-dienoil } -L-2-amminobutirril-N-metil-glicil-N-metil-L-leucil-L-valil-N-metil-L-leucil-L-alanil-D-alanil-N-metil-L-leucil-N-metil-L-leucil-N-metil-L-valil }	Trattamento dell'uveite cronica non infettiva
Latvian	Ciklo { { (E,Z)-(2s,3r,4r)-3-hidroksi-4-metil-2-(metilamino)nona-6,8-dienoil } -L-2-aminobutiril-N-methyl-glicil-N-metil-L-leicil-L-valil-N-metil-L-leicil-L-alanil-D-alanil-N-metil-L-leicil-N-metil-L-leicil-N-metil-L-valil }	Hroniskā neinfekciozā uveīta ārstēšana
Lithuanian	Ciklo { { (E,Z)-(2s,3r,4r)-3-hidroksi-4-metil-2-(metilamino)nona-6,8-dienoil } -L-2-aminobutiril-N-metil-glicil-N-metil-L-leucil-L-valil-N-metil-L-leucil-L-alanil-D-alanil-N-metil-L-leucil-N-metil-L-leucil-N-metil-L-valilas }	Lėtinės neinfekcinio uveito gydymas
Maltese	Cyclo { { (E,Z)-(2s,3r,4r)-3-Hydroxy-4-Methyl-2-(Methylamino)Nona-6,8-Dienoyl } -L-2-Aminobutyryl-N-Methyl-Glycyl-N-Methyl-L-Leucyl-L-Valyl-N-Methyl-L-Leucyl-L-Alanyl-D-Alanyl-N-Methyl-L-Leucyl-N-Methyl-L-Leucyl-N-Methyl-L-Valyl }	Kura ta' l-ujejite kronika u mhux infettiva

Language	Active Ingredient	Indication
Polish	Cyklo { { (E,Z)-(2s,3r,4r)-3-hydroksy-4-metylo-2-(metylamino)nona-6,8-dienoilo } -L-2-aminobutyrylo-N-metylo-glicylo-N-metylo-L-leucylo-L-walilo-N-metylo-L-leucylo-L-alanylo-D-alanylo-N-metylo-L-leucylo-N-metylo-L-leucylo-N-metylo-L-walil }	Leczenie przewlekłego niezakaźnego zapalenia błony naczyniowej oka.
Portuguese	Ciclo { { (E,Z)-(2s,3r,4r)-3-Hidroxi-4-Metil-2-(Metilamino)Nona-6,8-Dienoil } -L-2-Aminobutiril-N-Metil-Glicil-N-Metil-L-Leucil-L-Valil-N-Metil-L-Leucil-L-Alanil-D-Alanil-N-Metil-L-Leucil-N-Metil-L-Leucil-N-Metil-L-Valil }	Tratamento da uveíte crónica não infecciosa.
Romanian	Ciclo { { (E,Z)-(2s,3r,4r)-3-Hidroxi-4-Metil-2-(Metilamino)Nona-6,8-Dienoil } -L-2-Aminobutiril-N-Metil-Glicil-N-Metil-L-Leucil-L-Valil-N-Metil-L-Leucil-L-Alanil-D-Alanil-N-Metil-L-Leucil-N-Metil-L-Leucil-N-Metil-L-Valil }	Tratamentul uveitei non-infectioase cronice
Slovak	Cyklo- [[(E,Z)-(2S,3R,4)-3-hydroxy-4-metyl-2-(metylamino)nona-6,8-dienoyl]-L-2-aminobutyryl-N-metyl-glycyl-N-metyl-L-leucyl-L-valyl-N-metyl-L-leucyl-L-alanyl-D-alanyl-N-metyl-L-leucyl-N-metyl-L-leucyl-N-metyl-L-valyl]	Liečba chronickej neinfekčnej uveitídy
Slovenian	ciklo { { (E,Z)-(2s,3r,4r)-3-hidroksi-4-metil-2-(metilamino)nona-6,8-dienoil } -L-2-aminobutiril-N-metil-glicil-N-metil-L-leucil-L-valil-N-metil-L-leucil-L-alanil-D-alanil-N-metil-L-leucil-N-metil-L-leucil-N-metil-L-valil }	Zdravljenje kroničnega neinfekcijskega uveitisa
Spanish	Ciclo { { (E,Z)-(2s,3r,4r)-3-Hidroxi-4-Metil-2-(Metil-amino)Nona-6,8-Dienoil } -L-2-Aminobutiril-N-Metil-Glicil-N-Metil-L-Leucil-L-Valil-N-Metil-L-Leucil-L-Alanil-D-Alanil-N-Metil-L-Leucil-N-Metil-L-Leucil-N-Metil-L-Valil }	El tratamiento de la uveitis crónica no infecciosa
Swedish	Cyklo { { (E,Z)-(2S,3R,4R)-3-hydroxi-4-metyl-2-(metylamino)-nona-6,8-dienoyl } -L-2-aminobutyryl-N-metyl-glycyl-N-metyl-L-leucyl-L-valyl-N-metyl-L-leucyl-L-alanyl-D-alanyl-N-metyl-L-leucyl-N-metyl-L-leucyl-N-metyl-L-valyl }	Behandling av kronisk icke infektiös uveit
Norwegian	Syklo { { (E,Z)-(2s,3r,4r)-3-hydroksy-4-metyl-2-(metylamino)nona-6,8-dienoyl } -L-2-aminobutyryl-N-metyl-glysyl-N-metyl-L-leucyl-L-valyl-N-metyl-L-leucyl-L-alanyl-D-alanyl-N-metyl-L-leucyl-N-metyl-L-leucyl-N-metyl-L-valyl }	Behandling av kronisk ikke-infeksiøs uveitt,
Icelandic	Cýkló { { (E,Z)-(2s,3r,4r)-3-hýdroxý-4-metýl-2-(metýlamínó)nóna-6,8-díenóýl } -L-2-amínóbútýrýl-N-metýl-glýcýl-N-metýl-L-leucýl-L-valýl-N-metýl-L-leucýl-L-alanýl-D-alanýl-N-metýl-L-leucýl-N-metýl-L-leucýl-N-metýl-L-valýl }	Til meðferðar á augnæðahjúpsbólgu sem ekki stafar af sýkingu