



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

(1S,4R,5R,7S)-3,4-dibenzyl-2-oxo-6,8-dioxa-3-azabicyclo[3.2.1]octane-7-carboxylic acid-L-lysine for the treatment of neurotrophic keratitis

On 16 December 2014, orphan designation (EU/3/14/1400) was granted by the European Commission to MIMETECH S.r.l., Italy, for (1S,4R,5R,7S)-3,4-dibenzyl-2-oxo-6,8-dioxa-3-azabicyclo[3.2.1]octane-7-carboxylic acid-L-lysine for the treatment of neurotrophic keratitis.

What is neurotrophic keratitis?

Neurotrophic keratitis is a condition of the cornea (the clear layer at the front of the eye) caused by damage to the trigeminal nerve, the nerve that allows the surface of the eye to feel things and which supplies growth factors and other substances needed for normal growth and repair of the eye's surface. This results in a lack of sensitivity in the cornea, and to dryness, ulceration and scarring that interferes with vision.

Neurotrophic keratitis is a long-lasting and debilitating condition due to damage to the cornea and possible loss of sight.

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

At the time of designation, neurotrophic keratitis affected less than 5 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 255,000 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?

No satisfactory methods were authorised for the treatment of neurotrophic keratitis in the EU at the time of designation. Management depended on the stage of the disease and included supportive measures such as eye drops to moisten the eye and antibiotics to prevent infections, or the use of protective contact lenses, as well as surgery where appropriate.

^{*}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 511,100,000 (Eurostat 2014).



How is this medicine expected to work?

Patients with neurotrophic keratitis have lower than normal levels of growth factors that are normally supplied by the trigeminal nerve and which play an important role in the growth and survival of the cells of the cornea. The medicine is a compound that can mimic the action of a growth factor called nerve growth factor. When given as eye drops to patients with neurotrophic keratitis, the medicine is expected to help restore some of the normal growth processes in the eye and reduce the damage to the cornea associated with the condition.

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 neurotrophic keratitis had been started.

At the time of submission, this medicine was not authorised anywhere in the EU for neurotrophic keratitis 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 13 November 2014 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	(1S,4R,5R,7S)-3,4-dibenzyl-2-oxo-6,8-dioxa-3-azabicyclo[3.2.1]octane-7-carboxylic acid-L-lysine	Treatment of neurotrophic keratitis
Bulgarian	(1S,4R,5R,7S)-3,4-добензил-2-оксо-6,8-диокса-3-азабицикло[3.2.1]октан-7-карбоксилна киселина-L-лизин	Лечение на невротрофичен кератит
Croatian	(1S, 4R,5R,7S)-3,4-dibenzil-2-okso-6,8-dioksa-3-azabiklo[3.2.1]oktan-7-karboksilatna kiselina-L-lizin	Liječenje neurotrofnog keratitisa
Czech	Kyselina(1S,4R,5R,7S)-3,4-dibenzyl-2-oxo-6,8-dioxa-3-azabicyclo[3.2.1]oktan-7-karboxylová-L-lysin	Léčba neurotrofické keratitidy
Danish	(1S,4R,5R,7S)-3,4-dibenzyl-2-oxo-6,8-dioxa-3-azabicyclo[3.2.1]oktan-7-carboxylsyre-L-lysin	Behandling af neurotrofisk keratitis
Dutch	(1S,4R,5R,7S)-3,4-dibenzyl-2-oxo-6,8-dioxa-3-azabicyclo[3.2.1]octaan-7-carbonzuur-L-lysine	Behandeling van neurotrofische keratitis
Estonian	(1S,4R,5R,7S)-3,4-dibensüül-2-okso-6,8-dioksa-3-asabitsüklo[3.2.1]oktaan-7-karboksüülhape-L-lüsiin	Neurotroofilise keratiidi ravi
Finnish	(1S,4R,5R,7S)-3,4-dibentsyyli-2-okso-6,8-dioksa-3-atsabisyklo[3.2.1]oktaani-7-karboksylihappo-L-lysiini	Neurotrofisen keratiitin hoito
French	Acide (1S,4R,5R,7S)-3,4-dibenzyl-2-oxo-6,8-dioxa-3-azabicyclo[3.2.1]octane-7-carboxylique-L-lysine	Traitement de la kératite neurotrophique
German	(1S,4R,5R,7S)-3,4-Dibenzyl-2-oxo-6,8-dioxa-3-azabicyclo[3.2.1]octan-7-carbonsäure-L-lysin	Behandlung der Neurotrophen Keratitis
Greek	(1S,4R,5R,7S)-3,4-διβενζυλ-2-οξο-6,8-διοξα-3-αζαδικυκλο[3.2.1] οκτάνιο-7-καρβοξυλικό οξύ-L-λυσίνη	θεραπεία της νευροτροφικής κερατίτιδας
Hungarian	(1S,4R,5R,7S)-3,4-dibenzil-2-oxo-6,8-dioxa-3-azabiklo[3.2.1]oktán-7-karbonsav-L-lizin	Neurotrofiás keratitis kezelése
Italian	Acido(1S, 4R, 5R, 7S)-3.4-dibenzil-2-oxo-6,8-diosso-3-azabiklo [3.2.1] ottano-7-carbossilico-L-lisina	Tattamento della cheratite neurotrofica
Latvian	(1S,4R,5R,7S)-3,4-dibenzil-2-okso-6,8-dioksa-3-azabiklo[3.2.1]oktān-7-karboksilskābes-L-lizīns	Neirotropā keratīta ārstēšana
Lithuanian	(1S,4R,5R,7S)-3,4-dibenzil-2-okso-6,8-dioksa-3-azabiklo[3.2.1]oktan-7-karboksirūgšties-L-lizinas	Neurotrofinio keratito gydymas

¹ At the time of designation

Language	Active ingredient	Indication
Maltese	(1S,4R,5R,7S)-3,4-dibenzyl-2-oxo-6,8-dioxa-3-azabicyclo[3.2.1]octane-7-carboxylic acid-L-lysine	Kura tal-keratite newrotrofika
Polish	(1S,4R,5R,7S)-3,4-dwubenzyl-2-okso-6,8-dioksa-3-azabicyklo[3,2,1]-oktan-7-kwas karboksylowy-L-lizyna	Leczenie neurotroficznego zapalenia rogówki
Portuguese	(1S,4R,5R,7S)-3,4-dibenzil-2-oxo-6,8-dioxa-3-azabicyclo[3.2.1]octano-7-ácido carboxílico-L-lisina	Tratamento da queratite neurotrófica
Romanian	Acid (1S,4R,5R,7S)-3,4-dibenzil-2-oxo-6,8-dioxa-3-azabicyclo[3.2.1]octan-7- carboxilic-L-lizină	Tratamentul keratitei neurotrofice
Slovak	(1S,4R,5R,7S)-3,4-dibenzyl-2-oxo-6,8-dioxa-3-azabicyklo[3.2.1]oktán-7-karboxylovej kyseliny L-lyzín	Liečba neurotrofickej keratitídy
Slovenian	(1S,4R,5R,7S)-3,4-dibenzil-2-okso-6,8-dioksa-3-azabicyklo[3.2.1]oktan-7-karboksilna kislina-L-lizin	Zdravljenje nevrotrofičnega keratitisa
Spanish	3,4-dibencil-2-oxo-(1S,4R,5R,7S)-6,8-dioxa-3-azabicyclo[3.2.1]octano-7-ácido-carboxílico-L-lisina	Tratamiento de la queratopatía neurotrófica
Swedish	(1S,4R,5R,7S)-3,4-dibenzyl-2-oxo-6,8-dioxa-3-azabicyklo[3.2.1]oktan-7-karboxylsyra-L-lysin	Behandling vid neurotrofisk keratit
Norwegian	(1S,4R,5R,7S)-3,4-dibenzyl-2-oxo-6,8-dioxa-3-azabicyclo[3.2.1]oktan-7-karboxylsyre-L-lysin	Behandling av nevrotrofisk keratitt
Icelandic	(1S,4R,5R,7S)-3,4-dibensýl-2-oxó-6,8-díoxa-3-azabýcicló[3.2.1]octan-7-karboxýlsýru-L-lýsín	Meðferð við taugarýrnunar glærubólga