



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Doxycycline hyclate for the treatment of familial amyloid polyneuropathy

On 2 April 2012, orphan designation (EU/3/12/955) was granted by the European Commission to Giampaolo Merlini, Italy, for doxycycline hyclate for the treatment of familial amyloid polyneuropathy.

What is familial amyloid polyneuropathy?

Familial amyloid polyneuropathy (FAP) is a hereditary ('familial') disease caused by a defective gene for transthyretin, a protein that transports various substances in the blood. Transthyretin is primarily produced in the liver.

Patients with FAP have an abnormal transthyretin protein that breaks up easily and accumulates in various tissues in the body, especially tissues of the nervous system, in the form of insoluble, waxy 'amyloid' deposits. The condition mainly affects the heart and the nervous system causing symptoms such as muscle weakness in the limbs and, at later stages, inability to walk, problems affecting the stomach and the gut (leading to malnutrition), and bladder dysfunction.

FAP is a long-term debilitating disease due to the progressive worsening of nervous system symptoms. It is also life threatening because the amyloid deposits may accumulate in the heart and cause fatal heart conditions.

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

At the time of designation, FAP affected approximately 1.4 in 10,000 people in the European Union (EU)*. This is equivalent to a total of around 71,000 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 designation, the only medicine authorised in the EU to treat FAP was Vyndaqel (tafamidis). The only other treatment option was liver transplantation.

*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. This represents a population of 506,300,000 (Eurostat 2011).



The sponsor has provided sufficient information to show that doxycycline hyclate might be of significant benefit for patients with FAP because early studies show that it works in a different way to the existing medicine and might improve the treatment of patients with this condition. 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?

Doxycycline is a widely used antibiotic that belongs to the class 'tetracyclines'. In FAP, doxycycline is expected to work by disrupting the aggregation (sticking together) of abnormal transthyretin protein, which in turn is expected to make the 'amyloid' deposits dissolve. This is expected to reduce the symptoms of FAP.

What is the stage of development of this medicine?

The effects of doxycycline hyclate have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with doxycycline hyclate in patients with FAP were ongoing.

At the time of submission, doxycycline was authorised for other indications throughout Europe.

At the time of submission, doxycycline hyclate was not authorised anywhere in the EU for FAP 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 7 December 2011 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	Doxycycline hyclate	Treatment of familial amyloid polyneuropathy
Bulgarian	Доксициклин хиклат	Лечение на фамилна амилоидна полиневропатия
Czech	Doxycyklin hyklát	Léčba familiární amyloidové polyneuropatie
Danish	Doxycyclinhyclat	Behandling af familiær transthyretin amyloidose
Dutch	Doxycyclinehyclaat	Behandeling van familiale amyloid polyneuropathie
Estonian	Doksütsükliinhüklaat	Perekondliku amüloidse polüneuropaatia ravi.
Finnish	Doksisykliinihyklaatti	Familiaalisen amyloidipolyneuropatian hoito
French	Hyclate de doxycycline	Traitement de la amyloïde familiale liée à la transthyrétine
German	Doxycyclin-hyclat	Die Behandlung der Familiären Amyloid Polyneuropathie
Greek	Δοξυκυκλίνη (Doxycycline hyclate)	Θεραπεία της οικογενούς αμυλοειδικής πολυνευροπάθειας
Hungarian	Doxiciklin-hiklát	Familiáris amyloid polyneuropathia kezelése
Italian	Doxiciclina iclato	Trattamento della amiloidosi familiare da transtiretina
Latvian	Doksiciklīna hiklāts	Ģimenes amiloidās polineiropātijas ārstēšana
Lithuanian	Doksiciklino hiklatas	Šeiminės amiloidinės polineuropatijos gydymas
Maltese	Doxycycline hyclate	Trattament ta 'amyloidosis transthyretin familjali
Polish	Hyklan doksyliny	Leczenie rodzinnej amyloidozy transtyretynowej
Portuguese	Hiclato de doxiciclina	Tratamento da polineuropatia amiloidótica familiar..
Romanian	Doxiciclină hyclat	Tratamentul polineuropatiei amiloide familiale
Slovak	Doxycyklín hyklát	Liečba familiárnej amyloidovej polyneuropatie
Slovenian	Doksiciklinijev hiklat	Zdravljenje družinske amiloidoza transthyretin
Spanish	Hiclato de doxiciclina	Tratamiento de la polineuropatía amiloide familiar
Swedish	Doxycyclinhyklát	Behandling av familjär amyloidos med polyneuropati
Norwegian	Doksisyklinhyklát	Behandling av familiær amyloid polyneuropati
Icelandic	Doxýcyklín hýclat	Meðferð við ættgengum mýlildis fjöldaugakvilla

¹ At the time of designation