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EMA/COMP/50020/2015
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Nitroglycerin for the treatment of systemic sclerosis

On 12 February 2015, orphan designation (EU/3/15/1435) was granted by the European Commission to Covis Pharma S.à.r.l., Luxemburg, for nitroglycerin for the treatment of systemic sclerosis.

What is systemic sclerosis?

Systemic sclerosis is a complex disease in which the immune system (the body's natural defences) is overactive, causing inflammation and excess production of various proteins, particularly collagen. The reason why the immune system is overactive is not known. Collagen is an important component of connective tissue (the tissue that supports the skin and internal organs).

The overproduction of collagen leads to the abnormal growth of connective tissue, causing the skin to become thick and hard (fibrosis). It can also damage the blood vessel walls of the internal organs, such as the heart, lungs and kidneys. This makes it more difficult for the blood to flow through the vessels, causing tissue damage, circulation problems and high blood pressure.

Systemic sclerosis is a long-lasting, debilitating disease and may be life-threatening because of its possible effects on the gut, heart, lungs and kidneys.

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

At the time of designation, systemic sclerosis affected less than 3.5 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 180,000 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, there were no treatments for systemic sclerosis that could stop the build-up of collagen. Treatments authorised in the EU were aimed at relieving the symptoms of the disease and limiting the damage it causes. Several medicines were used to reduce inflammation and circulation

*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 512,900,000 (Eurostat 2015).

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problems. Bosentan was authorised in the EU specifically to treat patients with systemic sclerosis in whom poor blood circulation caused by the disease has led to the development of 'digital ulcers' (sores on the fingers and toes) and pulmonary hypertension (high blood pressure in the arteries of the lungs).

The sponsor has provided sufficient information to show that nitroglycerin might be of significant benefit for patients with systemic sclerosis because data from the scientific literature indicate that it might improve the outcome of patients with the condition, when compared with bosentan. 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?

Nitroglycerin is a well-known medicine that works as a 'vasodilator', by widening blood vessels. It has been used for many years for the treatment of angina pectoris (pains to the chest, jaw and back, brought on by physical effort and due to problems with the blood flow to the heart).

Patients with systemic sclerosis often suffer from Raynaud's phenomenon, a common condition where the blood vessels in the fingers and toes go into a temporary spasm which blocks the flow of blood, causing the affected area to change colour to white, then blue and then red as the blood flow returns. Nitroglycerin, applied as a gel in the affected area, is expected to cause the blood vessels to relax thereby relieving the symptoms of Raynaud's phenomenon including pain and numbness in the affected body parts, as well as its complications such as ulcers and tissue death.

What is the stage of development of this medicine?

The effects of nitroglycerin have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with nitroglycerin in patients with Raynaud's phenomenon had finished.

At the time of submission, nitroglycerin was not authorised anywhere in the EU for systemic sclerosis 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 9 January 2015 recommending the granting of this designation.

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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 languages[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	Nitroglycerin	Treatment of systemic sclerosis
Bulgarian	Нитроглицерин	Лечение на системна склероза
Croatian	Nitroglicerin	Liječenje sistemske skleroze
Czech	Nitroglycerin	Léčba systémové sklerodermie
Danish	Nitroglycerin	Behandling af systemisk sklerose
Dutch	Nitroglycerine	Behandeling van systeem sclerose
Estonian	Nitroglütseriin	Süsteemse sklerodermia ravi
Finnish	Nitroglyseriini	Systeemisen skleroosin hoito
French	Nitroglycérine	Traitement de la sclérose systémique
German	Nitroglycerin	Behandlung der systemischen Sklerose
Greek	Νιτρογλυκερίνη	Θεραπεία της συστηματικής σκλήρυνσης
Hungarian	Nitroglicerin	Szisztémás scleroderma kezelése
Italian	Nitroglicerina	Trattamento della sclerosi sistemica
Latvian	Nitroglicerīns	Sistēmiskas sklerozes ārstēšana
Lithuanian	Nitroglicerinas	Sisteminės sklerozės gydymas
Maltese	Nitroglicerina	Kura tas-sklerosi sistemika
Polish	Nitrogliceryna	Leczenie twardziny narządowej
Portuguese	Nitroglicerina	Tratamento da esclerose sistémica
Romanian	Nitroglicerină	Tratamentul sclerozei sistemice
Slovak	Nitroglycerín	Liečba systémovej sklerózy
Slovenian	Nitroglicerin	Zdravljenje sistemske skleroze
Spanish	Nitroglicerina	Tratamiento de la esclerosis sistémica
Swedish	Nitroglycerin	Behandling av systemisk skleros
Norwegian	Nitroglyserin	Behandling av systemisk sklerose
Icelandic	Nítróglýserín	Meðferð við dreifðum herslismeinum

[1] At the time of designation