European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

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Committee for Orphan Medicinal Products

Public summary of positive opinion for orphan designation of treprostinil diethanolamine for the treatment of systemic sclerosis

On 15 May 2009, orphan designation (EU/3/09/635) was granted by the European Commission to United Therapeutics Europe Ltd, United Kingdom, for treprostinil diethanolamine 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 overactivated, causing inflammation and overproduction of various proteins, particularly collagen. The reason why the immune system is activated 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 abnormal growth of connective tissue, causing the skin to become thick and hard. It also damages the tissues around the blood vessels of the internal organs, such as the heart, lungs and kidneys. This makes it more difficult for the blood to move through the vessels, causing tissue damage, circulation problems and high blood pressure. The high collagen levels can also stimulate the body's immune system to attack the collagen, increasing the inflammation in the body.
Systemic sclerosis is a debilitating disease that is long lasting and may be life threatening because of its effects on the heart, lungs and kidneys.

What is the estimated number of patients affected by the condition?
At the time of designation, systemic sclerosis affected between 1 and 3.5 in 10,000 people in the European Union (EU)[*]. This is equivalent to a total of between 50,000 and 180,000 people, and is below the threshold for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and 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 problems.
The sponsor has provided sufficient information to show that treprostinil diethanolamine might be of significant benefit for patients with systemic sclerosis mainly because the medicine is expected to be given to patients as tablets. This may contribute to the care of patients because it may allow the medicine to be given less often and may result in the levels of the medicine in the body being more

[*]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 504,800,000 (Eurostat 2009).

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stable over time. This medicine might also have improved safety and effectiveness compared with other treatments. These assumptions 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?
Treprostinil is already available as a solution for continuous infusion under the skin in some countries in the EU. Treprostinil is a substance that it is very similar to prostacyclin, a naturally occurring substance that causes blood vessels to dilate (widen). In systemic sclerosis, treprostinil is expected to act in the same way as prostacyclin to lower the blood pressure in the internal organs and improve the circulation problems.
Treprostinil diethanolamine is a new salt of treprostinil that is expected to be given to patients as sustained-release tablets (tablets that release treprostinil continuously over a few hours).

What is the stage of development of this medicine?
The effects of treprostinil diethanolamine have been evaluated in experimental models.
At the time of submission of the application for orphan designation, no clinical trials in patients with systemic sclerosis had been started.
At the time of submission, treprostinil diethanolamine was not authorised anywhere in the EU for systemic sclerosis or designated as 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 2 April 2009 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 Community) 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.

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Translations of the active ingredient and indication in all official EU languages, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Treprostinil diethanolamine	Treatment of systemic sclerosis
Bulgarian	Трепростинил диетаноламин	Лечение на системна склероза
Czech	Treprostinil diethanolamin	Léčba systémové sklerodermie
Danish	Treprostinil diethanolamin	Behandling af systemisk sklerose
Dutch	Treprostinil diethanolamin	Behandeling van Systeem Sclerose
Estonian	Treprostiniil dietanoolamiin	Süsteemse sklerodermia ravi
Finnish	Treprostiniili dietanoliamiini	Systeemisen skleroosin hoito
French	Tréprostinil diéthanolamine	Traitement de la sclérose systémique
German	Treprostinil Diethanolamin	Behandlung der systemischen Sklerose
Greek	Τρεπροστινίλ-διαιθαανολαμίνη	Θεραπεία της συστηματικής σκλήρυνσης
Hungarian	Treprostinil dietanolamin	Szisztémás scleroderma kezelése
Italian	Treprostinil dietanolammina	Trattamento della sclerosi sistemica
Latvian	Treprostinildietanolamīns	Sistēmiskas sklerozes ārstēšana
Lithuanian	Treprostinilo dietanolaminas	Sisteminės odos sklerozės gydymas
Maltese	Treprostinil diethanolamine	Kura tas-sklerosi sistemika
Polish	Treprostynylu dietanoloamina	Leczenie twardziny narządowej
Portuguese	Dietanolamina de treprostinil	Tratamento da esclerose sistémica
Romanian	Treprostinil dietanolamină	Tratamentul sclerozei sistemice
Slovak	Treptostinil dietanolamín	Liečba systémovej sklerózy
Slovenian	Treprostinil dietanolamin	Zdravljenje sistemske skleroze
Spanish	Treprostinil dietanolamina	Tratamiento de la esclerosis sistémica
Swedish	Treprostinildietanolamin	Behandling av systemisk skleros
Norwegian	Treprostinil-dietanolamin	Behandling av systemisk sklerose
Icelandic	Treprostiníl tvietanólamín	Meðferð við dreifðum herslismeinum