13 November 2015
EMA/COMP/609748/2015
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

2-(2-chlorophenyl)-4-[3-(dimethylamino)phenyl]-5-methyl-1H-pyrazolo[4,3-C]pyridine-3,6(2H,5H)-dione for the treatment of systemic sclerosis

On 9 October 2015, orphan designation (EU/3/15/1559) was granted by the European Commission to GenKyoTex Innovation S.A.S., France, for 2-(2-chlorophenyl)-4-[3-(dimethylamino)phenyl]-5-methyl-1H-pyrazolo[4,3-C]pyridine-3,6(2H,5H)-dione for the treatment of systemic sclerosis.

What is systemic sclerosis?

Systemic sclerosis, also known as scleroderma, 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. Initial symptoms include swollen fingers and hands, followed by thickened skin over the arms, legs, face and trunk. The disease can also damage the walls of the blood vessel of the internal organs, such as the heart, lungs and kidneys. This makes it more difficult for the blood to flow, causing tissue damage and circulation problems.

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).

[*]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).

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

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. Bosentan has been 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).

The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with systemic sclerosis because studies in experimental models show that the medicine may reduce the abnormal growth of connective tissue (fibrosis) and improve survival. 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?

The medicine is expected to work by blocking the action of some enzymes called 'NADPH oxidases'. These enzymes are thought to be responsible for the production of toxic molecules containing oxygen, which are involved in causing fibrosis. By blocking the actions of NADPH oxidases, the medicine is expected to reduce the fibrosis in systemic sclerosis patients, thereby improving the symptoms of the disease.

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 systemic sclerosis had been started.

At the time of submission, the medicine 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 3 September 2015 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

For details of the current sponsor of the orphan designation please refer to the information on the main web page of this Public Summary of Opinion.

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	2-(2-chlorophenyl)-4-[3-(dimethylamino)phenyl]-5-methyl-1H-pyrazolo[4,3-C]pyridine-3,6(2H,5H)-dione	Treatment of systemic sclerosis
Bulgarian	2-(2-хлорфенил)-4-[3-(диметиламино)фенил]-5-метил-1H-пиразоло[4,3-c]пиридин-3,6(2H, 5H)-дион	Лечение на системна склероза
Croatian	2-(2-klorofenil)-4-[3-(dimetilamino)fenil]-5-metil-1H-pirazolo[4,3-C]piridín-3,6(2H,5H)-dion	Liječenje sistemske skleroze
Czech	2-(2-chlorfenyl)-4-[3-(dimetylamino)fenyl]-5-methyl-1H-pyrazolo[4,3-c]pyridin-3,6(2H, 5H)-dion	Léčba systémové sklerodermie
Danish	2-(2-klorofenyl)-4-[3-(dimetylamino)fenyl]-5-methyl-1H-pyrazolo[4,3-c]pyridin-3,6(2H, 5H)-dion	Behandling af systemisk sklerose
Dutch	2-(2-chloorfenyl)-4-[3-(dimethylamino)fenyl]-5-methyl-1H-pyrazolo[4,3-c]pyridine-3,6(2H, 5H)-dion	Behandeling van systeem sclerose
Estonian	2-(2-klorofenüül)-4-[3-(dimetüülamino)fenüül]-5-metüül-1H-pürasolo[4,3-c]püridiin-3,6(2H, 5H)-dioon	Süsteemse sklerodermia ravi
Finnish	2-(2-kloorifenyyli)-4-[3-(dimetyyliamino)fenyyli]-5-metyyli-1H-pyratsolo[4,3-c]pyridiini-3,6(2H, 5H)-dioni	Systeemisen skleroosin hoito
French	2-(2-chlorophényl)-4-[3-(diméthylamino)phényl]-5-méthyl-1H-pyrazolo[4,3-c]pyridine-3,6(2H, 5H)-dione	Traitement de la sclérose systémique
German	2-(2-chlorphenyl)-4-[3-(dimethylamino)phenyl]-5-methyl-1H-pyrazolo[4,3-c]pyridin-3,6(2H, 5H)-dion	Behandlung der systemischen Sklerose
Greek	2-(2-χλωροφαινυλο)-4-[3-(διμεθυλάμινο)φαινύλ]-5-μεθυλο-1H-πυραζολο[4,3-c]πυριδινό-3,6(2H, 5H)-διόνη	Θεραπεία της συστηματικής σκλήρυνσης
Hungarian	2-(2-klorofenil)-4-[3-(dimetilamino)fenil]-5-metil-1H-pirazolo[4,3-c]piridin-3,6(2H, 5H)-dion	Szisztémás scleroderma kezelése
Italian	2-(2-clorofenil)-4-[3-(dimetilamino)fenil]-5-metil-1H-pirazolo[4,3-c]piridin-3,6(2H, 5H)- dione	Trattamento della sclerosi sistemica
Latvian	2-(2-hlorofenil)-4-[3-(dimetilamīn)fenil]-5-metil-1H-pirazolo[4,3-c]piridīn-3,6(2H, 5H)-dions	Sistēmiskas sklerozes ārstēšana
Lithuanian	2-(2-chlorofenil)-4-[3-(dimetilamino)fenil]-5-metil-1H-pirazolo[4,3-c]piridino-3,6(2H, 5H)-dionas	Sisteminės sklerozės gydymas
Maltese	2-(2-chlorophenyl)-4-[3-(dimethylamino)phenyl]-5-methyl-1H-pyrazolo[4,3-c]pyridine-3,6(2H, 5H)-dione	Kura tas-sklerosi sistemika
Polish	2-(2-chlorofenylo)-4-[3-(dimetyloamino)fenylo]-5-metylo-1H-pirazolo[4,3-c]pirydyno-3,6(2H,5H)-dion	Leczenie twardziny narządowej

[1] At the time of designation

Language	Active ingredient	Indication
Portuguese	2-(2-clorofenil)-4-[3-(dimetilamino)fenil]-5-metil-1H-pirazol[4,3-c]piridina-3,6(2H, 5H)-diona	Tratamento da esclerose sistémica
Romanian	2-(2-clorofenil)-4-[3-(dimetilamino)fenil]-5-metil-1H-pirazolo[4,3-c]piridin-3,6(2H, 5H)-dionă	Tratamentul sclerozei sistemice
Slovak	2-(2-chlórfenyl)-4-[3-(dimetylamino)fenyl]-5-metyl-1H-pyrazolo[4,3-c]pyridín-3,6(2H, 5H)-dión	Liečba systémovej sklerózy
Slovenian	2-(2-klorofenil)-4-[3-(dimetilamino)fenil]-5-metil-1H-pyrazolo[4,3-c]piridin-3,6(2H, 5H)-dion	Zdravljenje sistemske skleroze
Spanish	2-(2-clorofenil)-4-[3-(dimetilamino)fenil]-5-metil-1H-pirazol [4,3-c]piridina-3,6(2H, 5H)-diona	Tratamiento de la esclerosis sistémica
Swedish	2-(2-klorfenyl)-4-[3-(dimetylamino)fenyl]-5-metyl-1H-pyrazolo[4,3-c]pyridin-3,6(2H, 5H)-dion	Behandling av systemisk skleros
Norwegian	2-(2-klorfenyl)-4-[3-(dimetylamino)fenyl]-5-metyl-1H-pyrazolo[4,3-c]pyridin-3,6(2H, 5H)-dion	Behandling av systemisk sklerose
Icelandic	2-(2-klórófenýl)-4-[3-(tvímetýlamínó)fenýl]-5-metýl-1H-pýrazóló[4,3-c]pýridín-3,6(2H, 5H)-díón	Meðferð við dreifðum herslismeinum