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EMA/COMP/646194/2014
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

1-(6-Benzothiazolylsulfonyl)-5-chloro-1H-indole-2-butanoic acid for the treatment of systemic sclerosis

On 19 November 2014, orphan designation (EU/3/14/1361) was granted by the European Commission to Inventiva, France, for 1-(6-benzothiazolylsulfonyl)-5-chloro-1H-indole-2-butanoic acid 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. 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 move 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 approximately 3.5 in 10,000 people in the European Union (EU). This was equivalent to a total of around 179,000 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 511,100,000 (Eurostat 2014).

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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 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).

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

This medicine is a chemical substance that is expected to work by activating some cell receptors called peroxisome proliferator-activated receptors (PPARs). PPARs are thought to regulate fibrosis. By activating PPARs, this medicine is expected to reduce the fibrosis seen in systemic sclerosis, thereby relieving the symptoms of this condition.

What is the stage of development of this medicine?

The effects of 1-(6-benzothiazolylsulfonyl)-5-chloro-1H-indole-2-butanoic acid 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 9 October 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 languages[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	1-(6-benzothiazolylsulfonyl)-5-chloro-1H-indole-2-butanoic acid	Treatment of systemic sclerosis
Bulgarian	1-(6-бензотиазолилсулфонил)-5-хлоро-1H-индол-2-бутанова киселина	Лечение на системна склероза
Croatian	1-(6-benzotiazolilsulfonil)-5-kloro-1H-indol-2-butanoatna kiselina	Liječenje sistemske skleroze
Czech	1-(6-benzothiazolylsulfonyl)-5-chloro-1H-indol-2-kyselina máselná	Léčba systémové sklerodermie
Danish	1-(6-benzothiazolylsulfonyl)-5-chloro-1H-indol-2-butansyre	Behandling af systemisk sklerose
Dutch	1-(6-benzothiazolylsulfonyl)-5-chloor-1H-indool-2-butaanzuur	Behandeling van systeem sclerose
Estonian	1-(6-bensotiasoolüülsulfonüül)-5-kloro-1H-indool-2-butanoonhape	Süsteemse sklerodermia ravi
Finnish	1-(6-bentsotiatsolyylisulfonyyli)-5-kloori-1H-indoli-2-butaanihappo	Systeemisen skleroosin hoito
French	1-(6-benzothiazolylsulfonyl)-5-chloro-1H-indole-2-acide butanoïque	Traitement de la sclérose systémique
German	1-(6-Benzothiazolylsulfonyl)-5-chlor-1H-indol-2-butansäure	Behandlung der systemischen Sklerose
Greek	1-(6-βενζοθειαζολυλσουλφονυλ)-5-χλωρο-1H-*ινδολο*-2-βουτανοϊκό οξύ	Θεραπεία της συστηματικής σκλήρυνσης
Hungarian	1-(6-benzo-tiazolil-szulfonil)-5-klóro-1H-indol-2-vajsav	Szisztémás scleroderma kezelése
Italian	Acido 1-(6-benzotiazolilsulfonil)-5-cloro-1H-indolo-2-butanoico	Trattamento della sclerosi sistemica
Latvian	1-(6-benzotiazolilsulfonil)-5-hloro-1H-indola-2-sviestskābe	Sistēmiskas sklerozes ārstēšana
Lithuanian	1-(6-benzotiazolilsulfonil)-5-chloro-1H-indolo-2-butano rūgštis	Sisteminės sklerozės gydymas
Maltese	1-(6-benzothiazolylsulfonyl)-5-chloro-1H-indole-2-butanoic acid	Kura tas-sklerosi sistemika
Polish	Kwas 1-(6-benzotiazolilosulfonylo)-5-chloro-1H-indolo-2-butanowy	Leczenie twardziny narządowej
Portuguese	Ácido 1-(6-benzotiazolilsulfonil)-5-cloro-1H-indol-2-butanóico	Tratamento da esclerose sistémica
Romanian	acid 1-(6-benzotiazolilsulfonil)-5-cloro-1H-indol-2-butanoic	Tratamentul sclerozei sistemice
Slovak	Kyselina 1-(6-benzotiazolylsulfonyl)-5-chlór-1H-indol-2-butánová	Liečba systémovej sklerózy

[1] At the time of designation

Language	Active ingredient	Indication
Slovenian	1-(6-benzotiazolilsulfonil)-5-kloro-1H-indol-2-butanojska kislina	Zdravljenje sistemske skleroze
Spanish	Ácido 1-(6-benzotiazolilsulfonil)-5-cloro-1H-indol-2-butanoico	Tratamiento de la esclerosis sistémica
Swedish	1-(6-benzotiazolylsulfonyl)-5-kloro-1H-indol-2-butansyra	Behandling av systemisk skleros
Norwegian	1-(6-benzotiazolylsulfonyl)-5-klor-1H-indol-2-butansyre	Behandling av systemisk sklerose
Icelandic	1-(6-benzótíazólýlsúlfónýl)-5-klóró-1H-indól-2-smjörsýra	Meðferð við dreifðum herslismeinum