



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

26 March 2013
EMA/COMP/86745/2013
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

2-[4-Methoxy-3-(2-m-tolyl-ethoxy)-benzoylamino]-indan-2-carboxylic acid for the treatment of systemic sclerosis

On 12 March 2013, orphan designation (EU/3/13/1108) was granted by the European Commission to Sanofi-Aventis Groupe, France, for 2-[4-methoxy-3-(2-m-tolyl-ethoxy)-benzoylamino]-indan-2-carboxylic 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 overactivated, causing inflammation and excess production of various proteins, particularly collagen. The reason why the immune system is overactivated 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 tissues in 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 less than 3.5 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 178,000 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 27), Norway, Iceland and Liechtenstein. This represents a population of 509,000,000 (Eurostat 2013).



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 who have pulmonary hypertension (high blood pressure in the lungs) or 'digital ulcers' (sores on the fingers and toes).

The sponsor has provided sufficient information to show that the medicine '2-[4-methoxy-3-(2-m-tolyl-ethoxy)-benzoylamino]-indan-2-carboxylic acid' might be of significant benefit for patients with systemic sclerosis because early studies in experimental models show that it might be effective at reducing the formation of the fibrous connective tissue, a main feature of the disease which is not targeted by existing treatments. 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 expected to work mainly by blocking the action of a substance called lysophosphatidic acid (LPA). LPA is produced at the site of inflammation or injury by different types of cells, and is thought to be involved in the formation of the fibrous connective tissue in systemic sclerosis. By blocking its action, the medicine is expected to reduce the formation of fibrous connective tissue in the skin and various organs, thereby relieving the symptoms of the disease.

What is the stage of development of this medicine?

The effects of 2-[4-methoxy-3-(2-m-tolyl-ethoxy)-benzoylamino]-indan-2-carboxylic acid have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with the medicine in patients with systemic sclerosis were ongoing.

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 6 February 2013 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:

Sanofi-Aventis Groupe
54 rue de la Boétie
75008 Paris
France
Telephone: +33 153 7740 00
Telefax: +33 153 7741 33
E-mail: <http://en.sanofi.com/contact/contact.aspx>

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	2-[4-Methoxy-3-(2-m-tolyl-ethoxy)-benzoylamino]-indan-2-carboxylic acid	Treatment of systemic sclerosis
Bulgarian	2-[4-Метокси-3-(2-м-толуил-етокси)-безоиламино]-индан-2-карбоксилова киселина	Лечение на системна склероза
Czech	Kyselina 2-[4-Methoxy-3-(2-m-tolyl-ethoxy)-benzoylamino]-indan-2-karboxylová	Léčba systémové sklerodermie
Danish	2-[4-methoxy-3-(2-m-tolyl-ethoxy)-benzoylamino]-indan-2-carboxylsyre	Behandling af systemisk sklerose
Dutch	2-[4-methoxy-3-(2-m-tolyl-ethoxy)-benzoylamino]-indaan-2-carboxylzuur	Behandeling van systeem sclerose
Estonian	2-[4-metoksü-3-(2-m-tolüül-etoksü)-bensoüülamino]-indaan-2-karboksüülhape	Süsteemse sklerodermia ravi
Finnish	2-[4-Metoksi-3-(2-m-tolyyli-etoksi)-bentsoyyliamino]-indaani-2-karboksyylihappo	Systeemisen skleroosin hoito
French	Acide 2-[4-Méthoxy-3-(2-m-tolyl-éthoxy)-benzoylamino]-indan-2-carboxylique	Traitement de la sclérose systémique
German	2-[4-Methoxy-3-(2-m-benzyl-ethoxy)-benzoylamino]-indan-2-carbonsäure	Behandlung der systemischen Sklerose
Greek	2-[4-μεθοξυ-3-(2-μ-τολυλ-αιθοξυ)-βενζοϋλάμινο]-ινδαν-2-καρβοξυλικό οξύ	Θεραπεία της συστηματικής σκλήρυνσης
Hungarian	2-[4-metoxi-3-(2-m-tolil-etoxi)-benzoilamino]-indán-2-karboxilsav	Szisztémás scleroderma kezelése
Italian	Acido 2-[4-Metossi-3-(2-m-tolil-etossi)-benzoilamino]-indan-2-carbossilico.	Trattamento della sclerosi sistemica
Latvian	2-[4-metoksi-3-(2-m-tolil-etoksi)-benzoilamino]-indān-2-karboksilskābe	Sistēmiskas sklerozes ārstēšana
Lithuanian	2-[4-metoksi-3-(2-m-tolil-etoksi)-benzoilamino]-indano-2-karboksilo rūgštis	Sisteminės sklerozės gydymas
Maltese	2-[4-Methoxy-3-(2-m-tolyl-ethoxy)-benzoylamino]-indan-2-carboxylic acid	Kura tas-sklerosi sistemika
Polish	Kwas 2-[4-metoksy-3-(2-m-toliloetoksy)-benzylamino]-indano-2-karboksylowy	Leczenie twardziny narządowej
Portuguese	Ácido 2-[4-Metoxi-3-(2-m-tolil-etoxi)-benzoilamino]-indan-2-carboxílico	Tratamento da esclerose sistémica
Romanian	Acid 2-[4-metoxi-3-(2-m-tolil-etoxi)-benzoilamino]-indan-2-carboxilic	Tratamentul sclerozei sistemice
Slovak	Kyselina 2-[4-metoxi-3-(2-m-tolyl-etoxy)-benzoylamino]-indan-2-karboxylová	Liečba systémovej sklerózy
Slovenian	2-[4-metoksi-3-(2-m-tolil-etoksi)-benzoilamino]-indan-2-karboksilna kislina	Zdravljenje sistemske skleroze

¹ At the time of designation

Language	Active ingredient	Indication
Spanish	Ácido 2-[4-metoxi-3-(2-m-tolil-etoxi)-benzoilamino]-indan-2-carboxílico	Tratamiento de la esclerosis sistémica
Swedish	2-[4-metoxi-3-(2-m-tolyl-etoxi)-benzoylamino]-indan-2-karboxylsyra	Behandling av systemisk skleros
Norwegian	2-[4-metoksy-3-(2-m-tolyl-etoksy)-benzoylamino]-indan-2-karboksylsyre	Behandling av systemisk sklerose
Icelandic	2-[4-metoxý-3-(2-m-tólýl-etoxý)-benzóýlamínó]-indan-2-karboxýlsýra	Meðferð við dreifðum herslismeinum