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EMA/COMP/512680/2016
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Nintedanib for the treatment of systemic sclerosis

On 29 August 2016, orphan designation (EU/3/16/1724) was granted by the European Commission to Boehringer Ingelheim International GmbH, Germany, for nintedanib 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 excessive production of some 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).

Overproduction of collagen leads to 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 blood vessels of 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 513,700,000 (Eurostat 2016).

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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 and abnormal growth of connective tissue. 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 nintedanib might be of significant benefit for patients with systemic sclerosis. This is because laboratory studies suggest that it works in a different way to existing treatments and can reduce 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?

Nintedanib works by blocking the activity of some enzymes known as tyrosine kinases. These enzymes are present in certain receptors (such as VEGF, FGF and PDGF receptors) in cells called fibroblasts which are involved in the abnormal growth of connective tissue. By blocking these enzymes, nintedanib helps to reduce the the abnormal development of connective tissue, thereby helping to prevent the symptoms of systemic sclerosis from getting worse.

What is the stage of development of this medicine?

The effects of nintedanib have been evaluated in experimental models.

At the time of submission of the application for orphan designation, a clinical trial with nintedanib in patients with systemic sclerosis associated interstitial lung disease (SSc-ILD) was ongoing.

At the time of submission, nintedanib was not authorised anywhere in the EU for sytemic sclerosis or designated as an orphan medicinal product elsewhere for this condition. The medicine has been authorised in the EU as Ofev for the treatment of idiopathic pulmonary fibrosis since 2015, and as Vargatef for the treatment of lung cancer since 2014.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 13 July 2016 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:

Contact details of the current sponsor for this orphan designation can be found on EMA website, on the medicine's rare disease designations page.

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	Nintedanib	Treatment of systemic sclerosis
Bulgarian	нинтеданиб	Лечение на системна склероза
Croatian	Nintedanib	Liječenje sistemske skleroze
Czech	Nintedanib	Léčba systémové sklerodermie
Danish	Nintedanib	Behandling af systemisk sklerose
Dutch	Nintedanib	Behandeling van systeem sclerose
Estonian	Nintedaniib	Süsteemse sklerodermia ravi
Finnish	Nintedanibi	Systeemisen skleroosin hoito
French	Nintedanib	Traitement de la sclérodermie systémique
German	Nintedanib	Behandlung der systemischen Sklerose
Greek	Νιντεντανίμπη	Θεραπεία της συστηματικής σκλήρυνσης
Hungarian	Nintedanib	Szisztémás scleroderma kezelése
Italian	Nintedanib	Trattamento della sclerosi sistemica
Latvian	Nintedanibs	Sistēmiskas sklerozes ārstēšana
Lithuanian	Nintedanibas	Sisteminės sklerozės gydymas
Maltese	Nintedanib	Kura tas-sklerosi sistemika
Polish	Nintedanib	Leczenie twardziny narządowej
Portuguese	Nintedanib	Tratamento da esclerose sistémica
Romanian	Nintedanib	Tratamentul sclerozei sistemice
Slovak	Nintedanib	Liečba systémovej sklerózy
Slovenian	Nintedanib	Zdravljenje sistemske skleroze
Spanish	Nintedanib	Tratamiento de la esclerosis sistémica
Swedish	Nintedanib	Behandling av systemisk skleros
Norwegian	Nintedanib	Behandling av systemisk sklerose
Icelandic	Nintedaníb	Meðferð við dreifðum herslismeinum

[1] At the time of designation