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Public summary of opinion on orphan designation

(1'R,6'R)-3-(benzylamine)-6-hydroxy-3'-methyl-4-pentyl-6'-(prop-1-en-2-yl)-[1,1'-bi(cyclohexane)]-2',3,6-triene-2,5-dione for the treatment of systemic sclerosis

On 12 October 2017, orphan designation (EU/3/17/1933) was granted by the European Commission to Quintiles Ireland Limited, Ireland, for (1'R,6'R)-3-(benzylamine)-6-hydroxy-3'-methyl-4-pentyl-6'-(prop-1-en-2-yl)-[1,1'-bi(cyclohexane)]-2',3,6-triene-2,5-dione (also known as VCE-004.8 and EHP-101) 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 swelling of fingers and hands, followed by a thickening of the 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 515,700,000 (Eurostat 2017).

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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 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. Laboratory studies showed that the medicine reduced the abnormal growth of connective tissue, which is the main problem with the disease and is not targeted by authorised 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?

The medicine attaches to receptors (targets) on the surface of cells called peroxisome proliferator-activated receptor gamma (PPAR-γ) and cannabinoid type 2 receptors (CB2) which are involved in the growth of connective tissue. By attaching to these receptors, the medicine is expected to reduce abnormal growth of connective tissue, and therefore improve the symptoms of the condition.

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. Orphan designation of the medicine had been granted in the United States for systemic sclerosis.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 5 October 2017 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	(1'R,6'R)-3-(benzylamine)-6-hydroxy-3'-methyl-4-pentyl-6'-(prop-1-en-2-yl)-[1,1'-bi(cyclohexane)]-2',3,6-triene-2,5-dione	Treatment of systemic sclerosis
Bulgarian	(1'R,6'R)-3-(бензиламин)-6-хидрокси-3'-метил-4-пентил-6'-(проп-1-ен-2-ил)-[1,1'-би(циклохексан)]-2',3,6-триен-2,5-дион	Лечение на системна склероза
Croatian	(1'R,6'R)-3-(benzilamin)-6-hidroksi-3'-metil-4-pentil-6'-(prop-1-en-2-il)-[1,1'-bi(cikloheksan)]-2',3,6-trien-2,5-dion	Liječenje sistemske skleroze
Czech	(1'R,6'R)-3-(benzylamin)-6-hydroxy-3'-methyl-4-pentyl-6'-(prop-1-en-2-yl)-[1,1'-bi(cyklohexan)]-2',3,6-trien-2,5-dion	Léčba systémové sklerodermie
Danish	(1'R,6'R)-3-(benzylamin)-6-hydroxy-3'-methyl-4-pentyl-6'-(prop-1-en-2-yl)-[1,1'-bi(cyclohexan)]-2',3,6-trien-2,5-dion	Behandling af systemisk sklerose
Dutch	(1'R,6'R)-3-(benzylamine)-6-hydroxy-3'-methyl-4-pentyl-6'-(prop-1-en-2-yl)-[1,1'-bi(cyclohexaan)]-2',3,6-trieen-2,5-dion	Behandeling van systeem sclerose
Estonian	(1'R,6'R)-3-(bensüülamiin)-6-hüdroksü-3'-metüül-4-pentüül-6'-(prop-1-een-2-üül)-[1,1'-bi(tsükloheksaan)]-2',3,6-trieen-2,5-dioon	Süsteemse sklerodermia ravi
Finnish	(1'R,6'R)-3-(bentsyyliamiini)-6-hydroksi-3'-metyyli-4-pentyyli-6'-(prop-1-en-2-yyli)-[1,1'-bi(sykloheksaani)]-2',3,6-trieeni-2,5-dioni	Systeemisen skleroosin hoito
French	(1'R,6'R)-3-(benzylamine)-6-hydroxy-3'-méthyl-4-pentyl-6'-(prop-1-en-2-yl)-[1,1'-bi(cyclohexane)]-2',3,6-triène-2,5-dione	Traitement de la sclérodermie systémique
German	(1'R,6'R)-3-(Benzylamin)-6-hydroxy-3'-methyl-4-pentyl-6'-(prop-1-en-2-yl)-[1,1'-bi(cyclohexan)]-2',3,6-trien-2,5-dion	Behandlung der systemischen Sklerose
Greek	(1'R,6'R)-3-(βενζυλαμινο)-6-υδροξυ-3'-μεθυλ-4-πεντυλ-6'-(προπ-1-εν-2-υλ)-[1,1'-δι(κυκλοεξανο)]-2',3,6-τριενο-2,5-διόνη	Θεραπεία της συστηματικής σκλήρυνσης
Hungarian	(1'R,6'R)-3-(benzilamin)-6-hidroxi-3'-metil-4-pentil-6'-(prop-1-én-2-il)-[1,1'-bi(ciklohexán)]-2',3,6-trién-2,5-dion	Szisztémás scleroderma kezelése
Italian	(1'R,6'R)-3-(benzilammina)-6-idrossi-3'-metil-4-pentil-6'-(prop-1-en-2-il)-[1,1'-bi(cicloesano)]-2',3,6-triene-2,5-dione	Trattamento della sclerosi sistemica
Latvian	(1'R,6'R)-3-(benzilamīn)-6-hidroksi-3'-metil-4-pentil-6'-(prop-1-en-2-il)-[1,1'-bi(cikloheksān)]-2',3,6-triēn-2,5-dions	Sistēmiskas sklerozes ārstēšana

[1] At the time of designation

Language	Active ingredient	Indication
Lithuanian	(1'R,6'R)-3-(benzilamino)-6-hidroksi-3'-metil-4-pentil-6'-(prop-1-en-2-il)-[1,1'-bi(cikloheksano)]-2',3,6-trien-2,5-dionas	Sisteminės sklerozės gydymas
Maltese	(1'R,6'R)-3-(benżilammina)-6-idrossi-3'-metil-4-pentil-6'-(prop-1-en-2-il)-[1,1'-bi(ċikloeżan)]-2',3,6-trijen-2,5-dijon	Kura tas-sklerosi sistemika
Polish	(1'R,6'R)-3-(benzylamino)-6-hydroksy-3'-metylo-4-pentylo-6'-(prop-1-en-2-yl)-[1,1'-dwu(cykloheksan)]-2',3,6-trieno-2,5-dion	Leczenie twardziny narządowej
Portuguese	(1'R,6'R)-3-(benzilamina)-6-hidroxi-3'-metil-4-pentil-6'-(prop-1-eno-2-il)-[1,1'-bi(ciclo-hexano)]-2',3,6-trieno-2,5-diona	Tratamento da esclerose sistémica
Romanian	(1'R,6'R)-3-(benzilamină)-6-hidroxi-3'-metil-4-pentil-6'-(prop-1-en-2-il)-[1,1'-bi(ciclohexan)]-2',3,6-trien-2,5-dionă	Tratamentul sclerozei sistemice
Slovak	(1'R,6'R)-3-(benzylamín)-6-hydroxy-3'-metyl-4-pentyl-6'-(prop-1-en-2-yl)-[1,1'-bi(cyklohexán)]-2',3,6-trién-2,5-dión	Liečba systémovej sklerózy
Slovenian	(1'R,6'R)-3-(benzilamin)-6-hidroksi-3'-metil-4-pentil-6'-(prop-1-en-2-il)-[1,1'-bi(cikloheksan)]-2',3,6-trien-2,5-dion	Zdravljenje sistemske skleroze
Spanish	(1'R,6'R)-3-(bencilamina)-6-hidroxi-3'-metil-4-pentil-6'-(prop-1-en-2-il)-[1,1'-bi(ciclohexano)]-2',3,6-trieno-2,5-diona	Tratamiento de la esclerosis sistémica
Swedish	(1'R,6'R)-3-(bensylamin)-6-hydroxi-3'-metyl-4-pentyl-6'-(prop-1-en-2-yl)-[1,1'-bi(cyklohexan)]-2',3,6-trien-2,5-dion	Behandling av systemisk skleros
Norwegian	(1'R,6'R)-3-(benzylamin)-6-hydroksy-3'-metyl-4-pentyl-6'-(prop-1-en-2-yl)-[1,1'-bi(sykloheksan)]-2',3,6-trien-2,5-dion	Behandling av systemisk sklerose
Icelandic	(1'R,6'R)-3-(benzýlamín)-6-hýdroxý-3'-metýl-4-pentýl-6'-(próp-1-en-2-ýl)-[1,1'-bí(cýklóhexan)]-2',3,6-tríen-2,5-díon	Meðferð við dreifðum herslismeinum