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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Sirolimus for the treatment of tuberous sclerosis

On 9 October 2015, orphan designation (EU/3/15/1557) was granted by the European Commission to Desitin Arzneimittel GmbH, Germany, for sirolimus for the treatment of tuberous sclerosis.

What is tuberous sclerosis?

Tuberous sclerosis is a genetic disease that causes growth of benign tumours in different organs of the body, including the brain, lungs, heart, kidneys, skin and eyes. The symptoms and severity of the disease vary greatly from patient to patient. Depending on where the tumours are located, symptoms may include epilepsy, learning difficulties, skin abnormalities and kidney problems.

Tuberous sclerosis is a long-term debilitating disease that can be life threatening in patients with severe symptoms, who may develop severe learning disability, uncontrollable seizures (fits) and kidney failure.

What is the estimated number of patients affected by the condition?

At the time of designation, tuberous sclerosis affected less than 1.2 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 62,000 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).

What treatments are available?

At the time of designation, the medicine Votubia (everolimus) was authorised in the EU for the treatment of tuberous sclerosis.

The sponsor has provided sufficient information to show that sirolimus might be of significant benefit for patients with tuberous sclerosis because it will be available in a formulation to be applied onto the skin, and early studies show that it may improve the skin symptoms of the condition. This assumption

*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).

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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?

Sirolimus works by blocking an enzyme called 'mammalian target of rapamycin' (mTOR), which has increased activity in patients with tuberous sclerosis. Since mTOR is involved in the control of cell division and the growth of blood vessels, sirolimus is expected to reduce the growth of tuberous sclerosis tumours by preventing the division of tumour cells and reducing their blood supply.

Sirolimus is already authorised in the EU for the prevention of organ rejection in patients undergoing kidney transplantation.

What is the stage of development of this medicine?

The sponsor has provided data in experimental models from the published literature to support its application for orphan designation.

At the time of submission of the application for orphan designation, no clinical trials with this medicine in patients with tuberous sclerosis were ongoing.

At the time of submission, sirolimus was not authorised anywhere in the EU for tuberous sclerosis. Orphan designation of the medicine had been granted in the United States 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.

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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

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	Sirolimus	Treatment of tuberous sclerosis
Bulgarian	Сиролимус	Лечение на туберозна склероза
Croatian	Sirolimus	Liječenje tuberozne skleroze
Czech	Sirolimus	Léčba tuberózní sklerózy
Danish	Sirolimus	Behandling af tuberøs sklerose
Dutch	Sirolimus	Behandeling van tubereuze sclerose
Estonian	Siroliimus	Tuberoosse skleroosi ravi
Finnish	Sirolimuusi	Tuberoosiskleroosin hoito
French	Sirolimus	Traitement de la sclérose tubéreuse
German	Sirolimus	Behandlung der tuberösen Sklerose
Greek	Σιρόλιμους	Θεραπεία της οζώδους σκλήρυνσης
Hungarian	Szirolimusz	Sclerosis tuberosa kezelése
Italian	Sirolimus	Trattamento della sclerosi tuberosa
Latvian	Sirolimus	Tuberozās sklerozes ārstēšana
Lithuanian	Sirolimuzas	Tuberozinės sklerozės gydymas
Maltese	Sirolimus	Kura tal-isklerosi tuberuża
Polish	Syrolimus	Leczenie stwardnienia guzowatego
Portuguese	Sirolimus	Tratamento da esclerose tuberosa
Romanian	Sirolimus	Tratamentul sclerozei tuberoase
Slovak	Sirolimus	Liečba tuberóznej sklerózy
Slovenian	Sirolimus	zdravljenje tuberozne skleroze
Spanish	Sirolimus	Tratamiento de la esclerosis tuberosa
Swedish	Sirolimus	Behandling av tuberös skleros
Norwegian	Sirolimus	Behandling av tuberøs sklerose
Icelandic	Sírólímus	Meðferð við hnjóskahersli (tuberous sclerosis)

[1] At the time of designation