29 January 2016
EMA/COMP/789714/2015
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Sirolimus for the treatment of beta-thalassaemia intermedia and major

On 14 December 2015, orphan designation (EU/3/15/1585) was granted by the European Commission to Rare Partners srl Impresa Sociale, Italy, for sirolimus for the treatment of beta-thalassaemia intermedia and major.

What is beta-thalassaemia intermedia and major?

Beta thalassaemia is an inherited disease in which patients are unable to make enough haemoglobin, the protein found in red blood cells that carry oxygen around the body. Beta thalassaemia major is a severe form of the disease in which patients need frequent blood transfusions, while beta thalassaemia intermedia is a less severe form, which may worsen with age. Both types of beta thalassaemia are caused by defects in the gene responsible for producing beta-globin, one of the components of haemoglobin, which result in low levels of haemoglobin in the blood.

Beta thalassaemia intermedia and major are life-long debilitating diseases. They may be life threatening because of severe anaemia (low red blood cell count due to lack of haemoglobin), the need for repeated blood transfusions and the risk of complications associated with them.

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

At the time of designation, beta-thalassaemia intermedia and major affected approximately 1 in 10,000 people in the European Union (EU). This was equivalent to a total of around 51,000 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 main treatments for beta thalassaemia intermedia and major were blood transfusions and the use of iron chelators (medicines for reducing 'iron overload' - the high iron levels in the body caused by repeated blood transfusions). In some cases, bone-marrow

*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).

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

transplantation was used to cure the disease. This involves destruction of the patient's bone marrow and replacing it with bone marrow from a matched donor, to allow the patient to produce healthy red blood cells with normal haemoglobin.

The sponsor has provided sufficient information to show that sirolimus might be of significant benefit for patients with beta thalassaemia intermedia and major. Sirolimus works in a different way to existing treatments and early studies in experimental models indicate that it may improve the outcome of patients with this condition by stimulating the production of a type of haemoglobin called fetal haemoglobin. 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?

In the womb, the baby produces a form of haemoglobin known as fetal haemoglobin but switches to adult haemoglobin at birth. However, patients with beta thalassaemia are unable to produce functional adult haemoglobin, because of their inability to produce beta-globin.

This medicine is expected to work by stimulating the bone marrow to start producing fetal haemoglobin again. As fetal haemoglobin works in the same way as the adult form, it can make up for the missing adult haemoglobin in patients with beta thalassaemia and thereby reduce the need for blood transfusions. Production of fetal haemoglobin is not compromised in beta thalassaemia patients because it does not contain beta-globin.

What is the stage of development of this medicine?

The effects of sirolimus have been evaluated in experimental models.

At the time of submission of the application for orphan designation, no clinical trials with sirolimus in patients with beta thalassaemia intermedia and major had been started.

At the time of submission, sirolimus was not authorised anywhere in the EU for beta thalassaemia intermedia and major 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 12 November 2015 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:

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	Sirolimus	Treatment of beta thalassaemia intermedia and major
Bulgarian	Сиролимус	Лечение на бета таласемия интермедия и майор
Croatian	Sirolimus	Liječenje beta-talasemije intermedije i major
Czech	Sirolimus	Léčení beta thalasémie intermedia a major
Danish	Sirolimus	Behandling af beta-thalassæmia intermedia og major
Dutch	Sirolimus	Behandeling van bètathalassemie intermedia en major
Estonian	Siroliimus	Keskmise ja raske beetatalasseemia ravi
Finnish	Sirolimuusi	Beetatalassemia intermedia-ja major-tyypin hoito
French	Sirolimus	Traitement de la bêta-thalassémie intermédiaire et majeure
German	Sirolimus	Behandlung der Beta-Thalassämie (Intermediäre und Major-Form)
Greek	Σιρόλιμους	Θεραπεία της β-μεσογειακής αναιμίας, ενδιάμεσης και μείζονος
Hungarian	Szirolimusz	Béta-talasszémia intermedia és major kezelése
Italian	Sirolimus	Trattamento della beta-talassemia intermedia e major
Latvian	Sirolimus	Vidēji izteiktas un izteiktas bēta talasēmijas ārstēšana
Lithuanian	Sirolimuzas	Vidutinio sunkumo ir sunkios β-talasemijos gydymas
Maltese	Sirolimus	Kura tal-beta talassemija intermedja u maġġuri
Polish	Syrolimus	Leczenie talasemii beta-intermedia i major
Portuguese	Sirolimus	Tratamento da beta talassémia intermédia e major
Romanian	Sirolimus	Tratamentul beta talasemiei intermediare şi majore
Slovak	Sirolimus	Liečba stredne závažnej a závažnej beta talasémie
Slovenian	Sirolimus	Zdravljenje srednje in velike talasemije beta
Spanish	Sirolimus	Tratamiento de la beta talasemia intermedia y mayor
Swedish	Sirolimus	Behandling av beta-thalassaemia intermedia och major
Norwegian	Sirolimus	Behandling av beta-thalassemia intermedia og beta-thalassemia major
Icelandic	Sírólímus	Meðferð á langvinnu járnofhleðslu sem krefst klómeðferðar

[1] At the time of designation