EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Levoglutamide for the treatment of sickle cell disease

On 4 July 2012, orphan designation (EU/3/12/1011) was granted by the European Commission to Emmaus Medical Europe Limited, United Kingdom, for levoglutamide for the treatment of sickle cell disease.

What is sickle cell disease?

Sickle cell disease is a genetic disease in which the red blood cells become rigid and sticky, and change from being disc-shaped to being crescent-shaped (like a sickle). The change in shape is caused by the presence of an abnormal form of haemoglobin, the protein in red blood cells that carries oxygen around the body. In patients with sickle cell disease, the abnormal red blood cells attach to the walls of blood vessels and block them, restricting the flow of nutrients to the internal organs such as the heart, lungs and spleen. Because the abnormal red blood cells have a shorter life span, they release haemoglobin into the blood circulation rather than carrying it to the internal organs where it is needed. This causes severe pain and damage to these organs as well as repeated infections and anaemia (low red blood cell counts).

Sickle cell disease is a severe disease that is long lasting and may be life threatening because of damage to the heart and the lungs, anaemia and infections.

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

At the time of designation, sickle cell disease affected not more than 2.1 in 10,000 people in the European Union (EU)[*]. This is equivalent to a total of not more than 106,000 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 only medicine authorised in the EU to treat sickle cell disease was hydroxycarbamide. The main treatment for sickle cell disease was blood transfusion. This was usually

[*]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 506,300,000 (Eurostat 2011).

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combined with ‘iron chelators’ (medicines used to reduce the high iron levels in the body caused by repeated blood transfusions), which are necessary in patients with long-term anaemias such as sickle cell disease. In some cases, haematopoietic (blood) stem cell transplantation was used (a complex procedure where the patient receives stem cells from a matched donor to help restore the bone marrow) to allow the patient to produce red blood cells containing normal haemoglobin.

The sponsor has provided sufficient information to show that levoglutamide might be of significant benefit for patients with sickle cell disease because it works in a different way to existing treatments, and early studies show that it might be used in combination with hydroxycarbamide to further reduce the risk of ‘sickle cell crises’ (painful episodes caused by sickle-shaped red blood cells obstructing blood vessels and restricting blood flow to an organ). 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 way that levoglutamide works in sickle cell disease is not well understood, but studies indicate that when taken up by the abnormal red blood cells in sickle cell disease, levoglutamide reduces the adhesiveness of these cells to the walls of blood vessels. This is expected to improve blood flow to the internal organs, thereby reducing the painful crises in sickle cell disease.

What is the stage of development of this medicine?

The effects of levoglutamide have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with levoglutamide in patients with sickle cell disease were ongoing.

At the time of submission, levoglutamide was not authorised anywhere in the EU for sickle cell disease. Orphan designation of the medicine had been granted in the United States of America for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 11 May 2012 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:

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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	Levoglutamide	Treatment of sickle cell disease
Bulgarian	Левоглутамид	Лечение на сърповидно-клетъчна анемия
Czech	Levoglutamid	Léčba srpkovité anémie
Danish	Levoglutamid	Behandling af seglcellesygdom
Dutch	Levoglutamide	Behandeling van sikkelcelaandoening
Estonian	Levoglutamiid	Sirprakulise aneemia ravi
Finnish	Levoglutamidi	Sirppisolusyndrooman hoito
French	Lévoglutamide	Traitement de la drépanocytose
German	Levoglutamid	Behandlung der Sichelzellanämie
Greek	Λεβογλουταμίδη	Θεραπεία της δρεπανοκυτταρικής αναιμίας
Hungarian	Levoglutamid	Sarlósejtes anaemia kezelése
Italian	Levoglutamide	Trattamento dell'anemia falciforme
Latvian	Levoglutamīds	Sirpjveida šūnu anēmijas ārstēšana
Lithuanian	Levoglutamidas	Siklemijos gydymas
Maltese	Levoglutamide	Kura tal-marda taċ-ċelluli sura ta' minġel
Polish	Lewoglutamid	Leczenie niedokrwistości sierpowatokrwinkowej
Portuguese	Levoglutamida	Tratmento do sindrome das células falciformes
Romanian	Levoglutamidă	Tratamentul anemiei cu celule falciforme
Slovak	Levoglutamid	Liečba kosáčikovej anémie
Slovenian	Levoglutamid	Zdravljenje bolezni srpastih celic
Spanish	Levoglutamida	Tratamiento de la anemia drepanocítica
Swedish	Levoglutamid	Behandling av sickle cell syndrom
Norwegian	Levoglutamid	Behandling av sigdcellesykdom
Icelandic	Levóglútamíð	Meðferð sigðkornablóðleysis

[1] At the time of designation