2 March 2011
EMA/COMP/740288/2010
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Deferiprone for the treatment of sickle cell disease

On 23 February 2011, orphan designation (EU/3/10/832) granted by the European Commission to Apotex Europe B.V., the Netherlands, for deferiprone 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 walls of blood vessels and block them, restricting the flow of nutrients and oxygen to the internal organs, such as the heart, the lungs, and the spleen. This causes severe pain and damage to these organs. Since the abnormal red blood cells have a shorter life span, the disease also causes anaemia (low red blood cell counts).

Sickle cell disease is a severe disease that is long lasting and may be life threatening because of its effects on the heart and the lungs.

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

At the time of designation, sickle cell disease affected less than 2.5 in 10,000 people in the European Union (EU)[*]. This is equivalent to a total of fewer than 127,000 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, there was one medicine authorised in the EU for sickle cell disease. The main treatment for sickle cell disease was blood transfusion. This was usually 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

[*]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 506,500,000 (Eurostat 2010).

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7523 7040
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union

some cases, haematopoietic 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 deferiprone might be of significant benefit for patients with sickle cell disease because early studies in experimental models show that it might be more effective in removing iron from red blood cells than other iron chelators, increasing their survival. 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?

Patients with sickle cell disease need frequent blood transfusions. When patients receive repeated transfusions, the transfused red blood cells bring iron into the body. However, the body does not have a natural way of removing excess iron, so it builds up. Over time, the excess iron can damage important organs such as the heart or liver.

Deferiprone is an iron chelator. It attaches to iron in the body to form a compound that can be excreted by the body, mainly in the urine, and to a lesser extent in the stools. This helps to correct the iron overload and prevent damage due to excess iron. The medicine is also expected to remove iron from the red blood cell membranes. This may improve their survival, which is reduced in sickle cell disease.

Deferiprone is already used for iron overload in thalassaemia, another disease where patients need repeated blood transfusions.

What is the stage of development of this medicine?

The effects of deferiprone have been evaluated in experimental models.

At the time of submission of the application for orphan designation, no clinical trials with deferiprone in patients with sickle cell disease had been started.

Deferiprone has been authorised in the EU since 1999 in the treatment of thalassaemia, an inherited disease in which patients are unable to make enough haemoglobin. Deferiprone has been granted orphan designation in the United States of America for the treatment of iron overload in patients with haematologic disorders requiring chronic transfusion therapy.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 10 November 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:

Apotex Europe B.V.
Darwinweg 20
2333 CR Leiden
The Netherlands
Telephone: + 31 71 5657 777
Telefax: + 31 71 5657 778
E-mail: ApotexEurope.RA@apotex.com

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	Deferiprone	Treatment of sickle cell disease
Bulgarian	Деферипрон	Лечение на сърповидно-клетъчна анемия
Czech	Deferipron	Léčba srpkovité anémie
Danish	Deferipron	Behandling af seglcellesygdom
Dutch	Deferipron	Behandeling van sikkelcelaandoening
Estonian	Deferiproon	Sirprakulise aneemia ravi
Finnish	Deferiproni	Sirppisolusairauden hoito
French	Déférirprone	Traitement de la drépanocytose
German	Deferipron	Behandlung der Sichelzellenanämie
Greek	Δεφεριπρόνη	Θεραπεία της δρεπανοκυτταρικής αναιμίας
Hungarian	Deferipron	Sarlósejtes anaemia kezelése
Italian	Deferiprone	Trattamento dell'anemia falciforme
Latvian	Deferiprons	Sirpjveida šūnu anēmijas ārstēšana
Lithuanian	Deferipronas	Siklemijos gydymas
Maltese	Deferiprone	Kura tal-marda taċ-ċelluli sura ta' minġel
Polish	Deferypron	Leczenie niedokrwistości sierpowatokrwinkowej
Portuguese	Deferriprona	Tratmento do sindrome das células falciformes
Romanian	Deferipronă	Tratamentul anemiei cu celule falciforme
Slovak	Deferiprón	Liečba kosáčikovej anémie
Slovenian	Deferipron	Zdravljenje bolezni srpastih celic
Spanish	Deferiprona	Tratamiento de la anemia drepanocítica
Swedish	Deferipron	Behandling av sicklecellsjukdom
Norwegian	Deferipron	Behandling av sigdcellesykdom
Icelandic	Deferiprón	Meðferð sigðkornablóðleysis

[1] At the time of designation