EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

7 May 2018
EMA/125843/2018

Public summary of opinion on orphan designation

Docosahexaenoic acid ethyl ester for the treatment of sickle cell disease

On 21 March 2018, orphan designation (EU/3/18/1991) was granted by the European Commission to TurnKey PharmaConsulting Ireland Limited, Ireland, for docosahexaenoic acid ethyl ester (also known as SC411) 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 other blood cells and to the walls of blood vessels and block them, restricting the flow of oxygen-rich blood 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. As a result, patients experience severe pain as well as repeated infections and anaemia (low red blood cell counts).

Sickle cell disease is a life-long disease 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 approximately 2 in 10,000 people in the European Union (EU). This was equivalent to a total of around 103,000 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 (hydroxyurea). The main treatment for sickle cell disease was blood transfusion.

*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 517,400,000 (Eurostat 2018).

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This was usually combined with 'iron chelators' (medicines used to reduce high iron levels in the body resulting from repeated blood transfusions). In some cases, haematopoietic (blood) stem cell transplantation was used. This is a procedure where the patient's bone marrow is cleared of cells and replaced by stem cells from a donor to form new bone marrow that produces healthy blood cells containing normal haemoglobin.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with sickle cell disease because early studies show that adding this medicine to treatment with hydroxycarbamide can further reduce the occurrence of vaso-occlusive crises (when blood vessels become blocked by the abnormal red blood cells, restricting the flow of blood 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?

This medicine is made of docosahexaenoic acid (DHA), an omega-3 fatty acid, which is an important component of the membrane of many cells, including red blood cells.

It is thought that abnormal red blood cells in sickle cell disease contain too little DHA in their cell membrane, and too much of another type of fatty acid, called omega-6. This imbalance is believed to cause inflammation and to contribute to sickle cells sticking together and causing vaso-occlusive crises. The medicine is thought to help re-balance the fatty acid composition of the red blood cells' membrane. This is expected to reduce the symptoms of the disease.

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, clinical trials with the medicine in patients with sickle cell disease were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for sickle cell disease. 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 15 February 2018 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	Docosahexaenoic acid ethyl ester	Treatment of sickle cell disease
Bulgarian	Етил естер на докозахексаеновата киселина	Лечение на сърповидно-клетъчна анемия
Croatian	Etil ester dokosaheksaenoične kiseline	Liječenje bolesti srpastih stanica
Czech	Ethylester kyseliny dokosahexaenové	Léčba srpkovité anémie
Danish	Docosahexaensyreethylester	Behandling af seglcellesygdom
Dutch	Docosahexaeenzuurethylester	Behandeling van sikkelcelaandoening
Estonian	Dokosaheksaeenhappe etüülester	Sirprakulise aneemia ravi
Finnish	Dokosaheksaeenihapon etyyliesteri	Sirppisolusyndrooman hoito
French	Ester éthylique d'acide docosahexaénoïque	Traitement de la drépanocytose
German	Docosahexaensäure-Ethylester	Behandlung der Sichelzellenanämie
Greek	Αιθυλεστέρας του δοκοσαεξαενοϊκού οξέος	Θεραπεία της δρεπανοκυτταρικής αναιμίας
Hungarian	Dokozahexaénsav-*etil-észter*	Sarlósejtes anaemia kezelése
Italian	Estere etilico dell'acido docosaesaenoico	Trattamento dell'anemia falciforme
Latvian	Dokozaheksaēnskābes etilesteris	Sirpjveida šūnu anēmijas ārstēšana
Lithuanian	Dokozaheksaeno rūgšties etilo esteris	Siklemijos gydymas
Maltese	Aċidu etil ester dokoseżenojku	Kura tal-marda taċ-ċelluli sura ta' minġel
Polish	Ester etylowy kwasu dokozaheksaenowego	Leczenie niedokrwistości sierpowatokrwinkowej
Portuguese	Éster etílico do ácido docosa-hexaenóico	Tratmento do sindrome das células falciformes
Romanian	Ester etilic al acidului docosahexaenoic	Tratamentul anemiei cu celule falciforme
Slovak	Etylester kyseliny dokozahexaénovej	Liečba kosáčikovej anémie
Slovenian	Etilni ester dokozaheksaenske kisline	Zdravljenje bolezni srpastih celic
Spanish	Éster etílico del ácido docosahexaenoico	Tratamiento de la anemia drepanocítica
Swedish	Dokosahexaensyraetylester	Behandling av sickle cell syndrom
Norwegian	Dokosaheksaensyreetylester	Behandling av sigdcellesykdom
Icelandic	Dókósahexaenóik sýruetýl ester	Meðferð sigðkornablóðleysis

[1] At the time of designation