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Public summary of opinion on orphan designation

Benserazide hydrochloride for treatment of sickle cell disease

On 11 January 2019, orphan designation (EU/3/18/2125) was granted by the European Commission to Isabelle Ramirez, Germany, for benserazide hydrochloride for 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 1 in 10,000 people in the European Union (EU). This was equivalent to a total of around 52,000 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. This was usually combined with 'iron chelators' (medicines used to reduce high iron levels in the body

*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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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. Preliminary results suggest that the medicine used in combination with existing treatments can increase the levels of fetal haemoglobin (the main type of haemoglobin in fetuses and newborns), which could improve symptoms of the disease. 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 expected to increase the amount of fetal haemoglobin in the blood. Blood cells with this type of haemoglobin do not attach to other blood cells and blood vessel walls as the abnormal red blood cells do. As a result, the amount of red blood cells and oxygen in the organs is expected to increase, thereby relieving the symptoms of the disease.

What is the stage of development of this medicine?

The effects of benserazide hydrochloride 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 planned.

Benserazide hydrochloride is authorised in some countries in combination with levodopa for the treatment of Parkinson’s disease.

At the time of submission, benserazide hydrochloride was not authorised anywhere in the EU for sickle cell disease 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 6 December 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 the EMA website.

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 orphan condition in all official EU languages[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	Benserazide hydrochloride	Treatment of sickle cell disease
Bulgarian	Бензеразид хидрохлорид	Лечение на сърповидно-клетъчна анемия
Croatian	Benzerazidklorid	Liječenje bolesti srpastih stanica
Czech	Benserazid hydrochlorid	Léčba srpkovité anémie
Danish	Benserazide hydrochloride	Behandling af seglcellesygdom
Dutch	Benserazide hydrochloride	Behandeling van sikkelcelaandoening
Estonian	Benseraziidhüdrokloriid	Sirprakulise aneemia ravi
Finnish	Benseratsidihydrokloridi	Sirppisolusyndrooman hoito
French	Chlorhydrate de bensérazide	Traitement de la drépanocytose
German	Benserazidhydrochlorid	Behandlung der Sichelzellenanämie
Greek	Υδροχλωρική βενσεραζίδη	Θεραπεία της δρεπανοκυτταρικής αναιμίας
Hungarian	Benserazid hidroklorid	Sarlósejtes anaemia kezelése
Italian	Benserazide cloridrato	Trattamento dell'anemia falciforme
Latvian	Benserazīda hidrohlorīds	Sirpjveida šūnu anēmijas ārstēšana
Lithuanian	Benserazido hidrochloridas	Siklemijos gydymas
Maltese	Benserazide hydrochloride	Kura tal-marda taċ-ċelluli sura ta' minġel
Polish	Benserazydu chlorowodorek	Leczenie niedokrwistości sierpowatokrwinkowej
Portuguese	Cloridrato de benserazida	Tratmento do sindrome das células falciformes
Romanian	Clorhidrat de benserazidă	Tratamentul anemiei cu celule falciforme
Slovak	Benserazid hydrochlorid	Liečba kosáčikovej anémie
Slovenian	Benserazidijev hidroklorid	Zdravljenje bolezni srpastih celic
Spanish	Clorhidrato de benserazida	Tratamiento de la anemia drepanocítica
Swedish	Benserazidehydroklorid	Behandling av sickle cell syndrom
Norwegian	Benserazidhydroklorid	Behandling av sigdcellesykdom
Icelandic	Benserazíð hýdróklóríð	Meðferð sigðkornablóðleysis

[1] At the time of designation