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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

2-hydroxy-6-((2-(1-isopropyl-1H-pyrazol-5-yl)pyridin-3-yl)methoxy)benzaldehyde for the treatment of sickle cell disease

On 18 November 2016, orphan designation (EU/3/16/1769) was granted by the European Commission to SynteractHCR Deutschland GmbH, Germany, for 2-hydroxy-6-((2-(1-isopropyl-1H-pyrazol-5-yl)pyridin-3-yl)methoxy)benzaldehyde (also known as GBT440) 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 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 approximately 3.2 in 10,000 people in the European Union (EU). This was equivalent to a total of around 164,000 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).

[*]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 513,700,000 (Eurostat 2016).

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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 combined with 'iron chelators' (medicines used to treat iron overload, 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. 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 showed that the medicine decreases the number of sickle-shaped red blood cells and reduces haemolysis (the breakdown of red blood cells). 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 sickle cell disease, sickling of the red blood cells occurs when the abnormal haemoglobin releases its oxygen and then clumps together to form rigid chains that make the cells change shape.

This medicine is expected to work by increasing the ability of the abnormal haemoglobin to take up and hold oxygen. With more oxygen attached to the haemoglobin, it is expected that the haemoglobin will be less likely to clump together and cause sickling. The number of sickle-shaped red blood cells will subsequently fall and the patient's symptoms should start to improve.

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 sickle cell disease.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 6 October 2016 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	2-hydroxy-6-((2-(1-isopropyl-1H-pyrazol-5-yl)pyridin-3-yl)methoxy)benzaldehyde	Treatment of sickle cell disease
Bulgarian	2-хидрокси-6-((2-(1-изопропил-1H-пиразол-5-ил)пиридин-3-ил)метокси)бензалдехид	Лечение на сърповидно-клетъчна анемия
Croatian	2-hidroksi-6-((2-(1-izopropil-1H-pirazol-5-il)piridin-3-il)metoksi)benzaldehid	Liječenje bolesti srpastih stanica
Czech	2-hydroxy-6-((2-(1-isopropyl-1H-pyrazol-5-yl)pyridin-3-yl)methoxy)benzaldehyd	Léčba srpkovité anémie
Danish	2-hydroxy-6-((2-(1-isopropyl-1H-pyrazol-5-yl)pyridin-3-yl)methoxy)benzaldehyd	Behandling af seglcellesygdom
Dutch	2-hydroxy-6-((2-(1-isopropyl-1H-pyrazol-5-yl)pyridine-3-yl)methoxy)benzaldehyde	Behandeling van sikkelcelaandoening
Estonian	2-hüdroksü-6-((2-(1-isopropüül-1H-pürasool-5-yl)püridiin-3-yl)metoksü)bensaldehüüd	Sirprakulise aneemia ravi
Finnish	2-hydroksi-6-((2-(1-isopropyyli-1H-pyratsoli-5-yyli)pyridiini-3-yyli)metoksi)bentsaldehydi	Sirppisolusyndrooman hoito
French	2-hydroxy-6-((2-(1-isopropyl-1H-pyrazol-5-yl)pyridine-3-yl)méthoxy)benzaldéhyde	Traitement de la drépanocytose
German	2-Hydroxy-6-((2-(1-isopropyl-1H-pyrazol-5-yl)pyridin-3-yl)methoxy)benzaldehyd	Behandlung der Sichelzellenanämie
Greek	2-υδροξυ-6-((2-(1-ισοπροπυλο-1H-πυραζολο-5-υλ)πυριδινο-3-υλ)μεθοξυ)βενζαλδεϋδη	Θεραπεία της δρεπανοκυτταρικής αναιμίας
Hungarian	2-hidroxi-6-((2-(1-izopropil-1H-pirazol-5-il)piridin-3-il)metoxi)benzaldehid	Sarlósejtes anaemia kezelése
Italian	2-idrossi-6-((2-(1-isopropil-1H-pirazolo-5-yl)piridina-3-yl)metossi)benzaldeide	Trattamento dell'anemia falciforme
Latvian	2-hidroksi-6-((2-(1-izopropil-1H-pirazol-5-il)piridīn-3-il)metoksi)benzaldehīds	Sirpjveida šūnu anēmijas ārstēšana
Lithuanian	2-hidroksi-6-((2-(1-izopropil-1H-pirazol-5-il)piridin-3-il)metoksi)benzaldehidas	Siklemijos gydymas
Maltese	2-idrossi-6-((2-(1-isopropil-1H-pirazol-5-yl)piridin-3-yl)metossi)benzaldeid	Kura tal-marda taċ-ċelluli sura ta' minġel
Polish	2-hydroksy-6-((2-(1-izopropylo-1H-pirazol-5-ylo)pirydyn-3-ylo)metoksy)benzaldehyd	Leczenie niedokrwistości sierpowatokrwinkowej
Portuguese	2-hidroxi-6-((2-(1-isopropil-1-pirazol-5-il)piridin-3-il) metoxi)benzaldeído	Tratmento do sindrome das células falciformes
Romanian	2-hidroxi-6-((2-(1-izopropil-1H-pirazol-5-il)piridin-3-il)metoxi)benzaldehidă	Tratamentul anemiei cu celule falciforme
Slovak	2-hydroxy-6-((2-(1-izopropyl-1H-pyrazol-5-yl)pyridín-3-yl)metoxy)benzaldehyd	Liečba kosáčikovej anémie

[1] At the time of designation

Language	Active ingredient	Indication
Slovenian	2-hidroksi-6-((2-(1-izopropil-1H-pirazol-5-il)piridin-3-il)metoksi)benzaldehid	Zdravljenje bolezni srpastih celic
Spanish	2-hidroxi-6-[(2-(1-isopropil-1H-pirazol-5-il)piridin-3-il)metoxi]benzaldehído	Tratamiento de la anemia drepanocítica
Swedish	2-hydroxi-6-((2-(1-isopropyl-1H-pyrazol-5-yl)pyridin-3-yl)metoxi)bensaldehyd	Behandling av sickle cell syndrom
Norwegian	2-hydroksy-6-((2-(1-isopropyl-1H-pyrazol-5-yl)pyridin-3-yl)metoksy)benzaldehyd	Behandling av sigdcellesykdom
Icelandic	2-hýdroxý-6-((2-(1-ísóprópýl-1H-pýrazól-5-ýl) pýridín-3-ýl)metoxý)bensaldehýð	Meðferð sigðkornablóðleysis