European Medicines Agency
*Pre-authorisation Evaluation of Medicines for Human Use*

London, 8 December 2009
Doc.Ref.: EMA/COMP/654109/2009

# Committee for Orphan Medicinal Products

## Public summary of positive opinion for orphan designation of pegylated carboxyhaemoglobin for the treatment of sickle cell disease

On 26 November 2009, orphan designation (EU/3/09/698) was granted by the European Commission to Voisin Consulting S.A.R.L., France, for pegylated carboxyhaemoglobin 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. Because 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 approximately 1 in 10,000 people in the European Union (EU)[*]. This is equivalent to a total of around 50,000 people, and is below the threshold for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and knowledge of the Committee for Orphan Medicinal Products (COMP).

**What treatments are available?**
At the time of designation, there was one medicine authorised for sickle cell disease in the EU. 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. In some cases, bone marrow transplantation was used (a complex procedure where the bone marrow of the patient is destroyed and replaced with bone marrow from a matched donor) to allow the patient to produce red blood cells containing normal haemoglobin.
The sponsor has provided sufficient information to show that pegylated carboxyhaemoglobin might be of significant benefit for patients with sickle cell disease because it might improve the treatment of patients with this condition. In particular, early studies in experimental models indicate that it could be used together with existing treatments to prevent 'sickle cell crises' (painful episodes caused by sickle-shaped red blood cells obstructing blood vessels and restricting blood flow to an organ). This

[*]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 504,800,000 (Eurostat 2009).

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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?**
Pegylated carboxyhaemoglobin is made up of haemoglobin extracted from human blood and combined with two substances: polyethylene glycol and carbon monoxide. This medicine has been designed to carry carbon monoxide into the blood. In the blood, carbon monoxide is expected to work by stopping the red blood cells changing their shape and causing the blood vessels to widen to allow the blood to flow more easily. Once the carbon monoxide has been released, the resulting pegylated haemoglobin also has an effect, increasing the delivery of oxygen to organs. Together, these effects are expected to help to reduce the painful crises in sickle cell disease.

**What is the stage of development of this medicine?**
At the time of submission of the application for orphan designation, the evaluation of the effects of pegylated carboxyhaemoglobin in experimental models was ongoing.
At the time of submission of the application for orphan designation, no clinical trials with the designated product in patients with sickle cell disease had been started.
At the time of submission, pegylated carboxyhaemoglobin was not authorised anywhere in the EU for sickle cell disease or designated as 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 7 October 2009 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 Community) 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.

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**Translations of the active ingredient and indication in all official EU languages, Norwegian and Icelandic**

| Language | Active ingredient | Indication |
|---|---|---|
| English | Pegylated carboxyhaemoglobin | Treatment of sickle cell disease |
| Bulgarian | Карбоксихемоглобин, свързан с ПЕГ(полиетиленгликол)-вериги | Лечение на сърповидно-клетъчна анемия |
| Czech | Pegylovaný karboxyhemoglobin | Léčba srpkovité anémie |
| Danish | Pegyleret carboxyhæmoglobin | Behandling af seglcellesygdom |
| Dutch | Gepegyleerd carboxyhemoglobine | Behandeling van sikkelcelaandoening |
| Estonian | Pegüleeritud karbooksühemoglobiin | Sirprakulise aneemia ravi |
| Finnish | Pegyloitu karboksihemoglobiini | Sirppisolusyndrooman hoito |
| French | Carboxyhémoglobine pégylée | Traitement de la drépanocytose |
| German | Pegyliertes Carboxyhämoglobin | Behandlung der Sichelzellenanämie |
| Greek | PEG-ανθρακοξυαιμοσφαιρίνη | Θεραπεία της δρεπανοκυτταρικής αναιμίας |
| Hungarian | Pegilált karboxihemoglobin | Sarlósejtes anaemia kezelése |
| Italian | Carbossiemoglobina pegilata | Trattamento dell'anemia falciforme |
| Latvian | Pegilēts karboksihemoglobīns | Sirpjveida šūnu anēmijas ārstēšana |
| Lithuanian | Pegiliuotas karboksihemoglobinas | Siklemijos gydymas |
| Maltese | Karbossiemoglobina peġilata | Kura tal-marda taċ-ċelluli sura ta' minġel |
| Polish | Pegylowana karboksyhemoglobina | Leczenie niedokrwistości sierpowatokrwinkowej |
| Portuguese | Carboxihemoglobina peguilada | Tratmento do sindrome das células falciformes |
| Romanian | Carboxihemoglobină pegilată | Tratamentul anemiei cu celule falciforme |
| Slovak | Pegylovaný karboxyhemoglobín | Liečba kosáčikovej anémie |
| Slovenian | Pegiliran karboksihemoglobin | Zdravljenje bolezni srpastih celic |
| Spanish | Carboxihemoglobina pegilada | Tratamiento de la anemia drepanocítica |
| Swedish | Pegylerat kolmonoxidhemoglobin | Behandling av sickle cell syndrom |
| Norwegian | Pegylert karboksyhemoglobin | Behandling av sigdcellesykdom |
| Icelandic | Pegýleraður kolmonoxíðblóðrauði | Meðferð sigðkornablóðleysis |