



COMMITTEE FOR ORPHAN MEDICINAL PRODUCTS

**PUBLIC SUMMARY OF
POSITIVE OPINION FOR ORPHAN DESIGNATION
OF
hydroxyurea
for the treatment of sickle cell syndrome**

On 9 July 2003, orphan designation (EU/3/03/154) was granted by the European Commission to OTL Pharma, France, for hydroxyurea for the treatment of sickle cell syndrome. The sponsorship was transferred to Addmedica SAS, France, in October 2006.

What is sickle cell syndrome?

Sickle cell syndrome is a group of inherited diseases caused by a mutation in a blood protein called haemoglobin. The mutation leads to changes in the shape and behaviour of red blood cells. They become hard, sticky and shaped in the form of a sickle (the sharp hooks used to cut the wheat). This causes small blood clots that block blood flow, and cause repeated painful episodes, called crisis. In the long run, this causes severe damage to the organs in the body. The clinical picture of patients with sickle cell syndrome can be remarkably different. Some patients remain virtually without complaints, while others suffer repeated crises requiring admission to hospital from early childhood. The prototype disease in the sickle cell syndrome group, is the sickle cell anaemia, which is at the same time the most common and severe in the group.

What are the methods of treatment available?

No medicines exist that have been authorised for the treatment of sickle cell syndrome. Oxygen, blood transfusions, and narcotics for pain, help to improve the symptoms of the crisis. Bone marrow transplantation can provide a cure, but it is known to be effective and safe only in selected children.

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

Based on the information provided by the sponsor and previous knowledge of the Committee, sickle cell syndrome was considered to affect approximately 0.5 in 10,000 persons in the European Union, which, at the time of designation, corresponded to about 22,000 persons.

How is this medicinal product expected to act?

Hydroxyurea is a substance that has already been used for many years for the treatment of certain cancers. It inhibits DNA production and this can be used to kill cancer cells. In adult patients with sickle cell disease, certain studies reported that hydroxyurea reduced the frequency of painful crisis and the need for blood transfusions. Hydroxyurea was also found to increase the number of blood cells that produce a certain type of haemoglobin (haemoglobin F) that can prevent the formation of sickle cells in the blood. The exact mechanisms through which hydroxyurea might help the treatment of sickle cell syndrome are not fully known.

* Disclaimer: The number of patients affected by the condition is estimated and assessed for the purpose of the designation, for a European Community population of 377,000,000 (Eurostat 2001) and may differ from the true number of patients affected by the condition. This estimate is based on available information and calculations presented by the sponsor at the time of the application.

What is the stage of development of this medicinal product?

Clinical studies in children and adults with sickle cell anaemia are being conducted.

In the United States orphan drug status was granted on 10 January 1990 for treatment of patients with sickle cell anaemia as shown by the presence of haemoglobin S.

The Food and Drug Administration granted a marketing authorisation on 25 February 1998 for hydroxyurea with the indication “reduce the painful crises and reduce the need of blood transfusion in adults with sickle cell anaemia with recurrent moderate to severe painful crisis (generally at least 3 during the preceding 12 months)”.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 13 June 2003 a positive opinion recommending the grant of the above-mentioned designation.

Update: Hydroxyurea (Siklos) is authorised in the European Union as of 29 June 2007 for the prevention of recurrent painful vaso-occlusive crises including acute chest syndrome in paediatric and adult patients suffering from symptomatic Sickle Cell Syndrome..

For more information please see www.emea.europa.eu.

Opinions on orphan medicinal products designations are based on the following cumulative criteria: (i) the seriousness of the condition, (ii) the existence or not of alternative methods of diagnosis, prevention or treatment and (iii) either the rarity of the condition (considered to affect not more than five in ten thousand persons in the Community) or the insufficient return of development investments.

Designated orphan medicinal products are still investigational products which were considered for designation on the basis of potential activity. An orphan designation is not a marketing authorisation. As a consequence, demonstration of the quality, safety and efficacy will be necessary before this product can be granted a marketing authorisation.

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Translations of the active ingredient and indication in all EU languages

Language	Active Ingredient	Indication
English	Hydroxyurea	Treatment of sickle cell syndrome
Danish	Hydroyurinstof	Behandling af Seglcellesyndrom
Dutch	Hydroxyureum	Behandeling van sikkcelcelsyndroom
Finnish	Hydroksiurea	Sirppisolusyndroomin hoito
French	Hydroxyurée	Traitement du syndrome drépanocytaire
German	Hydroxyurea	Behandlung der Sichelzellenanämie
Greek	Υδροξουρία	Θεραπεία του Δρεπανοκυτταρικού Συνδρόμου
Italian	Idrossiurea	Trattamento dell'anemia falciforme
Portuguese	Hidroxiureia	Tratamento do Síndrome das células falciformes
Spanish	Hidroxiurea	Tratamiento de la anemia drepanocítica
Swedish	Hydroxiurea	Behandling av sickle cell syndrom